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The impact of vacuum sealing drainage on wound healing and infection control in diabetic foot ulcer patients

Li Wang¹, Xiaofeng Yang², Zhihong Wang¹ and Yingdong Tan^{1*}

Abstract

Purpose To describe observed associations between vacuum sealing drainage (VSD) and wound healing, infection control, and pain outcomes in a retrospective cohort of diabetic foot ulcer (DFU) patients.

Methods This single-center retrospective cohort study included 253 DFU patients (Wagner grades 2–3) divided into a conventional treatment group (n = 138) and a VSD group (n = 115, receiving standard care plus continuous-irrigation VSD). Treatment allocation was non-randomized and based on clinical suitability, physician discretion, patient preference, and logistics. Wound area, complete healing rate, healing time, infection control, inflammatory cytokines (IL-1 β , IL-6, IL-8), SF-MPQ pain scores, and adverse events were compared between groups. Logistic regression identified factors associated with poor healing and poor infection control.

Results In this cohort, VSD was associated with a higher complete healing rate (91.30% vs. 78.26%, $P = 0.005$; absolute difference 13.0%, NNT = 8), shorter median healing time (72 vs. 79 days; difference 7 days), better infection control (93.91% vs. 81.16%, $P = 0.003$), lower inflammatory cytokine levels, and lower SF-MPQ scores. Adverse events were fewer in the VSD group (9.57% vs. 20.29%, $P = 0.019$). Logistic regression identified VSD as a factor associated with reduced odds of poor healing (OR = 0.350) and poor infection control (OR = 0.285).

Conclusion In this retrospective, non-randomized cohort, continuous-irrigation VSD was associated with modestly better outcomes across several measured parameters. However, the absolute benefits were small, the study lacks data on cost, convenience, and treatment burden, and the findings are specific to the combined protocol used at this center. Given the observational design and the inherent risk of confounding by indication, these results should be interpreted as exploratory associations rather than as evidence of superiority. Prospective randomized trials are needed before any firm treatment recommendations can be made.

Keywords Vacuum sealing drainage, Diabetic foot ulcer, Wound healing, Infection control, Negative pressure wound therapy

Introduction

Diabetic foot ulcer (DFU) represents a significant and challenging complication of diabetes mellitus, affecting millions of patients worldwide. These chronic wounds are characterized by impaired healing processes due to underlying pathophysiological mechanisms such as neuropathy, ischemia, and infection [1, 2]. The burden of DFU is substantial, leading to high morbidity, prolonged hospital stays, and increased healthcare costs. Despite

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advancements in medical care, the prevalence of DFU remains high, necessitating innovative approaches for effective management [3, 4].

The pathogenesis of DFU involves multiple factors that complicate the healing process. Peripheral neuropathy, a common complication of diabetes, leads to loss of protective sensation, making patients susceptible to unnoticed trauma and subsequent ulceration. Additionally, vascular insufficiency contributes to poor perfusion, limiting the delivery of oxygen and nutrients necessary for tissue repair. Infection further exacerbates these challenges by promoting inflammation and delaying healing [5, 6]. Traditional treatments often focus on addressing these individual components through offloading, revascularization, and antimicrobial therapy. These strategies may not be sufficient for achieving complete wound closure, particularly in cases of large or deep ulcers [7, 8].

Negative pressure wound therapy (NPWT), including vacuum sealing drainage (VSD), has emerged as a widely adopted approach for managing chronic wounds. This technique involves applying controlled negative pressure to the wound bed, which promotes granulation tissue formation, enhances blood flow, and removes excess exudate [9, 10]. Several randomized controlled trials and meta-analyses have demonstrated the efficacy of NPWT in various types of chronic wounds, including those associated with diabetes [11–13].

However, the clinical value of NPWT remains an active area of debate. Recent high-quality evidence has tempered earlier enthusiasm. A large, multicenter, randomized SWHSI-2 trial published in *The Lancet* found no clear evidence that NPWT improved time to wound healing compared to usual care in surgical wounds healing by secondary intention, although that study was not limited to diabetic foot wounds [14]. Furthermore, a recent randomized non-inferiority trial demonstrated that copper oxide-impregnated dressings yielded similar healing outcomes to NPWT in diabetic wounds, while offering greater convenience and lower cost [15]. These findings raise important questions about the routine application of NPWT: when is negative pressure therapy truly justified, what is the magnitude of its benefit in specific patient subgroups, and how does it compare with simpler, less costly alternatives?

The present retrospective study does not aim to re-establish the efficacy of VSD, which has been shown in prior RCTs, nor does it attempt to claim superiority. Rather, it seeks to contribute to the ongoing clinical debate by providing real-world descriptive data from a Chinese patient population, with exploratory assessments of inflammatory cytokines (interleukin [IL]-1 β , IL-6, IL-8), pain improvement using the short-form McGill pain questionnaire (SF-MPQ), and risk factor

analysis for poor healing and infection control. These secondary outcomes and the identification of local risk factors represent the incremental contribution of this work. We explicitly acknowledge that any observed differences should be interpreted as associations observed in a selected retrospective cohort, and that the modest absolute benefits must be weighed against the additional costs, patient burden, and the availability of simpler alternative therapies.

Materials and methods

Design and grouping

A retrospective analysis was conducted on DFU patients who received treatment at our hospital from April 2020 to April 2024. Inclusion criteria were: (1) meeting the diagnostic criteria for DFU [16]; (2) Wagner grades [17] of 2 to 3; (3) age ≥ 18 years; (4) strict dietary control during treatment, with fasting blood glucose stabilized below 7.0 mmol/L and postprandial 2-h blood glucose controlled below 11.0 mmol/L; (5) ankle-brachial index (ABI) ≥ 0.7 ; (6) complete medical records. Exclusion criteria included: (1) severe heart, liver, or kidney dysfunction; (2) specific infections in the wound (*Mycobacterium tuberculosis*, *Clostridium tetani*); (3) acute complications of diabetes (hyperosmolar hyperglycemic state, diabetic ketoacidosis); (4) use of immunosuppressive agents or glucocorticoids affecting wound healing within the past 3 months; (5) intellectual disabilities, cognitive impairments, or mental illness; (6) malignancies, coagulation disorders, or active bleeding diseases; (7) pregnancy or lactation; (8) allergies to antibiotics or materials used during treatment.

Based on differences in treatment protocols, 253 patients who met the inclusion and exclusion criteria were defined into a conventional group ($n=138$) and a VSD group ($n=115$). The conventional group was defined as receiving only standard DFU treatments, including blood glucose control, anti-infection therapy, wound debridement, and local dressing changes, without the use of VSD devices. The VSD group was defined as receiving standard treatments supplemented with additional VSD therapy.

