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Original Article

Effects of skin flap grafting combined with vacuum sealing drainage on ulcer area, pain level, and serum inflammation in diabetic foot patients

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Abstract: Objective: To study the effects of skin flap grafting combined with vacuum sealing drainage (VSD) on ulcer area, pain level and serum inflammation in patients with diabetic foot (DF). Methods: In this retrospective study, 121 patients with DF who were treated in the Affiliated Hospital of Xinyang Vocational and Technical College between April 2018 and April 2022 were included as study subjects, including 50 cases receiving skin flap grafting (control group) and 71 cases receiving skin flap grafting combined with VSD (research group). Information on clinical efficacy, survival rate of the grafted flap, amputation and complications, ulcer area, rehabilitation (granulation tissue formation time, ulcer wound healing time), pain level (Visual Analogue Scale [VAS]), and serum inflammatory factors (interleukin [IL]-6, tumor necrosis factor [TNF]-α, and C-reactive protein [CRP]) were collected for comparative analyses. Univariate and multivariate analyses were conducted to screen the risk factors for patients' prognosis. Results: The overall response rate and the survival rate of the grafted flap in the research group were markedly higher compared with the control group, while the amputation rate was significantly lower (all $P<0.05$). Besides, the research group exhibited an evidently smaller post-treatment ulcer area, lower VAS, IL-6, TNF-α and CRP levels, and shorter granulation tissue formation time and ulcer wound healing time than the control group (all $P<0.05$). Neither group of patients experienced significant complications. The use of skin flap grafting + VSD was a protective factor for postoperative outcome. Conclusions: Skin flap grafting combined with VSD is effective in treating DF patients, which can validly reduce ulcer area and inhibit serum inflammation after treatment, thus accelerating rehabilitation.

Keywords: Skin flap grafting, vacuum sealing drainage, diabetic foot, ulcer area, serum inflammation

Introduction

Diabetes mellitus (DM), a chronic endocrine system disorder strongly linked to abnormal hyperglycemia, can damage blood vessels, kidneys, nerves and retina to varying degrees, triggering a series of complications [1]. Diabetic foot (DF) is one of the most serious DM-induced complications, which is associated with structural or functional abnormalities of the foot due to diabetic neuropathy and peripheral vascular diseases [2]. DF is clinically manifested with ulcers, pain, infection, gangrene, etc., accompanied by decreased sensitivity to temperature, vibration, and superficial touch, which may lead to hospitalization or amputation that restrains daily life [3-5]. Moreover, DF ulcers, as a serious clinical symptom of DF, can increase the ulcer area of the limbs and elevate the risk of invasive infection [6]. The pathological mechanism of DF is closely related to serum inflammation, with a persistent inflammatory reaction that interfere with wound healing and cause disease deterioration [7]. This study seeks to find more effective approaches to enhance the treatment efficacy in patients with DF and alleviate their clinical symptoms and improve mobility.

Skin flap grafting, a key surgical technique commonly used to repair skin damage, can be applied to clinical scenarios such as trauma repair, tumor resection, and foot ulcer treatment [8-10]. In the research of Yang L et al. [11],

