



# A systematic review of various types of conventional and modern diabetic foot ulcer surgeries and their outcomes: A beginners digest

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**Received:** 30 June 2023 **Revised:** 22 July 2023 **Accepted:** 16 August 2023 **e-Published:** 30 August 2023

## Abstract

**Background:** The diabetic foot constitutes one of the major diabetes-related morbidity. Diabetic foot ulcers (DFUs) are a disastrous consequence of the illness's course and are brought on by peripheral neuropathy, peripheral vascular disease, immunosuppression, and loss of glycemic control. Chronic ulcers must be treated surgically to prevent recurrences in cases with DFU. Every surgeon has to deal with this condition from very early in his career.

**Objectives:** To investigate the various forms of traditional and modern DFU procedures and their consequences, this study can provide very fruitful guidance to the surgeons.

**Methods:** In this study, we searched Google Scholar, PubMed, Embase, Cochrane Library, Web of Science, and Scopus from 2013 to 2023. The inclusion criteria were patients with DFUs, and patients with a known history of diabetes mellitus (type I or type II); the parameters included in the study were the occurrence of adverse responses, the rate of amputation, fatalities, recurrence rate and some other indications. Using the review manager (RevMan version 5.4), the risk of bias evaluation was done in this study, with risk assessment domains classified as high, unclear, or low risk. To check for biases for example reporting bias, performance bias, attrition bias, selection bias, etc., a recommended approach was used.

**Results:** The current review included 8 studies in total, with a total of 888 cases of DFUs. A recurrence rate of 24.51% was noted for the entire patient population. The recurrences noted in none of the three investigations. Overall mortality was 14.26%, according to three investigations.

**Conclusions:** It can be concluded that the patients treated with surgery show a lower recurrence rate of DFU as compared to the patients treated with only drug treatment. It is crucial to implement a new surgical treatment for DFUs to increase their success rate. A recently developed treatment program utilizing a multidisciplinary team approach and cooperation with referral hospitals is urgently required to improve the outcomes of DFU.

**Keywords:** Diabetic foot ulcer, Modern surgery, Conventional surgery, Wound management healing, Mortality, Recurrence.

## Introduction

In people with uncontrolled diabetes mellitus, diabetic foot ulcers are common complications.<sup>[1]</sup> DFUs are full-thickness wounds caused by poor glycemic control, peripheral vascular disease, neuropathy, or poor foot care which eventually leads to amputation of lower extremities which are commonly caused by osteomyelitis of the foot. Ulcers usually appear on the areas of the foot that are subjected to repetitive trauma and pressure.<sup>[1,2]</sup> Especially in the elderly, DFUs are a common problem for those with

diabetes. It has a high recurrence rate, which is attributed to a high risk of death and limb amputation, and is prohibitively expensive to treat.<sup>[3,4,5]</sup> Diabetes complications are one of the most frequent, severe, and expensive complications of diabetes, and diabetes-related hospitalization is one of the leading causes of diabetes-related death in the world.<sup>[2,6]</sup>

In the world, on average, 9.1 to 26.1 million people suffer from DFUs each year.<sup>[7]</sup> DFUs will develop in 15 to 25% of patients with diabetes mellitus over their lifetime.<sup>[8]</sup> These

figures are concerning since there are no insignificant clinical implications for the emergence of a DFU. In the United Kingdom, population-based cohort research found that DFUs are associated with death rates of 5% in the initial year and 42% in the next five. It has also been shown that diabetic patients with foot wounds are 2.5 times more likely to die than diabetic patients without foot wounds.<sup>[9]</sup> Moreover, patients with DFUs have significant morbidity, a decline in health-related quality of life, a worsening of their psychological adjustment, and a high burden of healthcare profiles.<sup>[10,11]</sup>

The premise of an effective therapeutic outcome for DFU, according to studies from the previous year, consists of not only blood glucose/HbA1c level control as well as infection prevention, but also medical interventions such as offloading, vascular status assessment, surgeries, biofilm control, dressing, cleaning, etc.<sup>[5,12]</sup> Among them, surgical treatment is essential to managing/curing DFU and includes dressing, off-loading, debridement, and the appropriate surgeries.<sup>[2, 5,13]</sup>