Ethics

The study protocol has been reviewed and approved by the Medical Ethics Committee of Shanghai First People's Hospital Jiuquan Hospital. The implementation of the study strictly adhered to the Declaration of Helsinki (revised in 2013), the Ethical Review Measures for Biomedical Research Involving Human Subjects, and other relevant medical ethics guidelines, ensuring the scientific integrity and ethical standards of the study. Given the retrospective design of this study, data were sourced from

archived medical records of previous treatments at the hospital. No additional interventions were performed on patients, and all data extraction processes did not involve current patient care or rights. After approval by the ethics committee, the requirement for informed consent was waived.

Treatment

Standard treatment

- (1) Blood glucose control: All patients received individualized blood glucose control protocols: ① Dietary Intervention: A clinical dietitian developed a low-sugar, high-fiber, high-quality protein diet plan to control total daily caloric intake and avoid high glycemic index (GI) foods. ② Blood Glucose Monitoring: Blood glucose was monitored 30 min before meals, 2 h after meals, and before bedtime daily. Glycated hemoglobin (HbA1c) was measured once a week. ③ Hypoglycemic Treatment: Based on blood glucose levels, oral hypoglycemic agents (such as metformin, SGLT-2 inhibitors, etc.) or subcutaneous insulin injections were selected. The target was to maintain fasting blood glucose ≤ 7.0 mmol/L, postprandial 2-h blood glucose ≤ 11.0 mmol/L, and HbA1c $\leq 7.5\%$.
- (2) Anti-infection therapy: During the initial treatment phase, wound exudates were collected for bacterial culture and antibiotic sensitivity testing. Sensitive antibiotics were selected based on the results to avoid empirical medication. Every 3 to 5 days, exudate cultures were repeated during treatment, and the type and duration of antibiotics were dynamically adjusted. Antibiotics were discontinued promptly after infection control to avoid misuse.
- (3) Wound debridement: Under sterile conditions, surgical debridement was performed to remove necrotic tissue and inflammatory granulation tissue from the wound surface. For Wagner grade 3 patients, the wound was expanded if necessary to expose and remove necrotic tendons and bone, ensuring debridement to healthy tissue margins. After debridement, the wound was sequentially irrigated with 3% hydrogen peroxide, repeatedly rinsed with 0.9% sodium chloride solution, disinfected with povidone-iodine solution, and finally dried with sterile gauze.
- (4) Local dressing changes: After basic wound care, conventional group patients followed a traditional dressing change protocol: ① The wound was covered with sterile petroleum jelly gauze (Approval No.: 20163142310, Shaoxing Fuqing Hygiene Products Co., Ltd., Zhejiang Province), which main-

tained a moist wound environment and reduced mechanical injury during dressing changes. ② The outer layer was wrapped with sterile gauze and elastic bandages moderately to avoid tightness affecting blood circulation. ③ Dressing Change Frequency: Initially (first 2 weeks), dressings were changed once daily. Once wound exudate decreased, the frequency was reduced to every other day, continuing for 12 weeks. ④ During each dressing change, the growth of granulation tissue, characteristics of exudate, and epithelial migration at the wound edges were observed, and the treatment plan was adjusted promptly.

- (5) Off-loading: All patients received appropriate off-loading therapy using non-removable knee-high off-loading boots or specialized custom-made therapeutic footwear, as indicated by wound location and severity. Off-loading was maintained throughout the treatment period to reduce pressure on the ulcer site.

VSD therapy

For the VSD group, after debridement, VSD dressings were cut according to the shape and size of the wound to ensure complete coverage and tight adherence without any dead space (Fig. 1). The drainage tubes were embedded within the dressings with side holes facing the wound. For larger or irregular wounds, multiple drainage tubes could be placed and combined into a single outlet using a three-way connector. The skin within a 3 cm perimeter around the wound was cleaned with normal saline, degreased with 70% alcohol, and then dried. After the alcohol had fully evaporated, a biocompatible transparent film was used to seal the dressing and surrounding skin to ensure a complete seal. The drainage tube outlet was connected to a central negative pressure device, and the negative pressure was adjusted to 20–50 kPa (equivalent to approximately 150–375 mmHg), initiating continuous negative pressure suction. A normal saline irrigation system was connected to continuously flush the VSD dressing at a rate of 10–20 mL/h. This irrigation was not a timed instillation-dwell cycle (as used in VeraFlo™ systems), but rather a continuous, low-volume flush primarily intended to prevent clotting or exudate blockage of the drainage tubing. The irrigation was applied throughout the entire duration of VSD therapy.

After using the VSD device (Approval No.: 20182142572, Wuhan Yijia Bao Biological Materials Co., Ltd., Hubei Province) for 1–2 weeks, treatment was adjusted based on granulation tissue growth and sinus tract formation. If the wound showed fresh granulation tissue with no sinus tract formation, the VSD negative



Fig. 1 A clinical photograph of the VSD setup. VSD, vacuum sealing drainage

pressure device was removed, and conventional petroleum jelly gauze dressing changes were initiated until the end of treatment. If granulation tissue growth was slow or sinus tracts were present, the wound was re-debrided, and the VSD procedure was repeated until the wound base was covered by granulation tissue, after which conventional dressing changes were resumed.

Treatment allocation

The choice between conventional treatment and VSD was not protocol-driven or randomized. Instead, it was based on a combination of physician discretion, patient preference, and, to a limited extent, device availability. In general, VSD was offered when: (a) the ulcer was suitable for negative pressure therapy (i.e., no exposed major vessels, nerves, or tendons without coverage, no active bleeding, and no untreated osteomyelitis); (b) the patient had adequate perfusion ($ABI \geq 0.7$); (c) the treating orthopedic surgeon had experience with VSD; and (d) the patient consented to the procedure and could comply with follow-up. Conventional treatment was chosen when VSD was not clinically indicated (e.g., very small wounds, inadequate seal possible, or concerns about patient adherence) or when the patient refused VSD. Logistical factors (e.g., temporary unavailability of the

VSD device or consumables) also influenced the choice in a small number of cases.

Observation indicators

- (1) **Wound healing:** The wound area, complete wound healing rate, and time to complete wound healing were recorded. High-resolution photographs of the wounds were taken using a calibrated ruler before treatment and after 2 weeks, 4 weeks, 8 weeks, and 12 weeks of treatment. The wound area (in cm^2) was calculated using ImageJ image analysis software. The complete wound healing rate refers to the percentage of patients in each group whose target ulcers met the "complete healing criteria" after 12 weeks of treatment. The complete healing criteria followed the IWGDF/IDSA Guidelines for the Diagnosis and Treatment of Diabetic Foot Infections [16]: ① The wound is completely covered by new epithelial tissue with no exposed granulation tissue; ② No local discharge, redness, swelling, or pain. The time to complete wound healing is defined as the number of days from the start of the first treatment until the wound first meets the complete healing criteria [16]. For patients who did not achieve complete healing within the 12-week study period, healing time was censored at day 84 (the end of follow-up) or at the date of last wound assessment if the patient was lost to follow-up earlier. No patient was excluded from the analysis because of non-healing.
- (2) **Infection control:** The infection control rate, duration of antibiotic use, and levels of inflammatory markers were recorded. The infection control rate refers to the percentage of patients in each group who achieved "effective infection control" after 2 weeks of treatment. The effective infection control criteria followed the IWGDF/IDSA Guidelines for the Diagnosis and Treatment of Diabetic Foot Infections [16]: ① Complete resolution of local signs of infection (redness, swelling, heat, pain, purulent discharge); ② Disappearance of systemic infection symptoms (fever, chills); ③ No need for continued systemic antibiotic therapy. The duration of antibiotic use is defined as the total number of days from the start of systemic antibiotics until discontinuation. Levels of interleukin (IL)-1 β , IL-6, and IL-8 were measured using the Inflammation 20-Plex Human ProcartaPlex™ Assay Panel (EPX200-12185–901, Thermo Fisher Scientific Inc., USA) before treatment and after 2 weeks of treatment.

