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The incidence of lower extremity amputation and its associated risk factors in patients with diabetic foot ulcers: A meta-analysis

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Abstract
This study analysed the incidence of lower extremity amputation and its associated risk factors in patients with diabetic foot ulcers. This study systematically searched both Chinese and English databases, including CNKI, Wanfang, VIP, PubMed, EMBASE and Web of Science, to identify cohort studies related to lower extremity amputation and associated risk factors in patients with diabetic foot ulcers up to October 2023. The patients were stratified based on whether they underwent lower extremity amputation, and relevant data, including basic information, patient characteristics, complications, comorbidities and pertinent laboratory test data, were extracted from the included studies. The literature quality assessment in this study utilized the Newcastle-Ottawa Scale to screen for high-quality literature, resulting in the inclusion of 16 cohort studies, all of which were of at least moderate quality. Meta-analysis of outcome indicators was conducted using the Stata 14.0 software. The results indicate that the overall amputation rate of lower extremities in patients with diabetic foot ulcers is 31% (0.25, 0.38). Among the 16 variables evaluated, gender (male), smoking history, body mass index (BMI), hypertension, cardiovascular disease, kidney disease, white blood cell count, haemoglobin and albumin levels were found to be correlated with the occurrence of lower extremity amputation in patients with diabetic foot ulcers. However, no significant correlation was observed between age, diabetes type, duration of diabetes, stroke, glycosylated haemoglobin, creatinine and total cholesterol levels and lower extremity amputation in patients with diabetic foot ulcers. This meta-analysis indicates that the overall amputation rate in patients with diabetic foot ulcers is 31%. Factors such as gender (male), smoking history, high BMI, hypertension, cardiovascular disease, kidney disease, white blood cell count,

haemoglobin and albumin levels are identified as significant risk factors for lower extremity amputation in diabetic foot ulcer patients. These findings suggest that attention should be focused on these risk factors in patients with diabetic foot ulcers to reduce the risk of lower extremity amputation. Therefore, preventive and intervention measures targeting these risk factors are of significant importance in clinical practice. (Systematic review registration: https://www.crd.york.ac.uk/PROSPERO/, identifier [CRD42024497538]).

KEYWORDS

diabetes mellitus, diabetic foot ulcer, lower extremity amputation, meta-analysis, risk factors

Key Messages

- The study underscores the significant incidence of lower extremity amputation (LEA) in patients with diabetic foot ulcers (DFU), with a notable overall rate of 31%, emphasizing the urgent need for effective preventive strategies.
- Several key risk factors, including male gender, smoking history, elevated body mass index, the presence of hypertension, cardiovascular disease and kidney disease, were identified as strong correlates of LEA in DFU patients, highlighting the importance of targeted interventions to mitigate these risks.
- While certain factors like age, diabetes type, duration of diabetes and laboratory parameters such as glycated haemoglobin and total cholesterol levels did not exhibit significant associations with LEA, further research is warranted to elucidate their potential role in DFU progression and inform comprehensive management strategies.

1 | INTRODUCTION

Diabetes mellitus (DM), a chronic disease, affects nearly 19% of the world's population.[1] According to projections by the International Diabetes Federation, the global diabetic population is expected to increase to 590 million by the year 2035.[2] Prolonged high blood sugar levels associated with DM can lead to immune deficiencies, particularly impairing white blood cell function. This impairment reduces the body's ability to combat bacteria within cells and slows down the wound-healing process, resulting in the occurrence of vascular and neurological complications. Among these complications, diabetic foot ulcers (DFU) are one of the most common and severe, often becoming the primary reason for hospitalization among diabetic patients.[3,4] Research indicates that the prevalence of foot ulcers among diabetic patients ranges from 4% to 10%, with a lifetime incidence as high as 25%.[5]

DFU is the primary cause of non-traumatic lower limb amputation.[6] Additionally, due to the delayed wound healing associated with diabetes, DFU may eventually lead to lower extremity amputation (LEA), significantly reducing patients' quality of life and increasing mortality rates.[7,8] Research indicates that DFU often lead to lower extremity amputations, with approximately 75% of lower extremity amputations occurring in diabetic patients. This is primarily attributed to factors such as lower limb vascular disease, neuropathic abnormalities, poor glycemic control and the presence of concomitant ulcers.[9] Given the substantial impact of DFU on patients' quality of life and the heavy burden it imposes on their families and society, there is an urgent need to deepen our understanding and identify the relevant risk factors (RFs) for DFU-associated LEA.

Research suggests that more than half of diabetic foot ulcers can be prevented through appropriate preventive measures, patient education and foot care. Proper foot care includes daily foot inspections, maintaining foot cleanliness and dryness, protecting feet from extreme temperatures, wearing properly fitted shoes, regular surgical debridement of wounds and dressing changes.[10]

Numerous studies have explored RFs for DFU-associated amputation, yet the results are inconsistent and the study quality varies. To address this challenge, the aim of the present review is to systematically search major Chinese and English databases and conduct a meta-analysis to comprehensively understand the amputation rate and significant RFs among patients with DFU, providing a reliable reference for clinical research and offering more scientific and effective strategies for early intervention and treatment of DFU.