An ulcer can form in a foot with normal morphology as a byproduct of an acute injury in the context of sensory neuropathy and a loss of protective feeling. The foot's structural deformity, which typically results from a long-lasting muscle imbalance linked to the neuropathy itself, causes abnormal pressure to develop more frequently<sup>[14]</sup> even though it is not an uncomplicated relationship.<sup>[15]</sup> Offloading is essential for both treating and avoiding ulcers. You can accomplish this with footwear, orthotics, and contact casts.<sup>[16-18]</sup> Although they are generally successful in the short term, ulcers typically return over time for a wide range of reasons, including patients' noncompliance. Within a mean of 126 days, Pound et al. observed a 40% recurrence rate.<sup>[19]</sup> Recurrence rates after 3 years were estimated by Armstrong et al. to be close to 60%.<sup>[20]</sup> Surgical treatment of foot abnormalities is a more effective method of unloading. The natural history of recurring or persistent ulcers is so grim that more aggressive and surgical treatment may be justified, even though any surgery in these individuals is a significant endeavor. The significant complication rates that were once discouraging may be reduced by newer less invasive surgical procedures. Retrospective results appear to be in favor of flexor tenotomies for toe ulcers.

For designing proper therapies, accurate and optimal knowledge of molecular pathways and cellular changes is a must. The processes of impaired healing and ulcer pathogenesis rely upon almost hundreds of contributing factors which involve macrophage function, angiogenic response, collagen accumulation, decreased or impaired

growth matters inventions, keratinocyte, fibroblasts migration as well as the proliferation, bone healing, number of epidermal nerves and also the balance stuck between the accumulation of ECM components and their remodeling through the MMPs.<sup>[21-25]</sup>

Molecular analysis of patient epidermis samples revealed pathogenic markers associated with slow wound healing. C-myc overexpression well as nuclear localization of -catenin are two examples of this.<sup>[26]</sup> Keratinocyte migration is prevented by the aforementioned mechanisms together with decreased and aberrant EGFR localization and activated glucocorticoid pathway<sup>[26,27]</sup> leading to non-healing ulceration. Among DFUs, keratinocytes fail to migrate, proliferate excessively, and differentiate appropriately. The phenotype of fibroblasts has changed and they are migrating and proliferating less.<sup>[27]</sup>

With the advent of knowledge about the molecular pathways governing DFU's, molecular surgery which is an integrated approach towards DFU is gaining the limelight. Molecular surgery is based on the molecular markers and pathological assessments of the wound to guide the surgeons for proper debridement of the wound by facilitating complete removal of hyperkeratotic, infected, and nonviable tissue from the wound which is necessary for accelerating the procedure of wound healing. The molecular markers are of immense value in these surgical procedures to evaluate the extent of debridement and it is recommended that the debridement should be done till no callus remains at the periphery or no scar tissue is left.<sup>[28-30]</sup>

### **Followings the surgical process for DFU management Surgical debridement**

A wound's debridement involves removing all necrotic and devitalized tissues as well as any callus that has formed. In callused areas, this procedure lowers plantar pressures and encourages the development of granulation tissue.<sup>[31]</sup> Debridement is crucial for the prohibition of toxicities because the devitalized tissues operate as a breeding place for bacteria, a physical barrier to antibiotics, and a constrained immune system response.<sup>[32]</sup> The Wound Healing Society (WHS) along with the Infectious Disease Society of America (IDSA) advise harsh debridement over topical debridement therapies (such as autolytic dressing or biological debridement).<sup>[13,31]</sup> Although there is a paucity of information generally, sharp debridement is effective in a few clinical studies.<sup>[33-35]</sup>

### **Dressings**

DFUs are diverse; hence no one dressing is the best alternative for all kinds of wounds. It is usually accepted

that the main motive of a dressing is to produce a moist environment that encourages, angiogenesis, granulation, and autolytic processes and also the faster movement of epidermal cells transversely the base of the wound.<sup>[31,32,36]</sup> Also, the specified dressing must be suitable for managing excessive wound exudates. There are many different types of dressings, and some are actively being researched. There is not enough data available at this time to suggest any specific dressing style.<sup>[31,33]</sup>

### The wound of loading

The horizontal component of ground response forces, plantar shear stress, and to a lesser extent, vertical plantar pressure are the key factors contributing to the development and insufficient healing of DFUs.<sup>[38]</sup> Since it promotes healing and avoids recurrence, reducing plantar pressure as well as shear stress from a DFU is an essential component of wound management. Many devices, like boots, orthotic walkers, and shoe modifications, can be used to offload.<sup>[32]</sup>

### Objectives

To investigate the various forms of traditional and modern DFU procedures and their consequences, this study can provide very fruitful guidance to the surgeons.