- (3) Pain Improvement: The SF-MPQ [18] was used to evaluate the pain rating index (PRI), visual analog scale (VAS), and present pain intensity (PPI) before treatment and after 12 weeks of treatment. The PRI consists of 15 descriptive pain terms, with items 1–11 assessing the sensory dimension of pain and items 12–15 assessing the affective dimension. Each item is scored on a scale from 0 to 3, where 0=no pain, 1=mild pain, 2=moderate pain, and 3=severe pain, yielding a total score range of 0–45. The VAS is a 10 cm line, where 0 represents "no pain" and 10 represents "the most intense pain." The PPI uses a six-level categorical scale, where 0 represents "no pain" and 5 represents "excruciating pain." The overall Cronbach's α for this scale is 0.933 [19].
- (4) Adverse event: The incidence of adverse events during treatment was recorded, including bleeding (active wound bleeding or subcutaneous hematoma), increased pain (an increase in VAS score of ≥ 2 points compared to baseline, excluding factors related to infection exacerbation), and local redness and swelling (an increase in the area of redness around the wound by ≥ 1 cm compared to baseline, with or without an increase in skin temperature).

Data analysis

Data were analyzed using SPSS version 29.0 (SPSS Inc., Chicago, IL, USA). Normality of continuous variables was assessed using the Shapiro–Wilk test. For variables with significant deviation from normality, non-parametric Mann–Whitney U tests were performed as sensitivity analyses; results were consistent with parametric tests, so parametric results are reported for comparability with prior literature. For wound area measured repeatedly (baseline, 2, 4, 8, 12 weeks), a linear mixed-effects model was used with treatment group, time (categorical), and the group $\times$ time interaction as fixed effects and a random intercept for each patient. Pairwise comparisons were adjusted using Bonferroni correction. Categorical variables were compared using χ^2 test or Fisher's exact test. Continuous variables at single time points were compared using independent samples t-tests or Mann–Whitney U tests as appropriate. The time to complete healing was analyzed using the Kaplan–Meier method. Patients who did not achieve healing by 12 weeks (84 days) were censored at that time. Patients who withdrew or were lost to follow-up were censored at their last documented wound assessment date. The log-rank test was used to compare healing curves between the VSD and conventional groups.

Univariate and multivariate logistic regression were performed with poor wound healing (incomplete healing at 12 weeks) and poor infection control (infection not controlled at 2 weeks) as dependent variables. Variable selection for multivariate models included VSD treatment (primary exposure), all variables with $p < 0.1$ in univariate analysis (duration of DM, Wagner grade, ABI, initial wound area). Multicollinearity was assessed using variance inflation factors (VIFs); all VIFs were < 2.0 . Events-per-variable (EPV) ratios were calculated (poor healing: $EPV \approx 5:1$; poor infection control: $EPV \approx 4:1$). All analyses are exploratory; odds ratio (OR) is presented with 95% confidence interval (CI), and $p < 0.05$ was considered statistically significant.

Results

General information

A total of 253 DFU patients were included, with 138 in the conventional group and 115 in the VSD group. No significant differences were observed between the two groups regarding demographics, comorbidities, diabetes-related indicators, or DFU-related characteristics (all $P > 0.05$, Table 1). Additionally, for patients in the VSD group, the median duration of a single VSD cycle was 14 days (interquartile range: 10–17 days), with a range of 7–21 days across all patients. Most patients (84.35%, $n=97$) completed treatment with a single VSD cycle, while 15.65% ($n=18$) required repeated debridement and 1–2 additional VSD cycles.

Wound healing

After 12 weeks of treatment, the VSD group achieved a significantly higher complete wound healing rate (91.30% vs. 78.26%, $P=0.005$; Table 2). The absolute risk difference for complete healing was 13.04%, corresponding to a number needed to treat (NNT) of 8 (95% CI 5–20). This means that approximately 8 patients would need to be treated with VSD (instead of conventional treatment) for one additional patient to achieve complete healing by 12 weeks. The median healing time was 72 days (95% CI 65–79 days) in the VSD group and 79 days (95% CI 72–87 days) in the conventional group. The Kaplan–Meier curves (Fig. 2) showed consistently better healing in the VSD group throughout the 12-week follow-up ($P < 0.001$). Of the 253 patients, 213 (84.19%) achieved healing within 84 days. Among the 40 non-healed patients, all were censored at day 84. No patient was lost to follow-up before 12 weeks. Therefore, the analysis includes all 253 patients with censoring applied only to the non-healed cases at the end of the study period.

The linear mixed-effects model revealed a significant group $\times$ time interaction ($F=3.840$, $P=0.004$), indicating that the reduction in wound area over the 12-week

Table 1 Comparison of general information between two groups of DFU patients

Parameter	Conventional group (n = 138)	VSD group (n = 115)	t/ χ^2	P
Demographics				
Age (years)	62.45 ± 10.23	61.89 ± 9.76	0.438	0.661
Gender [n(%)]			0.091	0.762
Male	79 (57.25%)	68 (59.13%)		
Female	59 (42.75%)	47 (40.87%)		
BMI (kg/m ²)	24.36 ± 3.87	23.98 ± 3.65	0.809	0.420
Comorbidities				
Hypertension [n(%)]	92 (66.67%)	72 (62.61%)	0.453	0.501
Coronary heart disease [n(%)]	41 (29.71%)	30 (26.09%)	0.408	0.523
Cerebrovascular disease [n(%)]	24 (17.39%)	18 (15.65%)	0.137	0.711
DM-related indicators				
Type of DM [n(%)]			0.041	0.840
T1DM	18 (13.04%)	16 (13.91%)		
T2DM	120 (86.96%)	99 (86.09%)		
Duration of DM (years)	15.67 ± 4.41	16.02 ± 4.88	0.602	0.548
DFU-related indicators				
Duration of DFU (days)	21.35 ± 5.19	22.64 ± 6.62	1.694	0.092
Ulcer location [n(%)]			0.871	0.929
Plantar	81 (58.70%)	72 (62.61%)		
Dorsal	18 (13.04%)	12 (10.43%)		
Lateral/Medial border	15 (10.87%)	10 (8.70%)		
Heel	12 (8.70%)	10 (8.70%)		
Toe	12 (8.70%)	11 (9.57%)		
Weight-bearing ulcer [n(%)]	58 (42.03%)	51 (44.35%)	0.138	0.711
Wagner grade [n(%)]			0.688	0.407
2	83 (60.14%)	75 (65.22%)		
3	55 (39.86%)	40 (34.78%)		
Deep wound [n(%)]	55 (39.86%)	45 (39.13%)	0.014	0.907
Tendon/bone exposure [n(%)]	30 (21.74%)	24 (20.87%)	0.028	0.867
Purulent drainage [n(%)]	76 (55.07%)	66 (57.39%)	0.137	0.711
Malodor [n(%)]	41 (29.71%)	38 (33.04%)	0.325	0.569
ABI	0.89 ± 0.08	0.90 ± 0.07	0.914	0.361
Single VSD cycle duration (days)			–	–
Median (IQR)	–	14 (10–17)		
Range	–	7–21		
Number of VSD cycles [n(%)]			–	–
1 cycle	–	97 (84.35%)		
2 cycles	–	15 (13.04%)		
≥ 3 cycles	–	3 (2.61%)		