2 | METHODS

2.1 | Inclusion criteria and exclusion criteria

2.1.1 | Inclusion criteria

The study population meets the following criteria: (1) Participants (P): Patients diagnosed with DFU, aged between 10 and 80 years old. (2) Intervention (I): The experimental group consists of DFU patients who undergo lower extremity amputation, while the control group comprises DFU patients receiving conservative treatment. (3) Comparison (C): Comparison of risk factors associated with amputation and non-amputation in DFU patients. (4) Outcome (O): Extraction of basic information, patient characteristics, complications, comorbidities and relevant laboratory test results from included cohort studies. (5) Study(S): Cohort study. Statistical analysis yielded the relative risk (RR) values, standardized mean difference (SMD) values and their 95% confidence intervals (95% CI), or they were calculated to complete the data.

2.1.2 | Exclusion criteria

Systematic reviews, comments, animal experiments and meta-analyses were excluded. Additionally, studies that did not match the research content or had inconsistent intervention measures or control measures were excluded. Non-cohort trials, literature with flawed experimental designs or mismatched experimental methods and literature with inconsistent outcome indicators were also excluded.

2.2 | Retrieval strategy

PubMed, Embase, Web of Science, Cochrane Library, CNKI, Wanfang Medicine and VIP database were searched. The search terms included 'diabetic foot', 'diabetic foot ulcer', 'lower extremity amputation', 'amputation' and 'risk factors'. Searches were conducted from the databases' date of inception to 30 October 2023, to retrieve all relevant literature on complications of DFU and the prevalence of LEA among patients with DFU (Table 1). Additionally, references cited in the retrieved studies were hand-searched to identify other relevant literature.

TABLE 1 Search strategy.

No.	Query
#1	('Diabetic Foot'[Mesh]) OR ((((Foot, Diabetic [Title/Abstract]) OR (Diabetic Feet [Title/Abstract])) OR (Feet, Diabetic [Title/Abstract])) OR (Foot Ulcer, Diabetic [Title/Abstract]))
#2	('Amputation, Surgical'[Mesh]) OR ((Amputation [Title/Abstract]) OR (Amputations [Title/Abstract]))
#3	('Risk Factors'[Mesh]) OR (((((((((((((((((Factor, Risk[Title/Abstract]) OR (Risk Factor[Title/Abstract])) OR (Social Risk Factors[Title/Abstract])) OR (Factor, Social Risk[Title/Abstract])) OR (Factors, Social Risk[Title/Abstract])) OR (Risk Factor, Social[Title/Abstract])) OR (Risk Factors, Social[Title/Abstract])) OR (Social Risk Factor[Title/Abstract])) OR (Health Correlates[Title/Abstract])) OR (Correlates, Health[Title/Abstract])) OR (Population at Risk[Title/Abstract])) OR (Populations at Risk[Title/Abstract])) OR (Risk Scores[Title/Abstract])) OR (Risk Score[Title/Abstract])) OR (Score, Risk [Title/Abstract])) OR (Risk Factor Scores[Title/Abstract])) OR (Risk Factor Score[Title/Abstract])) OR (Score, Risk Factor [Title/Abstract]))
#4	#1 AND #2 AND #3

2.3 | Data extraction

Two independent researchers extracted clinical data from the included studies. The data to be extracted from the literature included basic information (title, publication year, first author), general information about the study population (gender, age, sample size, smoking history, diabetes type), study design, intervention and control measures, outcome indicators, such as serum markers including Scr and Hb. Rates of amputation occurrence, RR and SMD values were calculated and statistically analysed. If there is any disagreement, the senoior most third investigator will make the decision.

2.4 | Literature quality evaluation

The quality of the literature was assessed using the Newcastle-Ottawa Scale (NOS), which allows for the quality evaluation of cohort studies. The scale comprises eight assessment criteria, with a maximum score of 9 points. Studies scoring 6–7 points are regarded as moderate quality, whereas those scoring 8–9 points are regarded as high quality.[11] The process of assessing literature quality was independently conducted by two researchers simultaneously. In the event of differing opinions between the two, consensus would be reached through negotiation, or a third party would be consulted for adjudication.

2.5 | Statistical analysis

All statistical analyses were conducted using the Stata 14.0 software.[12] Heterogeneity among the included studies was assessed, and based on the magnitude of the heterogeneity, either a fixed- or a random-effects model was selected. SMD and RR with 95% CI were used for continuous and dichotomous variables, respectively. Heterogeneity was assessed using the I^2 test. When $I^2 < 50\%$, indicating a low possibility of heterogeneity, a fixed-effects model was used; otherwise, a random-effects model was applied. Subgroup analyses were performed to explore the sources of heterogeneity, prioritizing study type. In instances where the number of included studies exceeded 10, funnel plots were constructed to assess publication bias. Begg's and Egger's tests were used to quantitatively evaluate the significance of publication bias, with the threshold for statistical significance set at p >0.05. Sensitivity analysis was conducted to assess the robustness of the results, especially in cases of high heterogeneity among studies, excessive weight of a single study or reversal of results due to different effect models.