### Methods

Based on the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) standard, this systematic review follows a protocol that provides more information about the study.

#### Literature Search

We use search engines like PubMed, Medline, Google Scholar, Wiley, Embase, and the Cochrane Library to find relevant articles. The relevant search phrases in the following examples include Conventional DFU surgeries, Modern DFU surgeries, DFUs with their side effects, and the recurrence rate of DFUs.

#### Eligibility criteria

Several eligibility factors, including inclusion and exclusion criteria, were taken into consideration when doing the study selection.

The inclusion criteria consisted of articles released from 2013 to 2023, patients with DFUs, and patients with diabetes mellitus (type I or type II).<sup>[4]</sup> The parameters included in the study were the occurrence of adverse responses, the rate of amputation, fatalities, recurrence rate and some other indications.<sup>[5]</sup> Only research that was conducted and published in English was approved for

inclusion. The exclusion criteria comprised non-English language literature, abstracts, letters, book chapters, presentations, and duplicate articles.

#### Data analysis

Following the initial search, a compilation of articles retrieved from the database was meticulously organized in an Excel sheet, wherein duplicates were subsequently identified and eliminated. The complete texts and abstracts of the articles were independently assessed by two authors. Each selected paper underwent thorough scrutiny before the final inclusion of this study.

### Results

#### Study selection

Based on the initial search, 625 articles were identified; some additional records were found i.e. about 3 articles. Additionally, 327 duplicate publications were removed. After that, we screened 301 records in which we excluded an additional 197 articles after screening them due to missing parameters in some articles, outcomes not relevant to DFU's, and articles that were irrelevant to our study. The study analyzed 104 full articles. Due to the short sample size, 92 papers, letters, case reports, and research that had not been published in English were omitted. This systematic review included 8 studies after complete screening and data analysis. Of which, 2 are randomized control trials, 2 retrospective studies, 1 clinic pathological study, 1 clinical study, 1 observational prospective study, and 1 cohort study [Figure 1].

#### Study characteristics

There are 888 cases of DFUs documented in the 8 research studies that comprise the current study. Type I diabetes was detected in 11.15% of the patients, whereas type II diabetes was found in 88.85% of the cases. The type of diabetes mellitus was not mentioned in two studies of the included papers.<sup>[44,45]</sup> Among the overall patients included in the present study, a recurrence rate of 24.51% was observed. The recurrences were not mentioned in the three studies.<sup>[46,45,39]</sup> Three studies showed an overall mortality rate of 14.26%.<sup>[40,42,46]</sup> The results of another five studies did not indicate any mortality<sup>[39,41,43,44,45]</sup> shown in Table 1.

#### Quality assessment criteria

In this review, we used the Cochrane-related tool and RevMan software version 5.4 to assess the risk of bias for randomized control trials. The risk of bias in random control trials (RCTs) included in the evaluation was evaluated by two separate reviews and differences were settled by a third reviewer. The risk of individual research

was categorized as low, unclear, or high based on the domains and criteria. Risk assessment domains were classified as high, unclear, or low risk based on attrition bias (incomplete outcome data), selection bias (formation of random sequence), selective reporting (reporting bias), performance bias (blinding of patients and staff), and other biases. The total risks for the various trials were therefore valued as low risk (+), high risk (-), and unclear risk (?). The risk of bias evaluation for the 8 included researches is shown in the figure. 2. All studies were found to have substantial methodological issues in at least one bias category. Randomization was insufficient or nonexistent in the most problematic categories, with low outcome assessor blinding (60% of the trials) and unclear risk in 40% of the trials.

### Discussion

One of the most difficult effects of diabetes is diabetic foot ulceration or DFU. DFUs might affect up to one-third of diabetic mellitus (DM) patients at some point in their lives. One of the main factors contributing to morbidity in DM patients is DFU.<sup>[47]</sup> Patients with DM are at a significant risk of developing DFUs, which can progress to infection, gangrene, amputation, and eventually death from sepsis with a multi-organ failure syndrome.<sup>[48,49]</sup> Consequently, it is necessary to take a proactive strategy to avoid the development of DFUs by providing patients and doctors with the necessary knowledge. Therefore, in the present review, we mainly focused on the various types of conventional and modern DFU surgeries and their outcomes.