DFU, diabetic foot ulcer; VSD, vacuum sealing drainage; BMI, body mass index; DM, diabetes mellitus; ABI, ankle-brachial index

Table 2 Comparison of complete wound healing between two groups of DFU patients

Parameter	Conventional group (n = 138)	VSD group (n = 115)	t/ χ^2	P
Complete wound healing rate (after 12 weeks of treatment) [n(%)]	108 (78.26%)	105 (91.30%)	8.018	0.005
Median healing time (days, 95% CI)	79 (72–87)	72 (65–79)	–	< 0.001

DFU, diabetic foot ulcer; VSD, vacuum sealing drainage; CI, confidence interval

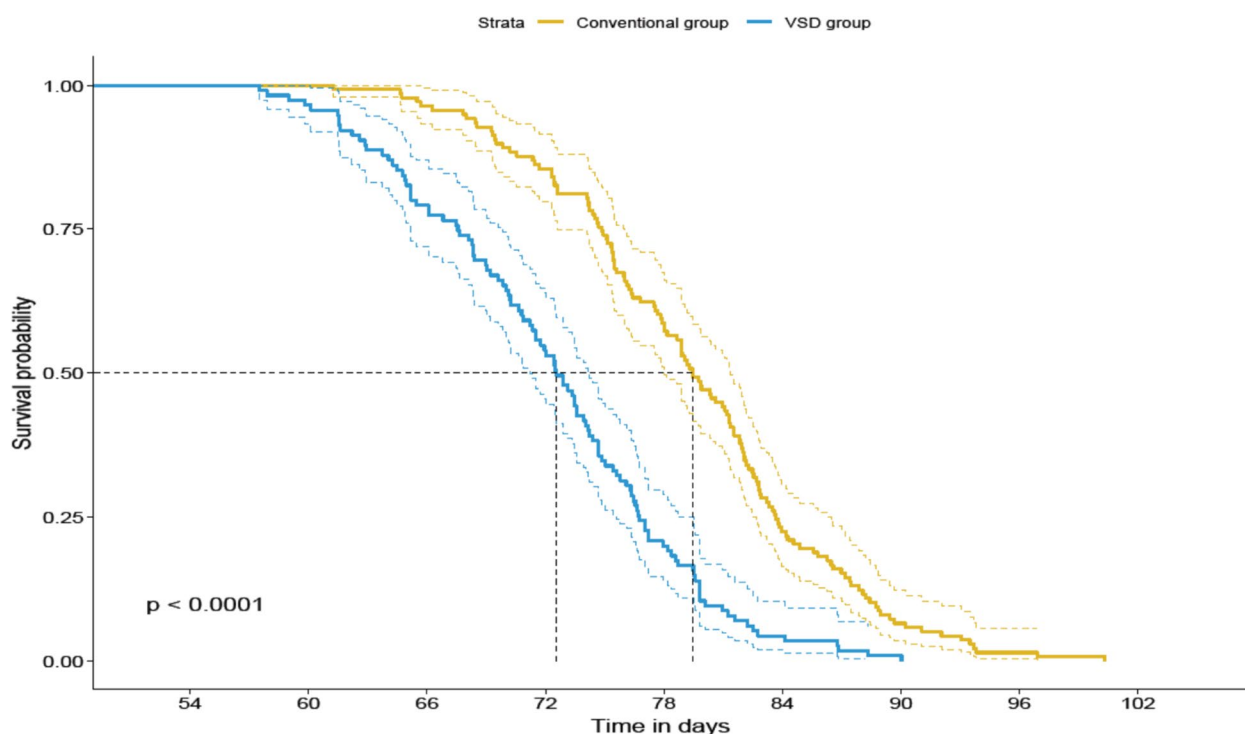


Fig. 2 Kaplan–Meier survival curves for time to complete wound healing

period differed significantly between the VSD and conventional treatment groups. Post-hoc comparisons with Bonferroni correction showed that while baseline wound area was similar between groups (15.73 vs. 15.68 cm², $P=0.860$), the VSD group had significantly smaller wound areas at all subsequent follow-up time points: at 2 weeks (12.34 vs. 13.41 cm², $P=0.003$), 4 weeks (8.01 vs. 8.74 cm², $P=0.006$), 8 weeks (3.23 vs. 3.69 cm², $P=0.002$), and 12 weeks (0.96 vs. 1.05 cm², $P=0.016$). These results are consistent with the pattern shown in Fig. 3.

Infection control

As shown in Table 3, the VSD group had a superior infection control rate after 2 weeks (93.91% vs. 81.16%, $P=0.003$) and required a shorter duration of antibiotic therapy (12.08 vs. 14.92 days, $P<0.001$) compared to the conventional group.

Table 4 presents the levels of inflammatory cytokines. While baseline levels were similar (all $P>0.05$), after 2 weeks of treatment, the VSD group exhibited significantly greater reductions in IL-1 β , IL-6, and IL-8 levels compared to the conventional group (all $P<0.01$).