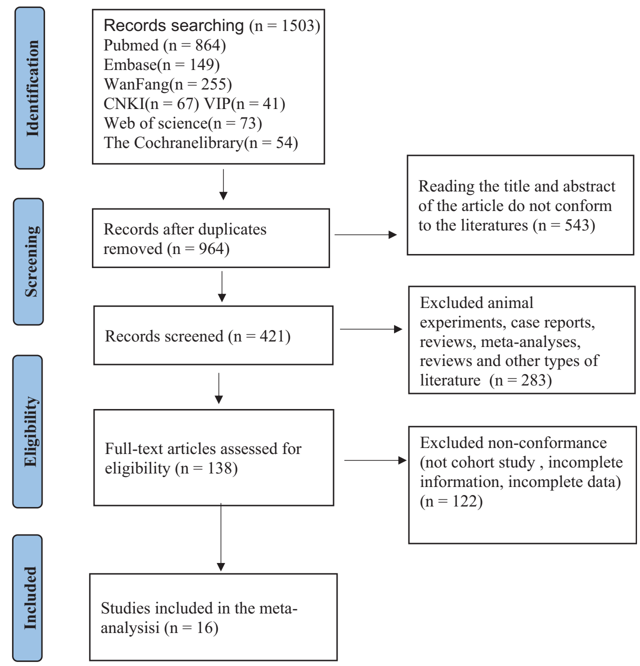

FIGURE 1 Flow chart showing inclusion and exclusion of literature.

3 | RESULTS

3.1 | Retrieval situation and basic information

An initial screening yielded 1503 articles. After excluding duplicates, irrelevant studies and those not meeting the PICOS criteria, our study ultimately included 16 cohort studies (Figure 1). The included studies collectively comprised 5689 patients.[13–28] Among them, 1815 cases were in the DFU amputation group, while 3874 cases were in the DFU non-amputation group. The selected literature, based on the NOS method, had quality scores of 6 or above, including six prospective cohort studies and 10 retrospective cohort studies. Details of the baseline characteristics and quality assessment of the literature are presented in Table 2.

3.2 | Meta-analyses

3.2.1 | Incidence of amputation among patients with diabetic foot ulcers

Sixteen studies reported the incidence of LEA among patients with DFU. After heterogeneity testing, I^2 was calculated as 96.57%, and the Q test demonstrated p <0.1, indicating high heterogeneity among the studies. Therefore, a random-effects model was employed for the meta-analysis, revealing an LEA incidence of 31%. Egger's test ($p = 0.96$) and Begg's test ($p = 0.964$) suggested no publication bias, and sensitivity analysis indicated that no single study significantly influenced the results. The findings of this study are stable, although the source of heterogeneity could not be determined. Figure 2A–C present the details. Subgroup analysis was conducted based on study methodology, geographical region, quality score and publication year (Table 3).

3.2.2 | Analysis of risk factors related to amputation among patients with DFU

The analysis of RFs associated with LEA among patients with DFU is presented in Table 2. Notably, gender (male) (RR = 1.09; 95% CI, 1.04, 1.14), smoking history (RR = 1.17; 95% CI, 1.08, 1.26), BMI (RR = −0.27; 95% CI, −0.37, −0.17), hypertension (RR = 1.09; 95% CI, 1.04, 1.14), cardiovascular disease (RR = 1.30; 95% CI, 1.18, 1.43), kidney disease (RR = 1.29; 95% CI, 1.03, 1.60), white blood cell count (SMD = 0.49; 95% CI, 0.14, 0.85), haemoglobin (SMD = −0.54; 95% CI, −0.9, −0.09) and albumin (SMD = −0.54; 95% CI, −0.72, −0.18) were all identified as RFs for LEA among patients with DFU. Conversely, age (SMD = 0.13; 95% CI, −0.88, 0.33), diabetes type (RR = 1; 95% CI, 0.96, 1.03), diabetes duration (SMD = 0.02; 95% CI, −0.21, 0.24), stroke (RR = 1.11; 95% CI, 0.95, 1.29), glycosylated haemoglobin

TABLE 2 Basic characteristics of included studies.