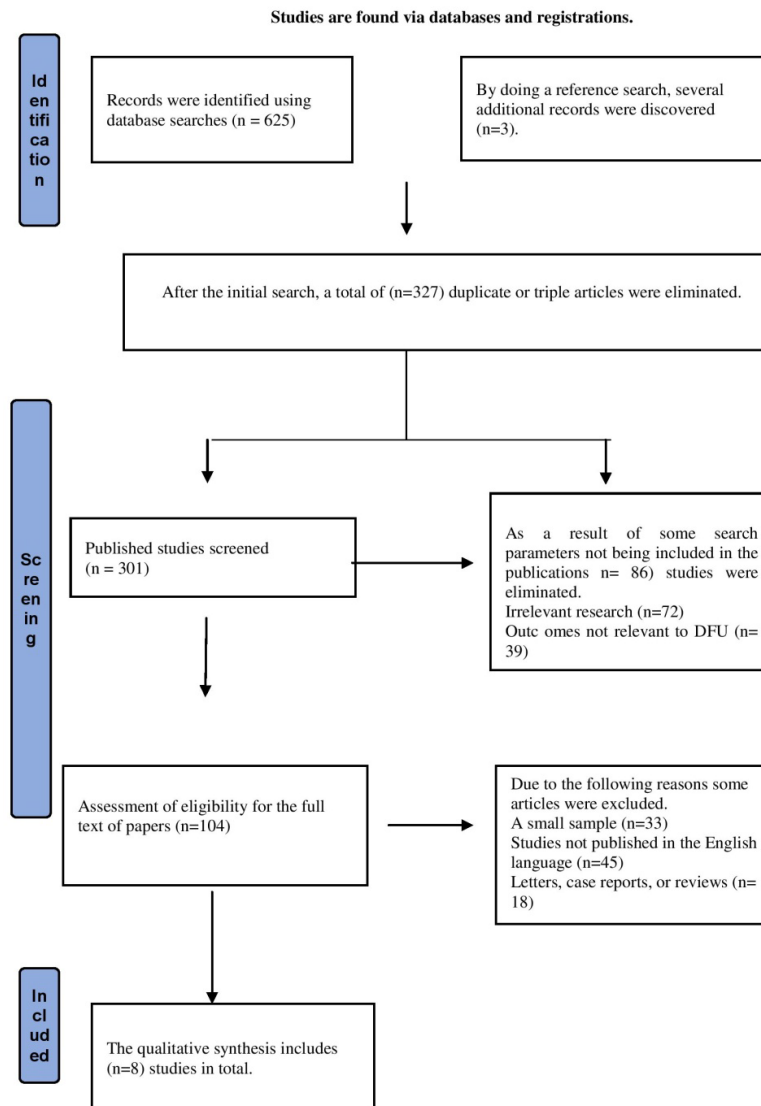


Figure-1. Flowchart of study

**Table 1.** Characteristics of the included studies

Author/ year	Study design	Sample size	Diabetic type	Surgical/ Non- surgical treatment	Ulcer recurrence	Outcomes
<b>Wu et al., (2022)</b> <sup>[39]</sup>	Randomized control study	There was a total of 112 patients.	53 cases were analyzed with type 2 diabetes.	76 patients were treated with the surgery treatment i.e. (surgery group) as well and the 36 patients were treated with drug treatment i.e. (Drug group).	Ns	The outcome of the study shows that in comparison to the drug group, the surgical group had a much greater cure rate and recovery rate.
<b>Sikhondze et al., (2022)</b> <sup>[40]</sup>	Cohort study	62 cases	Type I: 4 cases (6.5%) Type II: 58 cases (93.5%)	Antidiabetic drugs and general antibiotic treatment were given to all patients with DFUs. 31 individuals (50.0%) had their ulcers surgically debrided, while 29 (46.8%) had lower extremity amputations (LEA) done as the first surgical procedure following admission. 15 (24.2%) patients experienced minor LEA, while 14 (22.6%) underwent severe amputations. During the research period, no revascularization procedures were performed.	Recurrence was found in 11 cases as well as recurrence gangrene found in 5 patients. A total of 25.81% of cases were found with ulcer recurrence.	The patients, more than half of whom had advanced DFUs (Wagner grades 3–5). Late presentations and poor glycemic control were frequent. Lower extremity amputation was frequently used as the first line of therapy for DFUs. Lower extremity routine For DFU patients, Doppler ultrasonography is advised to evaluate peripheral arterial disease. For proper antibiotic coverage, a wound swab for culture and sensitivity testing is suggested. Inpatient stays lasted an average of 17.0 11.1 days, with a mortality rate of 1.6%.
<b>Hutting, K.H. et al., (2021)</b> <sup>[41]</sup>	A retrospective multicenter cohort study	They were the subject's total of 64 cases.	Type1 diabetes:5 cases Type2: 59 cases	Patients were treated with gentamicin-loaded calcium sulfate-hydroxyapatite (CaS-HA).	18.75% recurrence was found in this study.	Surgical treatment with gentamicin-loaded CaS-HA biocomposite was feasible in this study of patients with DFO and successful in 66% of patients. A prospective trial of this treatment regimen, based on uniform treatment protocols, is required.