Pain improvement

Pain assessment results are detailed in Table 5. At baseline, scores for the PRI, VAS, and PPI were similar

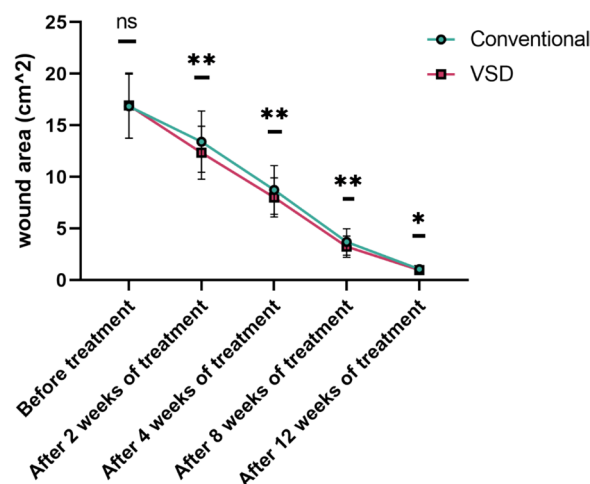


Fig. 3 Comparison of wound area between two groups of DFU patients (cm²). Data are presented as mean $\pm$ SD. The linear mixed-effects model showed a significant group $\times$ time interaction ($F=3.840$, $P=0.004$). Pairwise comparisons at each time point were performed using Bonferroni-adjusted t-tests. ns: no significant difference; * $P<0.05$; ** $P<0.01$. DFU, diabetic foot ulcer; VSD, vacuum sealing drainage

between groups (all $P>0.05$). After 12 weeks, the VSD group reported significantly lower final scores than the conventional group across all three components: PRI

Table 3 Comparison of infection control outcomes between two groups of DFU patients

Parameter	Conventional group (n = 138)	VSD group (n = 115)	t/ χ^2	P
Infection control rate (after 2 weeks of treatment) [n(%)]	112 (81.16%)	108 (93.91%)	8.996	0.003
Duration of antibiotic use (days)	14.92 ± 2.44	12.08 ± 1.51	11.289	< 0.001

DFU, diabetic foot ulcer; VSD, vacuum sealing drainage

Table 4 Comparison of inflammatory cytokine levels between two groups of DFU patients (pg/mL)

Parameter	Conventional group (n = 138)	VSD group (n = 115)	t	P
IL-1 β				
Before treatment	35.24 ± 3.15	35.18 ± 3.22	0.156	0.876
After 2 weeks of treatment	18.35 ± 2.24	17.56 ± 1.95	2.971	0.003
IL-6				
Before treatment	88.43 ± 6.32	87.92 ± 6.85	0.623	0.534
After 2 weeks of treatment	52.18 ± 4.87	50.65 ± 3.92	2.766	0.006
IL-8				
Before treatment	3.87 ± 0.92	3.91 ± 0.89	0.423	0.673
After 2 weeks of treatment	1.24 ± 0.39	1.12 ± 0.27	2.688	0.008

DFU, diabetic foot ulcer; VSD, vacuum sealing drainage; IL-interleukin

Table 5 Comparison of SF-MPQ scores between two groups of DFU patients (points)

Parameter	Conventional group (n = 138)	VSD group (n = 115)	t	P
PRI				
Before treatment	25.83 ± 4.12	26.15 ± 3.98	0.641	0.522
After 12 weeks of treatment	9.45 ± 2.14	8.89 ± 1.46	2.466	0.014
VAS				
Before treatment	7.86 ± 1.23	7.92 ± 1.19	0.437	0.663
After 12 weeks of treatment	2.93 ± 0.81	2.71 ± 0.67	2.376	0.018
PPI				
Before treatment	3.77 ± 0.51	3.78 ± 0.53	0.136	0.892
After 12 weeks of treatment	1.78 ± 0.39	1.69 ± 0.32	2.062	0.040

SF-MPQ, short-form McGill pain questionnaire; DFU, diabetic foot ulcer; VSD, vacuum sealing drainage; PRI, pain rating index; VAS, visual analogue scale; PPI, present pain intensity

(8.89 vs. 9.45, $P=0.014$), VAS (2.71 vs. 2.93, $P=0.018$), and PPI (1.69 vs. 1.78, $P=0.040$).

Adverse events

The incidence of treatment-related adverse events was significantly lower in the VSD group (9.57% vs. 20.29%, $P=0.019$), as detailed in Table 6.

Logistic regression analysis

Table 7 displays the logistic regression analysis for factors associated with poor wound healing (incomplete healing at 12 weeks). In the multivariate model, VSD treatment was identified as a significant independent protective

factor (OR=0.350, 95% CI 0.162–0.756, $P=0.006$). Conversely, a longer duration of diabetes (OR=1.040, $P=0.019$), a higher Wagner grade 3 (OR=2.200, $P=0.010$), and a larger initial wound area (OR=1.090, $P=0.005$) were independent risk factors for poor healing. A higher ABI value was also an independent protective factor (OR=0.820, $P=0.015$).

Table 8 shows the logistic regression analysis for factors affecting poor infection control (failure at 2 weeks). In the final multivariate model, VSD treatment remained a strong independent protective factor (OR=0.285, 95% CI 0.118–0.689, $P=0.004$), while a higher Wagner grade 3 was a significant independent risk factor (OR=2.000,

Table 6 Comparison of adverse events incidence rate between two groups of DFU patients during treatment [n(%)]

Parameter	Conventional group (n = 138)	VSD group (n = 115)	χ^2	P
Adverse events incidence rate	28 (20.29%)	11 (9.57%)	5.533	0.019
Bleeding	5 (3.62%)	7 (6.09%)		
Increased pain	16 (11.59%)	4 (3.48%)		
Local redness and swelling	12 (8.70%)	5 (4.35%)		

DFU, diabetic foot ulcer; VSD, vacuum sealing drainage

Table 7 Univariate and multivariate logistic regression analysis of risk factors affecting poor wound healing in DFU patients

Parameter	Univariate analysis			Multivariate analysis		
	P	OR	95%CI	P	OR	95%CI
VSD treatment (vs. conventional treatment)	0.005	0.343	0.159–0.736	0.006	0.350	0.162–0.756
Duration of DM	0.010	1.020	1.012–1.089	0.019	1.040	1.006–1.075
Wagner grade 3 (vs. grade 2)	0.005	2.500	1.332–4.692	0.010	2.200	1.205–4.015
ABI	0.009	0.800	0.680–0.941	0.015	0.820	0.695–0.967
Wound area (before treatment)	0.001	1.100	1.040–1.163	0.005	1.090	1.026–1.158

DFU, diabetic foot ulcer; VSD, vacuum sealing drainage; DM, diabetes mellitus; ABI, ankle-brachial index; OR, odds ratio; CI, confidence interval

Table 8 Univariate and multivariate logistic regression analysis of risk factors affecting poor infection control in DFU patients

Parameter	Univariate analysis			Multivariate analysis		
	P	OR	95%CI	P	OR	95%CI
VSD treatment (vs. conventional treatment)	0.003	0.279	0.116–0.671	0.004	0.285	0.118–0.689
Duration of DM	0.050	1.030	1.000–1.061	0.078	1.025	0.997–1.054
Wagner grade 3 (vs. grade 2)	0.011	2.200	1.205–4.015	0.019	2.000	1.120–3.571
ABI	0.048	0.850	0.723–0.996	0.067	0.860	0.732–1.010
Wound area (before treatment)	0.045	1.070	1.000–1.145	0.081	1.060	0.988–1.137

DFU, diabetic foot ulcer; VSD, vacuum sealing drainage; DM, diabetes mellitus; ABI, ankle-brachial index; OR, odds ratio; CI, confidence interval

P=0.019). The associations for diabetes duration, ABI, and initial wound area did not reach statistical significance in the multivariate analysis (all P > 0.05).