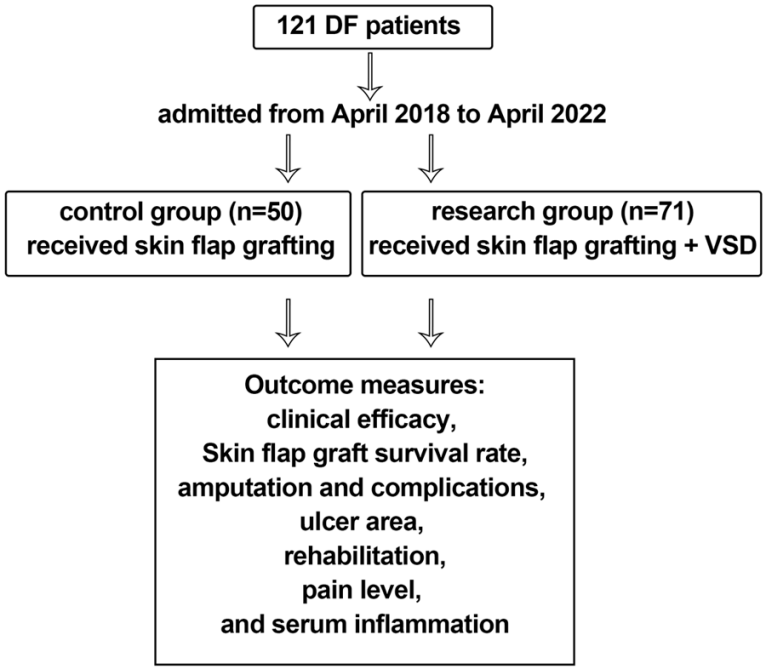

Figure 1. Flowchart of the study. DF, diabetic foot; VSD, vacuum sealing drainage.

the application of skin flap grafting in the treatment of Wagner grade 3 and 4 DF has achieved favorable effects, shortened course of disease, and improved local blood flow of patients, suggesting certain therapeutic value of this technique in DF. However, this procedure also comes with problems such as inadequate preoperative infection control and ulcer debridement that can lead to decreased survival of the grafted flap and poor wound healing, which limits its application and inversely impact the treatment effect to a certain extent [12, 13]. Vacuum sealing drainage (VSD) is a treatment to promote wound healing by applying negative pressure to the wound surface, which has the advantages of non-invasiveness, easy application, and high drainage efficiency [14]. It has a good therapeutic effect on skin and soft tissue defects in the elderly with bone exposure, which increases the survival rate of skin grafting while speeding up wound healing [15]. In addition, it has good application value in necrotizing fasciitis, shortening wound healing time and reducing the frequency of dressing change while being cost-effective [16]. Previous randomized controlled clinical studies have also demonstrated significant clinical advantages of VSD in DF, such as improving wound healing rate and reducing amputation risk [17, 18].

At present, there are few relevant studies on the clinical effects of skin flap grafting combined with VSD in DF patients, mainly focusing on the use of flap grafting or VSD as a single intervention in the treatment of DF, with limited clinical indicators analyzed or sample size. Therefore, it is necessary to verify the clinical advantages of this treatment mode from the perspective of clinical efficacy, survival of the grafted flap, ulcer area, pain level and serum inflammation to provide a better choice for DF patients, which is also the novelty of this research.

Materials and methods

General information

This retrospective study selected 121 DF patients who were treated in the Affiliated Hospital of Xinyang Vocational and Technical College between April 2018 and April 2022 as the research participants. The control group (n = 50) received skin flap grafting, and the research group (n = 71) received skin flap grafting plus VSD. The two groups were clinically comparable without notable differences in general data (P>0.05). This research was ratified by the hospital's ethics committee. **Figure 1** displays the flow chart of this study.

Criteria for patient enrollment and exclusion

Inclusion criteria: In accordance with the diagnostic criteria for DF; single foot lesions; no contraindications to skin flap grafting or VSD; age ≥18; normal communication and cognitive abilities; complete case data and evaluation results of relevant outcome measures after receiving appropriate treatment; willingness to cooperate with the research.

Exclusion criteria: Acute phase of cardio-cerebrovascular events; poor physical condition and intolerance to surgical treatment; cardiopulmonary insufficiency or severe liver and kidney function damage; immune system disor-

ders; foot ulcers caused by other factors; use of other treatment schemes before enrollment; mental disorders; defective clinical data.

Data collection

Preoperative data of eligible patients, including age, gender, age, BMI, course of disease, ulcer site (pelma, toe, acrotarsium), education level (below high school, high school and above), smoking and drinking history were collected from the patient records.

Postoperative data, comprising the occurrence of the adverse events, ulcer area, the amputation rate, serum inflammation index levels, were also extracted.