<b>Thewjitcharoen et al., (2020)</b> <sup>[42]</sup>	Retrospective study	There were a total of 290 patients.	Type II: 99.4% of cases	PTA was performed on 82 patients with ischemia and neuro-ischemic DFU (217 ulcers), while open surgical bypass was only performed on 6 individuals.	Within three years, there was a 78.6% recurrence rate.	This research showed a depressing change in the healing rate of DFU and a constant pattern of major amputation, despite significant achievement in lowering major amputations during the previous ten years. The outcomes of DFU treatments were impacted by the considerable rise in PAD prevalence among Thai patients receiving DFU. Poorer outcomes were linked to more advanced illnesses and more comorbidity.
<b>Lakhani et al., (2019)</b> <sup>[43]</sup>	Observational prospective study	100 cases with DFU's were diagnosed.	100 patients present with type 2 diabetic mellitus.	76 patients were using oral hypoglycemic drugs, 4 were receiving only injectable insulin therapy, and 8 were receiving both injectable insulin and oral hypoglycemic drug therapy. Out of 100 patients, 12 were being treated for diabetes with diet and exercise. All patients received insulin by injection after admission. Patients should have needed insulin or improved diabetes mellitus control since they were under stress.	Ulcer recurrences were found in 2% of cases.	In this research, the rate of amputations was greater (74%), likely as a result of neglected illness and late presentation caused by peripheral neuropathy, which lessens pain perception. In this trial, there was no death.
<b>Finestone et al., (2018)</b> <sup>[44]</sup>	Randomized control trial	100 patients were subjected to this study.	NS	In Group 1 (surgery), 40 patients underwent surgery within a week. 60 patients in Group 2 (controls) were given instructions to	Recurrence in group 1 is anticipated to be no more than an additional 10%, resulting in a 20% failure rate overall after two years. In group 2a,	The need for improved treatments than the non-surgical alternatives that are now available is justified by the high rate of recurrence of foot ulcers and their serious implications.

				wear an offloading cast for up to 12 weeks (based on clinical considerations).	recurrence is probably about 50%.	
<b>Khan AA et al., (2016)</b> <sup>[45]</sup>	Clinical study	The study included 60 patients with DFUs in total.	NS	5 patients had conservative therapy, 46 patients underwent debridement, 8 underwent severe amputation, 14 underwent disarticulation, and 2 underwent pus drainage. Thirteen individuals underwent split skin grafting as a last alternative.	NS	Controlling diabetes with human insulin, using antibiotics, simple dressing, debridement of the wound, and slough removal are all examples of conservative therapy. The other therapeutic options were split skin grafting, disarticulation, below-knee amputation as well and above-knee amputation. There was no mortality found in this study.
<b>Mummidi DS et al., (2015)</b> <sup>[46]</sup>	Clinicopathological study.	100 patients were diagnosed with DFU.	Patients present with diabetic mellitus (Exact types were not mentioned.)	Out of 100 patients, 12 (12%) were treated conservatively, which included slough excision, daily dressing, antibiotics, and diabetes management. Debridement of the wounds was used to treat 28 (28%) patients, SSG was used to treat 10 (10) patients, I&D was used to treat 6 (6% of the patients), J fasciotomy was used to treat 5 (10) patients who had abscesses, and M was used to treat 6 (16%) patients who had gangrene of the toes and phalanges.	NS	From the outcomes of the study researcher showed that the patients with diabetes who are susceptible to foot lesions need to be informed about the dangers. It has been shown that the multidisciplinary team approach to diabetic foot issues is the best way to obtain favorable rates of limb salvage in high-risk diabetic patients. An infection in a diabetic foot poses a risk to one's leg and is constantly in need of immediate diagnostic and treatment attention. The mortality rate in the present study was 2%.