Author	Year	Country	Method	Total (n)	LEA (n)	LEA (%)	Qualityscore
Sena	2009	Turkey	Prospective	574	213	37.11	8
Jaffar	2009	Saudi Aramco	Prospective	62	12	19.35	8
Moham	2012	India	Prospective	162	46	28.4	8
Jui-Hung	2012	Taiwan	Retrospective	789	338	42.84	9
Yufeng	2015	China	Retrospective	669	133	19.88	8
Fengning	2015	China	Retrospective	364	62	17.03	8
Saleem	2017	Pakistan	Prospective	112	31	27.68	9
Se-Young	2018	Korea	Retrospective	141	37	26.24	9
Imad	2018	Saudi Arabia	Prospective	82	33	40.24	7
Jeong	2018	Korea	Retrospective	192	113	58.85	7
Jeyara	2019	Australia	Prospective	513	263	51.27	9
Carmine	2021	Italy	Retrospective	583	79	13.55	8
Shiqi	2022	America	Retrospective	362	75	20.72	6
Sarah	2022	Australia	Retrospective	564	186	32.98	8
Denizhan	2022	Turkey	Retrospective	407	157	38.57	9
Husakova	2022	Czech Republic	Retrospective	113	37	32.74	6

Abbreviation: LEA, lower extremity amputation.

(SMD = 0.02; 95% CI, −0.11, 0.15), creatinine (SMD = −0.11; 95% CI, −0.83, −0.61) and total cholesterol (SMD = −0.08; 95% CI, −0.2, 0.04) demonstrated no statistically significant correlation with LEA among patients with DFU (Table 4).

3.3 | Sensitivity analysis

In the included studies, there was an issue of excessive weight attributed to hypertension and cardiovascular disease. However, upon excluding studies involving patients with excessive weight, the results remained unchanged, suggesting the findings were relatively stable. Sequential removal of studies examining gender (male), smoking, BMI, renal disease, white blood cell count, haemoglobin and albumin levels did not alter the results upon reanalysis, indicating overall stability in the findings. Figure 3A,B display the details of the sensitivity analysis.

3.4 | Publication bias

Funnel plot analysis was conducted for outcome indicators from studies with ≥10 articles. Evaluation of publication bias was separately performed for gender (male), smoking history and hypertension. The Egger's test ($p = 0.848$) and Begg's test ($p = 0.827$) for gender (male), the Egger's test ($p = 0.894$) and Begg's test ($p = 0.855$) for smoking and the Egger's test ($p = 0.407$) and Begg's test ($p = 0.837$) for hypertension all resulted in $p > 0.05$, indicating symmetrical funnel plots without publication bias. Visual representations are provided in Figure 4A–C.

4 | DISCUSSION

The main objective of this study was to comprehensively analyse the incidence of LEA in DFU patients and its associated risk factors. Through a systematic review and meta-analysis of existing literature, we synthesized the evidence regarding DFU-related LEA, resolved inconsistencies in previous studies and provided reliable reference for clinical decision-making.

Our analysis revealed an overall amputation rate of 31% in DFU patients. Furthermore, through rigorous assessment of 16 cohort studies, we identified several risk factors associated with LEA in DFU patients, including gender (male), smoking history, BMI, hypertension, cardiovascular disease, kidney disease, white blood cell count, haemoglobin levels and albumin levels. These findings provide valuable insights into the multifaceted nature of DFU-related amputations and underscore the importance of addressing these RFs in clinical practice.

Regarding gender, the risk of LEA among male patients was 1.09 times higher than among females, consistent with previous research findings that demonstrated a higher risk among males compared to females.[29]