Discussion

The beneficial effect of NPWT on DFU healing has been demonstrated in prior RCTs. The primary contribution of the present retrospective study is not to demonstrate this benefit de novo, but to provide real-world descriptive data from a single Chinese center, along with exploratory analyses of pain scores, inflammatory cytokine changes, and risk factors for poor outcomes. All findings should be interpreted as associations, not as causal evidence.

One of the key outcomes of our study was the higher rate of complete wound healing observed in the VSD group. The possible mechanism underlying this benefit may be multifactorial. VSD creates a controlled negative pressure environment around the wound, which

promotes granulation tissue formation and enhances blood flow. This increased perfusion supports the delivery of oxygen and nutrients to the wound site, facilitating faster healing. The continuous suction provided by VSD helps remove excess exudate and debris, reducing the risk of bacterial colonization and infection. By maintaining a clean wound bed, VSD allows for more effective epithelialization and reduces the likelihood of wound breakdown or recurrence [20–22].

Kaplan–Meier analysis confirmed that VSD was associated with a significantly shorter time to healing, with a median difference of 7 days. This could be attributed to the continuous negative pressure applied by VSD, which not only accelerates the formation of granulation tissue but also stimulates the migration of keratinocytes and fibroblasts. These cells play a critical role in the repair process, contributing to the closure of the wound. Moreover, the removal of fluid from the wound bed prevents

maceration, a condition where the skin becomes overly moist and vulnerable to breakdown. By keeping the wound dry and clean, VSD facilitates quicker healing and reduces the duration of treatment [14, 23, 24].

Infection control is another area where VSD demonstrated superior performance. The reduction in infection rates in the VSD group can be linked to the mechanical effects of negative pressure, which help to clear bacteria and other contaminants from the wound. The controlled environment created by VSD minimizes the exposure of the wound to external pathogens, thereby reducing the need for prolonged antibiotic therapy [25, 26]. This is particularly beneficial for diabetic patients who are at higher risk of developing antibiotic-resistant infections due to their compromised immune systems. By minimizing the duration of antibiotic use, VSD not only reduces the risk of resistance but also lowers the potential for side effects associated with long-term antibiotic therapy [27]. Beyond the effects of negative pressure alone, the continuous saline irrigation component in our VSD protocol may have contributed to the observed outcomes. As suggested by recent literature, instillation combined with NPWT enhances the removal of necrotic debris and bacteria, potentially improving the micro-environment of the wound bed more effectively than suction alone [10].

Additionally, the beneficial effects of VSD observed in this study may be mechanistically linked to the stimulation of nitric oxide (NO) production. Mechanical stretch and shear stress induced by negative pressure have been shown to upregulate endothelial NO synthase (eNOS), increasing local NO bioavailability. NO plays a pivotal role in vasodilation, angiogenesis, collagen synthesis, and anti-inflammatory processes, all of which are crucial for diabetic wound healing [28, 29]. Our findings of reduced inflammatory cytokines and improved healing rates align with this NO-mediated pathway.

Pain relief is an essential aspect of DFU management, as chronic wounds can cause significant discomfort and affect patients' quality of life. Our results suggest that VSD is linked to better pain relief compared to conventional treatments. The mechanism behind this effect is likely related to the reduction in wound size and improved healing, which directly contributes to less pain. The negative pressure applied by VSD may have an analgesic effect by stimulating nerve endings in the wound bed, leading to a reduction in pain perception. This dual action of promoting healing and providing pain relief makes VSD a valuable option for managing DFU [30–32].

The incidence of adverse events was lower in the VSD group, indicating that this method is not only effective but also safer than conventional treatments. The reduced occurrence of complications such as bleeding, increased pain, and local redness and swelling suggests that VSD

minimizes trauma to the surrounding tissues. This is particularly important in diabetic patients, whose compromised vascular function and impaired healing responses make them more susceptible to complications. By reducing the risk of these adverse events, VSD enhances patient safety and improves overall treatment outcomes [33, 34].

The logistic regression analysis provides a broader clinical context for our findings. It confirmed VSD as a strong independent protective factor for poor wound healing and infection control, while also identifying longer diabetes duration, more severe Wagner grade, lower ABI, and larger initial wound area as risk factors for poor wound healing. This reinforces the concept that DFU management is multifaceted. VSD is a powerful adjunctive tool that addresses local wound pathophysiology, but its success is interdependent with optimal systemic management of diabetes, perfusion, and overall patient health.

While most comparisons reached statistical significance, the absolute magnitude of the clinical benefits was modest. The complete healing rate was 13% higher with VSD (NNT=8). The median healing time was shortened by 7 days (from 79 to 72 days)—a reduction of approximately 11%. The reduction in antibiotic duration was about 3 days, and the decrease in VAS pain scores (0.22 points) was below the MCID. The most clinically relevant benefit was the lower incidence of adverse events (9.6% vs. 20.3%, NNT≈9). Therefore, while VSD appears to offer some advantages, the overall clinical benefit is modest and should not be overstated.

However, recent high-quality evidence suggests a more nuanced role for NPWT. A large, multicenter, randomized SWHSI-2 trial published in *The Lancet* recently found no clear evidence that NPWT improved the time to wound healing compared to usual care in surgical wounds healing by secondary intention, although that study was not limited to diabetic foot wounds [14]. Furthermore, a recent randomized non-inferiority trial demonstrated that copper oxide-impregnated dressings yielded similar healing outcomes to NPWT in diabetic wounds, while offering greater convenience and lower cost [15]. The discrepancies between our findings and these studies may be explained by several factors. First, patient selection and wound characteristics differ significantly. Our study focused exclusively on DFUs, which have unique pathophysiological features such as peripheral neuropathy, microvascular disease, and impaired cellular response, where the mechanical and biologic effects of NPWT (e.g., increased local blood flow, reduction of edema, and bacterial clearance) might be particularly beneficial. In contrast, the SWHSI-2 trial included a broader spectrum of surgical wounds, which may have diluted the treatment effect. Second, the control

interventions in the comparative trials varied. The non-inferiority of copper dressings highlights that for certain wound types, simpler and more economical modalities can achieve comparable results, challenging the necessity of routine NPWT. Therefore, while our study supports the efficacy of VSD/NPWT in promoting healing in DFUs, these recent findings underscore the importance of individualized treatment decisions. NPWT should be considered as part of a comprehensive DFU management plan rather than a universal solution, weighing its clinical benefits against cost and convenience on a case-by-case basis.