Short keys: NS: not stated, DFO: DFU's.

	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and personnel (performance bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)
Finestone et al. (2018)	+	+	?	+	?
Hutting, K.H. et al. (2021)	?	?	+	+	+
Khan AA et al. (2016)	+	+	?	+	?
Lakhani et al. (2019)	+	?	?	+	+
Mummidi DS et al. (2015)	+	?	+	+	+
Sikhondze et al. (2022)	?	+	?	+	+
Thewjitcharoen et al.(2020)	?	?	?	+	+
Wu et al.(2022)	+	+	?	+	?

Figure 2. Graphical representation of the risk of bias for the involved studies

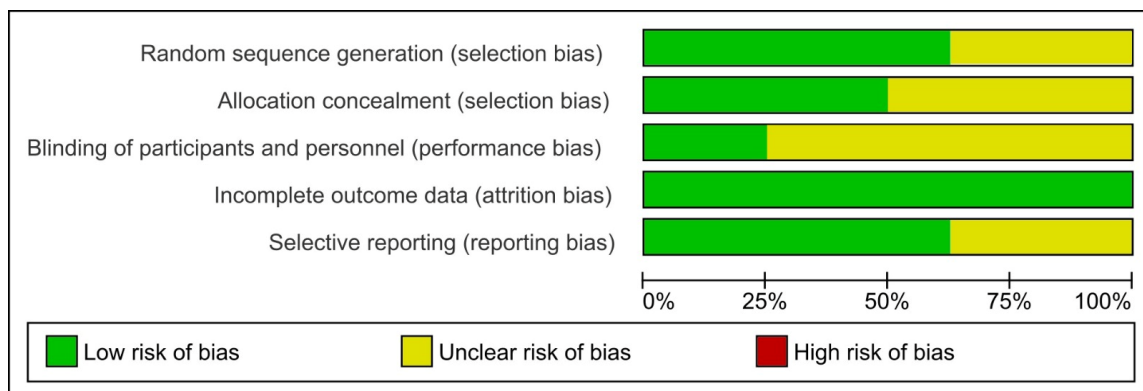


Figure 3. Percentage of the biases

The current study consists of eight research papers, which have documented 888 cases of diabetic foot ulcers (DFUs). Among the patients included in the study, 11.15% were identified with type I diabetes, while the remaining 88.85% were diagnosed with type II diabetes. It is worth noting that the specific type of diabetes mellitus was not specified in two of the included studies.<sup>[44, 45]</sup>

In this review, we found overall, a recurrence rate of 24.51% in cases of DFU was observed in five studies. Whereas, recurrences were not mentioned in the three studies.<sup>[39,45,46]</sup> Similar to Huang et al. meta-analysis, the

outcomes of this one indicated that the risk of DFU recurrence in male patients was 1.38 times greater than that in female patients (OR=1.38, 95% CI, 1.07-1.78, P=0.05), which was in line with those of a prior investigation.<sup>[50]</sup> Furthermore, research conducted by Dubsk et al.,<sup>[51]</sup> and Khalifa et al.,<sup>[52]</sup> reported that DFU recurrence was not associated with gender, although the authors did not justify this discouraging finding, probably because of the small sample size. In the included trials, researchers found that patients with a history of smoking had a greater probability of developing DFU again.<sup>[52]</sup>



Despite several studies being published,<sup>[51-54]</sup> these studies were constrained by their small sample sizes and concluded that smoking was not a risk factor for DFU recurrence. Whereas, Huang et al.,<sup>[50]</sup> reported that 44.2% (178/403) of cases found in the DFU recurrence group and 34.2% (195/570) in the DFU group gave a history of smoking previously.

In this review, three investigations revealed a 14.26% overall mortality rate.<sup>[40,42,46]</sup> Five further studies' findings showed no evidence of mortality which is presented in Table 1.<sup>[39,41,43,44,45]</sup> Despite the rise in the number of diabetic patients in our nation, there has been inadequate attention paid to the training of specialized nurses, such as those who specialize in diabetes or diabetic foot care. The invention of short-term training programs for nurses, the use of clinical guidelines and algorithms for treating diabetic feet in clinics and hospitals, as well as ongoing education about novel diabetic foot care techniques, appear to have the potential to temporarily increase the focus on diabetes and foot care. Moreover, the vast array of programs, which incorporates the Master of Sciences in Nursing for growing diabetic expert nurses and the creation of electronic health, might lessen this worldwide issue.<sup>[56]</sup> As a result, several colleges have established standards by putting in place specific programs for those just starting in the healthcare sector. One of the inventors in this field is the Endocrinology and Metabolism Research Institute of Tehran University of Medical Sciences, which created the clinical guidelines for diabetic feet, translated the clinical care of diabetic feet, designed the diabetic foot website,<sup>[57,58]</sup> established the virtual clinic for diabetes education's section on diabetic feet, and created the network of diabetic foot health centers.