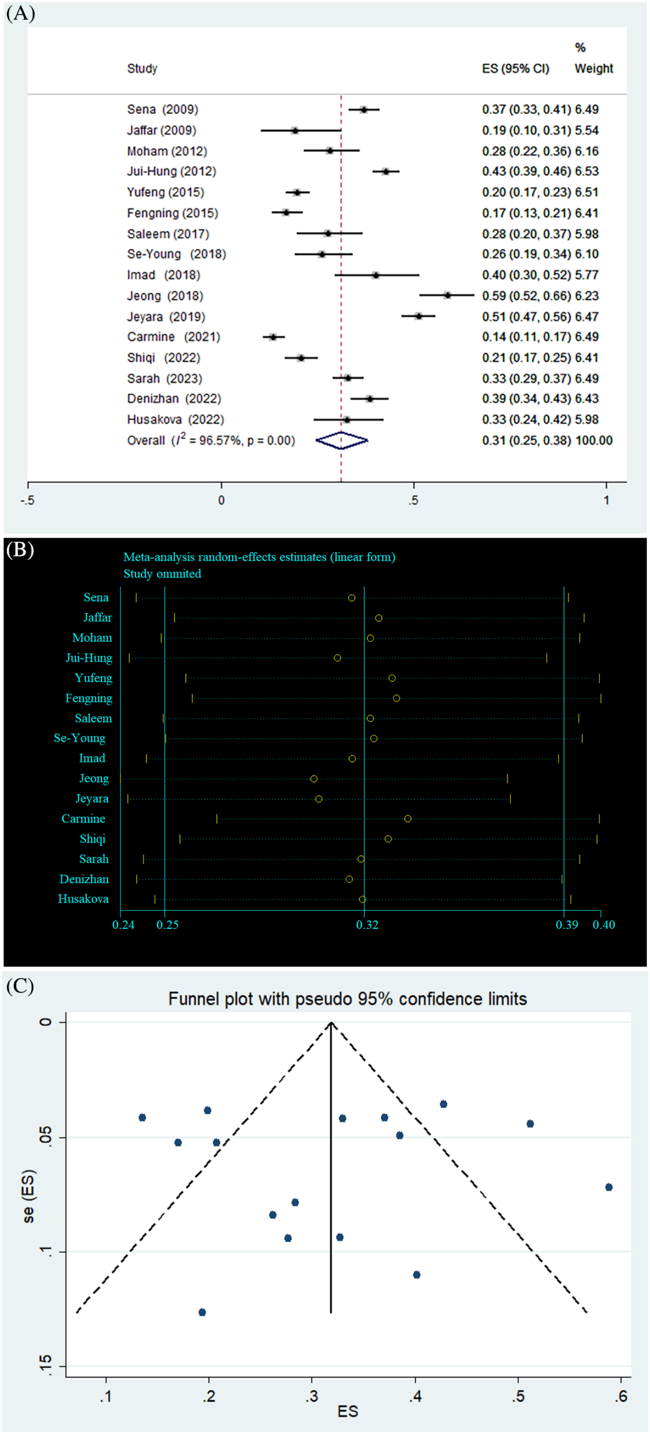

FIGURE 2 Meta-analysis of the incidence of lower extremity amputation (A) forest map, (B) sensitivity analysis map and (C) publication bias funnel map.

Possible reasons for this gender difference include the fact that males are more likely to engage in prolonged physical labour, leading to increased oxygen consumption in the lower limbs and thereby making their feet more susceptible to lower limb vascular disease.[30] Additionally, oestrogen protects blood vessels and potentially lowers the risk of LEA in females. Poor compliance with foot care among male patients is also a significant contributing factor to their susceptibility.[31]

Regarding smoking history, there was a higher risk of LEA among patients with a history of smoking. This observation could be attributed to the impact of smoking on glycemic control among patients with diabetes, leading to vascular constriction and impaired blood flow. Consequently, ischemia may occur, thereby slowing ulcer healing and increasing the risk of LEA.[32,33]

The association between BMI and the incidence of LEA among DFU patients with and without limb amputation was evaluated. A lower BMI was associated with a higher rate of limb amputation. Existing studies have demonstrated a significant J-shaped association between BMI and diabetic foot ulcers.[34] Patients with higher BMI may have better nutritional support and greater capacity to cope with the metabolic demands of chronic diseases, indicating a significant protective effect of high BMI on the risk of DFU.[35]

The complications and comorbidities of diabetes may increase the incidence of LEA among patients with DFU. Hypertension, cardiovascular disease and renal disease, which were included in this study, all had substantial impacts on the incidence of LEA in DFU patients.

Additionally, studies have demonstrated that patients with diabetes accompanied by hypertension have a significantly higher mortality rate from cardiovascular and cerebrovascular events compared to those with diabetes alone.[36] This observation may be attributed to the dysregulation of metabolic processes in patients with diabetes, leading to the release of several vasoactive substances that damage endothelial function, thereby increasing the risk of cardiovascular diseases, renal diseases and other complications.[37] Furthermore, patients with DFU who have underlying diseases and multiple comorbidities often present with more severe conditions, longer bedridden periods and are more prone to muscle weakness and metabolic abnormalities. The decreased ability to cope with physiological stressors further increases the risk of LEA.[38] This study reaffirms that complications and comorbidities associated with diabetes can increase the incidence of LEA, emphasizing the need for strict blood pressure and blood sugar control in patients with DFU.

Furthermore, the analysis of biochemical markers showed that white blood cell count and albumin are risk factors for LEA. Elevated white blood cell levels suggest a more severe infection among patients, and persistent severe infections can lead to edema and exudation, impairing granulation tissue growth and resulting in non-healing wounds, which may eventually lead to amputation.[39] Furthermore, the body's metabolic rate also increases, leading to symptoms such as fever and

TABLE 3 Subgroup analysis of the prevalence of lower extremity amputation among patients with diabetic foot ulcers.

Project	Number of studies	Heterogeneity I^2 (%)	Heterogeneity p	Prevalence (95%CI)
Method				
Prospective cohort	6	63.1	0.019	0.4 (0.35, 0.45)
Retrospective cohort	10	86	0	0.29 (0.26, 0.32)
Region				
Europe	4	58.4	0.065	0.42 (0.37, 0.47)
Asia	9	81.6	0	0.31 (0.27, 0.33)
United States	1	-	-	0.21 (0.1, 0.31)
Australia	2	90.8	0.001	0.23 (0.17, 0.29)
Quality score				
6 or 7	4	83.9	0	0.34 (0.27, 0.42)
8	7	75.1	0.01	0.25 (0.21, 0.28)
9	5	62.8	0.029	0.42 (0.38, 0.47)
Publication (y)				
<2020	11	83.69	0	0.35 (0.32, 0.38)
≥2020	5	83.4	0	0.26 (0.22, 0.31)

Abbreviation: CI, confidence intervals.