This study has several limitations that need to be acknowledged. First and foremost, this was a single-center, retrospective, non-randomized comparative study. The decision to use VSD was based on physician discretion, patient preference, and logistical factors, not on a predefined protocol. This introduces a high risk of confounding by indication. When a sicker or more complex patient receives an advanced therapy, the observed outcome may be biased either positively (if the therapy works well) or negatively (if uncontrolled severity worsens the outcome). Our baseline comparability on measured variables does not eliminate this risk. Unlike studies that use propensity score matching, although we adjusted for known confounders such as the duration of diabetes, Wagner grade, ABI, and initial wound area using multivariate regression, we cannot entirely rule out the influence of unmeasured confounders (such as the surgeon's experience, patient compliance with dressing changes, and wound bacterial load). Therefore, the results should be interpreted as associations, not as strong evidence of VSD's superiority. Additionally, for adverse events, we cannot rule out that the treating physicians systematically avoided VSD in wounds they judged to be at higher risk of bleeding or pain exacerbation (confounding by contraindication). This could artificially lower the event rate in the VSD group and is a major reason why no causal safety claims can be made. Second, the study only included patients with Wagner grades 2–3, and thus, the conclusions cannot be generalized to more severe DFU populations. Therefore, the findings of this study should be interpreted cautiously, and further validation through multicenter prospective randomized controlled trials is needed to confirm the efficacy of VSD. Third, the VSD intervention protocol in this study was not fully standardized: negative pressure values, whether to use saline irrigation, and the duration of application were all adjusted based on individual patient conditions, leading to heterogeneity in the intervention measures. We cannot determine which combination of parameters is the core driver of VSD benefits. This limitation necessitates individualized parameter selection based

on patient wound characteristics when implementing VSD in clinical practice. Future research should include dose–response studies with standardized parameters to identify the optimal VSD implementation protocol. Fourth, the VSD system used in this study differs from standard NPWT (without irrigation) in two fundamental ways: it uses a central vacuum source (rather than a portable pump) and it incorporates continuous saline irrigation. Because our study did not include a control group receiving standard NPWT without irrigation, the specific contribution of the irrigation component cannot be isolated. Consequently, the findings of this study should not be directly generalized to standard NPWT (without irrigation) or to other NPWTi systems (e.g., VeraFlo™ with intermittent instillation-dwell). Our results apply specifically to continuous-irrigation VSD as defined above. Whether standard NPWT (no irrigation) would produce similar results remains unknown from this study. Fifth, although baseline comparisons showed no group differences in ulcer location and weight-bearing status, the potential interaction between VSD and off-loading remains unclear. For instance, VSD dressings may provide additional cushioning to plantar ulcers, indirectly enhancing the effects of prescribed off-loading devices (e.g., total contact casts). Conversely, if VSD was disproportionately applied to non-weight-bearing ulcers (despite balanced baseline proportions), the observed healing benefit might be partially attributed to reduced mechanical stress rather than negative pressure alone. Future studies should explicitly document ulcer location and quantify off-loading compliance to isolate the specific effects of VSD. Sixth, we used ABI as the primary non-invasive vascular screening tool. However, ABI is known to be unreliable in diabetic patients due to medial arterial calcification, which can produce falsely elevated values (≥ 1.3) and mask underlying ischemia. Moreover, we did not perform more advanced perfusion assessments such as transcutaneous oxygen pressure (TcPO₂) or skin perfusion pressure. Therefore, residual differences in tissue perfusion between groups cannot be completely excluded, even though ABI values were similar. This is an important limitation, as compromised perfusion is a key determinant of healing failure in DFU. Future prospective studies should incorporate laser Doppler flowmetry or oxygen saturation imaging for more precise perfusion assessment. Seventh, the limited sample size resulted in a low EPV ratio in the logistic regression model, which may increase the risk of overfitting. Therefore, the predictive model should be interpreted with caution and validated in larger cohorts. Finally, we did not perform a formal cost-effectiveness analysis, nor did we collect detailed resource utilization data (e.g., nursing time, number of dressing changes, outpatient visits) or patient-reported

outcomes on convenience, mobility limitation, or treatment burden. Therefore, we cannot comment on the economic value or the practical acceptability of VSD relative to conventional treatment. This is an important gap, as cost and patient convenience are major determinants of treatment adoption in routine practice.

Conclusion

In conclusion, this retrospective, single-center, non-randomized exploratory analysis observed associations between the use of a continuous-irrigation VSD protocol and modestly improved healing and infection-related outcomes in a selected cohort of Wagner grade 2–3 DFU patients. However, because of the observational design, the non-randomized treatment allocation, and the inherent risk of confounding by indication, these findings cannot establish causality and do not support a general recommendation for VSD over conventional treatment. The absolute clinical benefits were small—a 13% absolute increase in healing (NNT=8) and a 7-day reduction in median healing time—and must be interpreted in the absence of data on cost, patient convenience, mobility restriction, or treatment burden. Moreover, the results apply strictly to the specific continuous-irrigation VSD protocol used at this center and are not generalizable to standard NPWT without irrigation or to other NPWT with instillation systems. Given these substantial limitations, VSD should be considered only as an individualized adjunctive therapy within a multidisciplinary framework, with its use carefully weighed against its additional costs and patient burden on a case-by-case basis. Firm conclusions regarding its routine clinical application cannot be drawn from this study alone, and well-designed prospective randomized controlled trials are essential to confirm these exploratory observations and to identify which patient subgroups might derive the most benefit.

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Author contributions

Li Wang: Conceptualization, Formal analysis, Investigation. Xiaofeng Yang: Methodology, Formal analysis, Data Curation. Yingdong Tan: Conceptualization, Formal analysis, Data Curation. Zhihong Wang: Data Curation, Methodology, Writing—Original Draft.

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Data availability

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Declarations

Ethics approval and consent to participate

The study protocol has been reviewed and approved by the Medical Ethics Committee of Shanghai General Hospital Jiuquan Hospital (People's Hospital

of Jiuquan). The implementation of the study strictly adhered to the Declaration of Helsinki (revised in 2013), the Ethical Review Measures for Biomedical Research Involving Human Subjects, and other relevant medical ethics guidelines, ensuring the scientific integrity and ethical standards of the study. Given the retrospective design of this study, data were sourced from archived medical records of previous treatments at the hospital. No additional interventions were performed on patients, and all data extraction processes did not involve current patient care or rights. After approval by the ethics committee, the requirement for informed consent was waived.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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References