A comprehensive investigation was conducted on a range of conventional and modern surgical interventions for diabetic foot ulcers (DFUs), revealing their respective limitations. The study examined various surgical techniques used to treat DFUs, including:

1. Debridement: A conventional method involving the removal of dead or infected tissue from the ulcer. Limitations include the potential for incomplete removal, leading to delayed healing or recurrent infection.

2. Skin grafting: A procedure that involves transplanting healthy skin to cover the ulcer site. Limitations may include graft failure, poor integration, and limited availability of suitable donor sites.

3. Flap reconstruction: This approach involves transferring healthy tissue, often with its blood supply, to the ulcer area. Limitations include the need for a skilled surgeon, prolonged healing time, and the risk of flap

failure.

4. Negative pressure wound therapy (NPWT): A modern technique that uses a vacuum system to promote wound healing. Limitations include the need for regular equipment changes, discomfort for some patients, and limited evidence regarding its long-term efficacy.

5. Hyperbaric oxygen therapy (HBOT): This method involves exposing the patient to increased oxygen levels, which can enhance healing. Limitations include the need for specialized facilities, multiple sessions, and limited evidence supporting its efficacy in DFU treatment.

6. Bioengineered skin substitutes: Modern advancements in tissue engineering have led to the development of bioengineered skin substitutes. Limitations include their high cost, limited availability, and the need for further research to establish their long-term effectiveness.

7. Amputation: In severe cases where other interventions fail or complications arise, amputation may be necessary. However, it is considered a last resort due to the significant impact on the patient's quality of life.

It is important to note that the choice of surgical intervention depends on various factors, including the severity of the DFU, the patient's overall health, and the expertise of the healthcare team. Each surgical approach has its benefits and limitations, and a personalized treatment plan should be developed based on individual patient needs and circumstances.

## Conclusions

Based on the outcomes of this review, we can conclude that the patients treated with surgery show a lower recurrence rate of DFU as compared to the patients treated with only drug treatment. It is crucial to implement a new surgical treatment for DFUs to increase their success rate. To enhance the results of DFU, a newly established system of treatment with a multidisciplinary team approach and collaboration with referral hospitals is urgently needed. Our review sheds light upon the more successful outcomes-oriented treatment protocol to be added to the curriculum of trainee doctors. The article also recommends a meticulous training section to beginners doctors, and nurses who deal with the treatment of DFU.

## Acknowledgment

None.

## Competing interests

The authors declare that they have no competing interests.

## Abbreviations

Diabetic foot ulcers: DFUs  
 Wound Healing Society: WHS;  
 Infectious Disease Society of America: IDSA;  
 Preferred Reporting Items for Systematic Reviews and  
 Meta-Analyses: PRISMA;  
 random control trials: RCTs;  
 diabetic mellitus: DM;  
 Negative pressure wound therapy: NPWT;  
 Hyperbaric oxygen therapy: HBOT.

## Authors' contributions

All authors read and approved the final manuscript. All authors take responsibility for the integrity of the data and the accuracy of the data analysis.

## Funding

None.

## Role of the funding source

None.

## Availability of data and materials

The data used in this study are available from the corresponding author on request.

## Ethics approval and consent to participate

The study was conducted in accordance with the Declaration of Helsinki. Institutional Review Board approval was obtained.

## Consent for publication

By submitting this document, the authors declare their consent for the final accepted version of the manuscript to be considered for publication.

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**How to Cite this Article:**

Chawada MJ, Singh MR, Swami G, Patond HW, Anmod GL. A systematic review of various types of conventional and modern diabetic foot ulcer surgeries and their outcomes: A beginners digest. *Arch Trauma Res*. 2023;12(3):112-123. [doi:10.48307/ATR.2023.178214](https://doi.org/10.48307/ATR.2023.178214)