TABLE 4 Summary of meta-analysis results.

Risk factor	Numbers	Amputation	No amputation	Heterogeneity p	Heterogeneity I^2 (%)	Effect model	Meta-analysis results Effect	Meta-analysis results 95%CI	Meta-analysis results p
Male (n)	14	1028	1997	0.168	26.7	FEM	RR = 1.09	(1.04, 1.14)	0
Age (y)	7	767	1233	0	75.4	REM	SMD = 0.13	(−0.88, 0.33)	0.224
Smoking (n)	13	619	1197	0.354	9.1	FEM	RR = 1.17	(1.08, 1.26)	0
BMI (kg/m^2)	5	624	1496	0.094	19.5	FEM	SMD = −0.27	(−0.37, −0.17)	0.094
Type of DM	5	359	856	0.88	0	FEM	RR = 1	(0.96, 1.03)	0.857
Course (y)	7	1072	1635	0	85.6	REM	SMD = 0.02	(−0.21, 0.24)	0.867
Hypertension	12	894	1036	0.049	44.3	FEM	RR = 1.09	(1.04, 1.14)	0
Cardiovascular disease	9	329	688	0.054	47.6	FEM	RR = 1.30	(1.18, 1.43)	0
Stroke	7	540	799	0	78.7	REM	RR = 1.11	(0.95, 1.29)	0.194
Nephropathya	8	385	705	0	73.7	REM	RR = 1.29	(1.03, 1.60)	0.026
HbA1c (%)	7	1072	1635	0.03	57.1	REM	SMD = 0.02	(−0.11, 0.15)	0.771
WBC ($\times 10^9$/L)	8	1325	2345	0	95.7	REM	SMD = 0.49	(0.14, 0.85)	0.07
Hb (g/dl)	7	1192	1809	0	96.8	REM	SMD = −0.54	(−0.9, −0.09)	0.2
Albumin (g/L)	4	695	1163	0	85.9	REM	SMD = −0.54	(−0.72, −0.18)	0.001
Cr (mmol/L)	4	754	1178	0	98.1	REM	SMD = −0.11	(−0.83, 0.61)	0.761
TC (mg/dl)	4	484	747	0.155	42.8	FEM	SMD = −0.08	(−0.2, 0.04)	0.194

Abbreviations: BMI, body mass index; CI, confidence intervals; DM, Diabetes mellitus; RR, relative risk; SMD, standardized mean difference.

anorexia. Increased energy expenditure and decreased food intake can lead to a decrease in albumin levels. In some diabetic patients with diabetic nephropathy, prolonged elevation of urinary protein levels can lead to hypoalbuminemia.[40] Additionally, renal dysfunction can lead to anaemia and secondary malnutrition, contributing to the progressive decline in haemoglobin and albumin levels.[41]