- Stone A, Donohue CM. Diabetic foot ulcers in geriatric patients. *Clin Geriatr Med*. 2024;40(3):437–47.
- Armstrong DG, Tan TW, Boulton AJM, et al. Diabetic foot ulcers: a review. *JAMA*. 2023;330(1):62–75.
- Rehman ZU, Khan J, Noordin S. Diabetic foot ulcers: contemporary assessment and management. *J Pak Med Assoc*. 2023;73(7):1480–7.
- Guo Q, Ying G, Jing O, et al. Influencing factors for the recurrence of diabetic foot ulcers: a meta-analysis. *Int Wound J*. 2023;20(5):1762–75.
- Sa B, Bermudez NM, Shimon SV, et al. Diabetic foot ulcers a review of debridement techniques. *Surg Technol Int*. 2024;44:31–5.
- Mohsin F, Javaid S, Tariq M, et al. Molecular immunological mechanisms of impaired wound healing in diabetic foot ulcers (DFU), current therapeutic strategies and future directions. *Int Immunopharmacol*. 2024;139:112713.
- Medeiros S, Rodrigues A, Costa R. Physiotherapeutic interventions in the treatment of patients with diabetic foot ulcers: a systematic literature review. *Physiotherapy*. 2023;118:79–87.
- JIMÉNEZ-GARCÍA JF, JIMÉNEZ-ABAD JF, LÓPEZ LA, et al. Diabetic foot ulcers: evaluating the role of the specialist advanced practice nurse in complex chronic wounds. *Br J Nurs*. 2024;33(15):S4–S15.
- Lu Y, Zhao D, Cao G, et al. Research progress on and molecular mechanism of vacuum sealing drainage in the treatment of diabetic foot ulcers. *Front Surg*. 2024;11:1265360.
- Zaver V, Marietta M, Kankanalu P. Negative pressure wound therapy. StatPearls. Treasure Island (FL). StatPearls Publishing Copyright © 2026, StatPearls Publishing LLC. 2026.
- Dalmedico MM, Do Rocio Fedalto A, Martins WA, et al. Effectiveness of negative pressure wound therapy in treating diabetic foot ulcers: a systematic review and meta-analysis of randomized controlled trials. *Wounds*. 2024;36(8):281–9.
- Wu Y, Shen G, Hao C. Negative pressure wound therapy (NPWT) is superior to conventional moist dressings in wound bed preparation for diabetic foot ulcers: a randomized controlled trial. *Saudi Med J*. 2023;44(10):1020–9.
- Widigdo DAM, Sofro ZM, Pangastuti HS, et al. The efficacy of negative pressure wound therapy (NPWT) on healing of diabetic foot ulcers: a literature review. *Curr Diabetes Rev*. 2024;20(8):1–11.
- Arundel C, Mandefield L, Fairhurst C, et al. Negative pressure wound therapy versus usual care in patients with surgical wound healing by secondary intention in the UK (SWHSI-2): an open-label, multicentre, parallel-group, randomised controlled trial. *Lancet (London, England)*. 2025;405(10490):1689–99.
- Melamed E, Dabbah J, Israel T, et al. Noninferiority of copper dressings than negative pressure wound therapy in healing diabetic wounds: a randomized clinical trial. *Adv Wound Care*. 2025. <https://doi.org/10.1089/wound.2024.0273>.

16. Senneville É, Albalawi Z, VAN Asten SA, et al. IWGDF/IDSA guidelines on the diagnosis and treatment of diabetes-related foot infections (IWGDF/IDSA 2023). *Diabetes Metab Res Rev.* 2023;40(3):e3687.
17. Wagner FW. The dysvascular foot: a system for diagnosis and treatment. *Foot Ankle.* 1981;2(2):64–122.
18. Melzack R. The short-form McGill pain questionnaire. *Pain.* 1987;30(2):191–7.
19. Tsui FPY, Wong SSC, Chan TCW, et al. A validation study of the Cantonese Chinese version of short form McGill pain questionnaire 2 in Cantonese-speaking patients with chronic pain in Hong Kong. *Pain Pract.* 2024;24(3):449–57.
20. Yin XL, Hu L, Li T, et al. A meta-analysis on the efficacy of vacuum sealing drainage combined with autologous platelet-rich plasma in the treatment of grade 2 and grade 3 diabetic foot ulcers. *Int Wound J.* 2023;20(4):1033–41.
21. Xu J, Hua Y, Lei J, et al. Effects of skin flap grafting combined with vacuum sealing drainage on ulcer area, pain level, and serum inflammation in diabetic foot patients. *Am J Transl Res.* 2023;15(12):6939–48.
22. Chen Q, Lu M, Liu X, et al. Comparison of customized vacuum sealing drainage and vacuum sealing drainage in the treatment of diabetic foot ulcers: a retrospective analysis. *J Orthop Surg Res.* 2023;18(1):803.
23. Zhong M, Guo J, Qahar M, et al. Combination therapy of negative pressure wound therapy and antibiotic-loaded bone cement for accelerating diabetic foot ulcer healing: a prospective randomised controlled trial. *Int Wound J.* 2024;21(10):e70089.
24. Gu H, Zhao X, Sun Y, et al. Negative-pressure wound therapy compared with advanced moist wound therapy: a comparative study on healing efficacy in diabetic foot ulcers. *Surgery.* 2025;180:109098.
25. Yammine K, Abdallah R, Stiban S, et al. Monitoring negative pressure wound therapy for diabetic foot ulcers using WhatsApp. *J Tissue Viability.* 2024;33(1):1–4.
26. Suludere MA, Malone M, Siah MC, et al. The infected diabetic foot: does negative pressure wound therapy with irrigation reduce bioburden and improve wound healing? *Int J Low Extrem Wounds.* 2024. <https://doi.org/10.1177/15347346241292125>.
27. Angulo AR, Caballero-Alvarado J, Sarmiento-Falen J, et al. Comparative assessment of negative pressure wound therapy versus standard treatment in diabetic foot ulcers: a systematic review and meta-analysis. *J Wound Ostomy Contin Nurs.* 2025;52(3):227–38.
28. Sano H, Ichioka S. Involvement of nitric oxide in the wound bed microcirculatory change during negative pressure wound therapy. *Int Wound J.* 2015;12(4):397–401.
29. Ghasemi A, Kashfi K, Bahadoran Z. The role of nitric oxide in type 2 diabetes. Bentham Science Publishers; 2022.
30. Tang Y, Ji H, Yan Y, et al. Enhancing diabetic foot ulcer healing: impact of the regulation of the FUS and ILF2 RNA-binding proteins through negative pressure wound therapy. *Int J Mol Med.* 2024;54(5):103.
31. Kadavan RA, Deans N, Punnackal Joseph R, et al. Unlocking the potential of negative pressure wound therapy in diabetic foot ulcers: a systematic review and meta-analysis. *Cureus.* 2025;17(11):e96474.
32. Huang Y, Yu Z, Xu M, et al. Negative pressure wound therapy promotes wound healing by down-regulating miR-155 expression in granulation tissue of diabetic foot ulcers. *Sci Rep.* 2025;15(1):6733.
33. Villalba-Aguilar C, Laredo-Aguilera JA, Villalba-Aguilar L, et al. Comparative efficacy of negative pressure wound therapy and conventional treatments in the management of diabetic foot ulcers: a systematic review and meta-analysis. *J Clin Med.* 2025. <https://doi.org/10.3390/jcm14228051>.
34. Tarricone A, Crisologo A, Killeen A, et al. Pooled study-level analysis of randomized controlled trials analyzing the effect of negative pressure wound therapy with irrigation vs traditional negative pressure wound therapy on diabetic foot outcomes. *Wounds.* 2023;35(4):66–70.

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