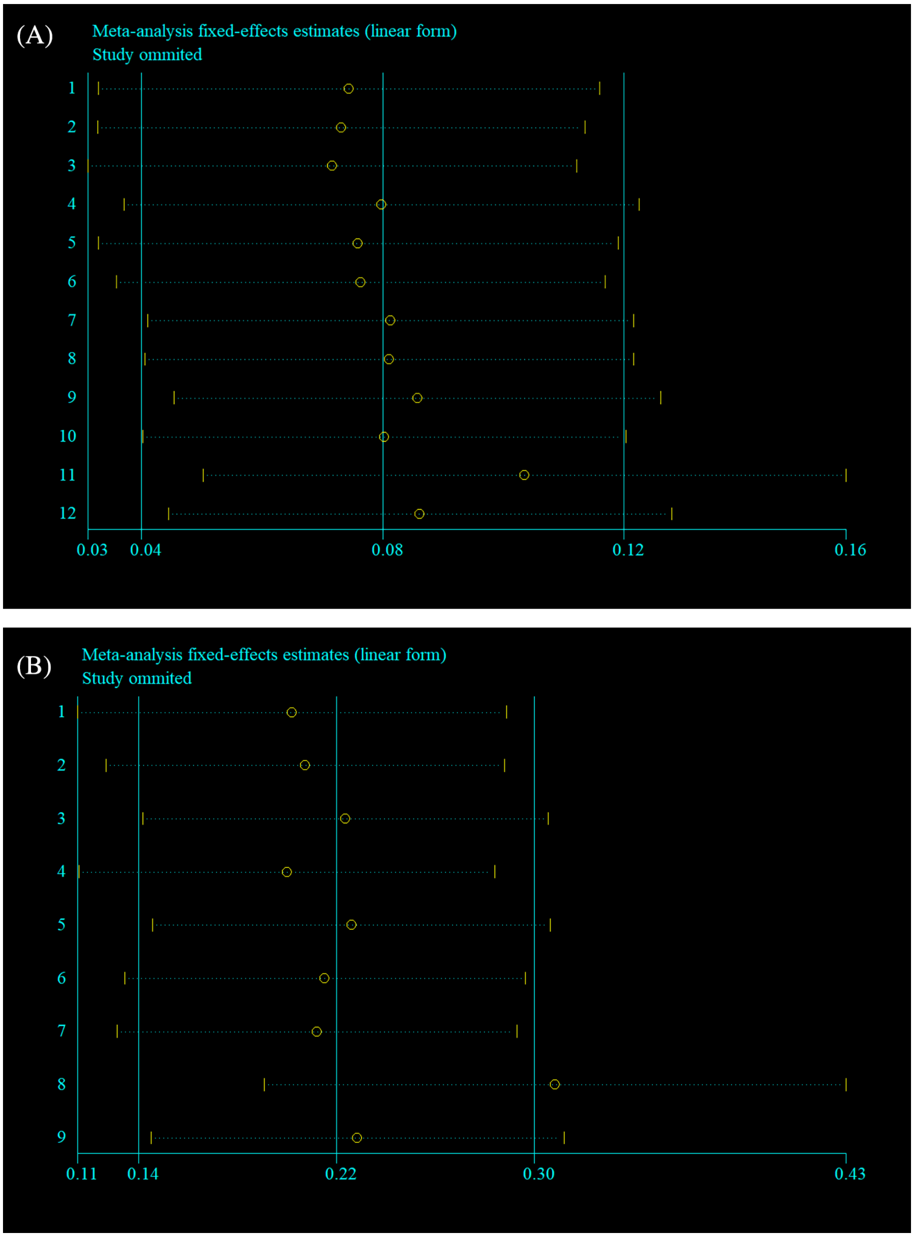

FIGURE 3 Sensitivity analysis results of (A) hypertension and (B) cardiovascular disease were included in the study.

Age, duration of diabetes, type of diabetes, stroke, glycated haemoglobin, creatinine and total cholesterol levels did not emerge as RFs for LEA. Notably, older age is associated with unfavourable prognoses, possibly due to the slower immune response to infections and the presence of other complications that delay healing, including impaired blood flow. Conversely, a longer duration of diabetes may correlate with more diabetes-related complications, including microvascular and macrovascular changes, which may play a critical role in skin breakdown and non-healing ulcers. There are two subtypes of DM: type 1 DM (DM1) and type 2 DM (DM2). Notably, all included studies enrolled patients with both types of diabetes to determine how the different types of diabetes affect patients with DFU undergoing amputation. Despite some differences in age, aetiology and symptoms between these two subtypes of diabetes, both DM1 and DM2 are associated with a higher incidence of LEA in DFU, with no significant differences between them.[42,43] The lack of significant difference between the two may be attributed to the fact that both types of diabetes can lead to complications such as peripheral neuropathy, peripheral vascular disease and impaired wound healing, all of which increase the risk of DFU and subsequent LEA. Additionally, current research has not identified a correlation between glycated haemoglobin and amputation, and there were no significant differences in baseline levels of glycated haemoglobin between the amputation and non-amputation groups.

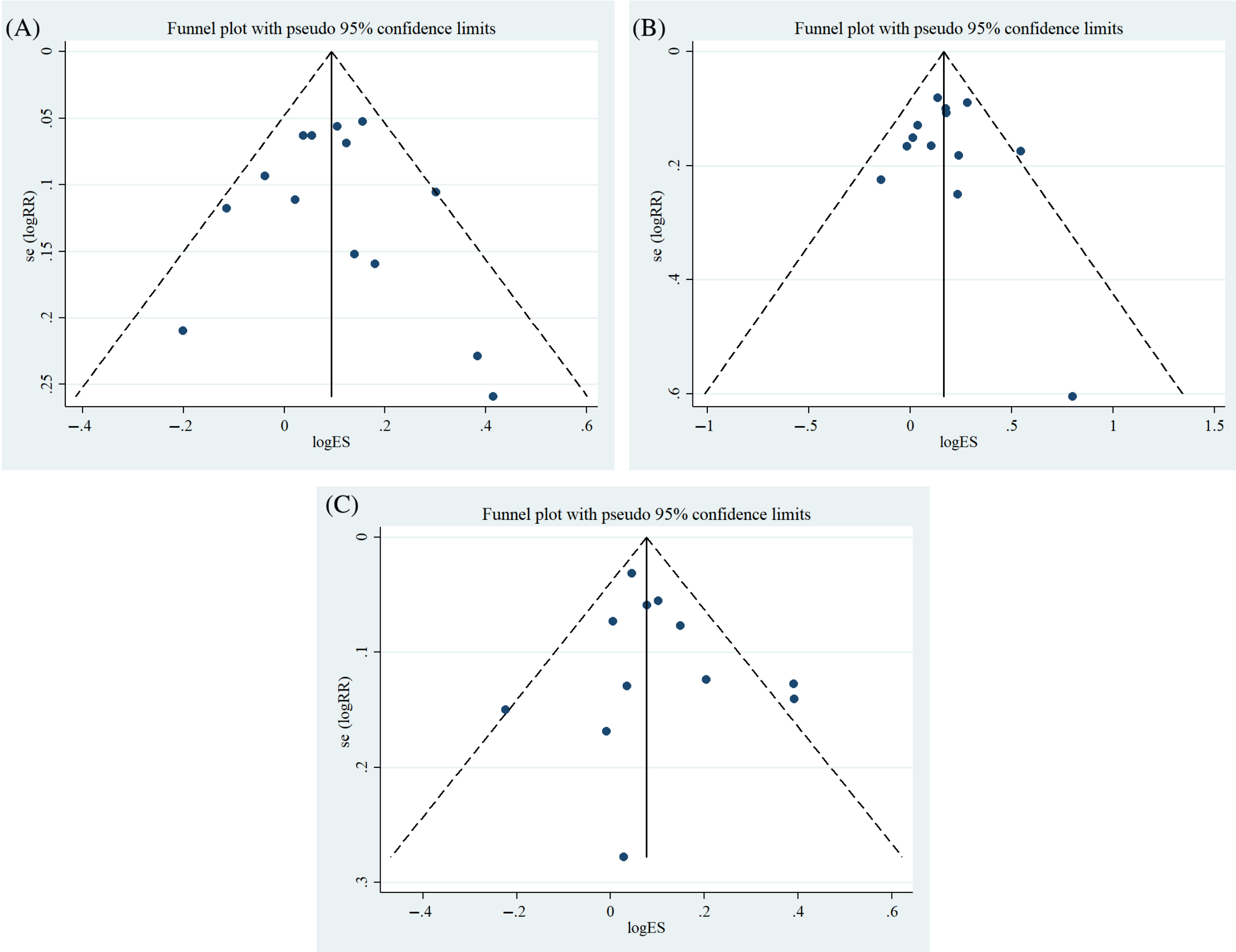

FIGURE 4 Funnel plot including indicators (A) gender, (B) smoking history and publication bias analysis of (C) hypertension.

The RFs for LEA among patients with DFU have been reported both domestically and internationally, but the conclusions are not entirely consistent, especially regarding gender, smoking history, certain laboratory tests, comorbidities and complications. These discrepancies may be related to differences in sample size, geographical location, time period and cultural factors across various studies. However, our meta-analysis also has some limitations. First, there is a lack of randomized studies on this topic, necessitating long-term and large-scale follow-up studies to validate these findings. Second, amputation in DFU involves multiple factors, thus requiring a more comprehensive analysis such as multivariate analysis. Among the 16 studies included, 10 were retrospective cohort studies, and six were prospective cohort studies.

Despite these limitations, our meta-analysis provides a valuable clinical reference. To the best of our knowledge, this is the first study to comprehensively analyse crucial laboratory test data associated with high amputation rates. The analysis confirms the impact of DFU and other RFs on the incidence of LEA, but further research is needed to validate these factors. Larger and more homogeneous samples are required to examine the importance and credibility of certain test parameters, including BMI and glycated haemoglobin.[44,45]

These findings hold significant clinical implications for the treatment and prevention of LEA in patients with DFU. Factors such as gender (male), smoking history, elevated BMI, hypertension, cardiovascular disease and renal disease have been identified as RFs for LEA, highlighting the importance of closely monitoring the progression of DFU and its complications. Furthermore, targeted education on DFU prevention and foot self-care should be provided to these high-risk patients to equip them with necessary knowledge and skills for minimizing the risk of LEA. Healthcare professionals should emphasize the importance of regular foot examinations, proper footwear and wound care to prevent DFU and reduce the incidence of LEA among DFU patients.

Additionally, future research should focus on validating identified RFs and exploring other factors contributing to the risk of LEA in DFU patients, utilizing larger and more diverse samples to enhance the reliability of study findings.

5 | CONCLUSION

The study concludes that the overall incidence rate of LEA among patients with DFU is 31%, providing important epidemiological data for medical practice. Gender (male), smoking history, BMI, hypertension, cardiovascular disease, kidney disease, white blood cell count, haemoglobin and albumin were closely associated with LEA, serving as significant RFs. Among these, BMI, haemoglobin and albumin were negatively correlated with the occurrence of DFU-related LEA, whereas the others demonstrated positive correlations. However, age, DM type, duration of diabetes, stroke, glycated haemoglobin, creatinine and total cholesterol levels were not found to be significant RFs. These findings help narrow the clinical focus, enabling clinicians to more accurately identify high-risk patients. Targeted and timely interventions should be implemented for high-risk patients, such as regular foot examinations, appropriate foot care education and early detection and treatment of foot ulcers.

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CONFLICT OF INTEREST STATEMENT

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

DATA AVAILABILITY STATEMENT

The original contributions presented in the study are included in the article/Supplementary Material. Further inquiries can be directed to the corresponding authors.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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