Treatment methods

All patients received routine hypoglycemic therapy to control their postprandial blood glucose within 6-10 mmol/L and the fasting blood glucose within 5-7 mmol/L. Wound exudate was collected for bacterial culture and susceptibility testing, based on which targeted treatment was administered to control local infection. In addition, the wound was disinfected, and the necrotic tissue and pus were removed. The wound was then repeatedly rinsed with normal saline, coated with an appropriate amount of povidone iodine cream, and covered with sterile gauze. The frequency of dressing change was once a day.

The control group received skin flap grafting. Patients underwent pedicled perforator flap grafting when fresh granulation tissue was observed. On this basis, VSD was given to patients in the research group. After debridement, the skin surrounding the ulcer was disinfected and cleaned using 75% alcohol, and the wound was rinsed with 0.9% sodium chloride. A VSD dressing, prepared according to the size of the wound, was placed over the ulcer surface, and a drainage tube was placed at the ulcer site. After wiping the area around the wound with sterile gauze, the dressing and the entire wound were closed with a semipermeable biofilm covering a range of more than 3 cm from the wound edge. Continuous negative pressure suction was then performed, with the suction tube attached to the dressing silicone tube and the central negative pressure suction device, respectively, to ensure a negative pressure between 125 and 450 mmHg. Obvious collapse of the biofilm and dressing indicated a favorable sealing effect. The dressing was removed a week after the procedure and the growth of granulation tissue was closely observed for 2 weeks.

Outcome measures

(1) Clinical efficacy. The response was assessed before and 4 weeks after treatment. Cure: most or complete healing of the wound after treatment, with no significant inflammatory response around the ulcer and the presence of fresh granulation tissue formation. Significant effectiveness: the formation of fresh granulation tissue and about 25-50% residual wound area. Effectiveness: visible scar tissue, no local formation of fresh granulation tissue on the wound, slight inflammatory reaction, and deep and large residual wound with an area of about 25%-50% of that before treatment. Ineffectiveness: no fresh granulation tissue formed in and around the wound surface nor no significant change in the size of the wound surface, with symptoms such as exudation and necrosis in the local area and redness and swelling in the surrounding area, even showing a trend of aggravation. The total effective rate = (cure cases + significant effectiveness cases + effectiveness cases)/total cases *100%.

(2) Incidence of adverse events. The incidence of amputation and complications in the two groups were observed 4 weeks after treatment.

(3) Ulcer area. The ulcer surface was photographed with a camera before and one and two weeks after treatment, and the images were imported into a computer to calculate the ulcer area using the graphic calculation software.

(4) Rehabilitation. The granulation tissue formation time and ulcer wound healing time of both groups were recorded 4 weeks after treatment.

(5) Pain level. Visual Analogue Scale (VAS; score range: 0-10) was used to evaluate the degree of patients' pain before and 4 weeks after treatment. The score was proportional to the pain degree.

(6) Serum inflammation. Before and 4 weeks after treatment, venous blood was collected

Table 1. General information of the two groups

	Control group (n = 50)	Research group (n = 71)	χ^2/t value	*P* value
Age (years)	53.22±7.33	55.54±10.24	1.373	0.172
Sex			0.602	0.438
Male	31 (62.00)	39 (54.93)		
Female	19 (38.00)	32 (45.07)		
Disease course (year)	2.84±0.62	2.94±0.81	0.734	0.464
BMI (kg/m^2)	22.38±2.59	22.52±2.77	0.281	0.779
Ulcer site			0.693	0.707
Pelma	28 (56.00)	35 (49.30)		
Toe	11 (22.00)	20 (28.17)		
Acrotarsium	11 (22.00)	16 (22.54)		
Educational level			0.009	0.754
Below high school	31 (62.00)	46 (64.79)		
High school and above	19 (38.00)	25 (35.21)		
Smoking history			2.922	0.087
Yes	20 (40.00)	18 (25.35)		
No	30 (60.00)	53 (74.65)		
Alcoholism history			3.245	0.072
Yes	22 (44.00)	20 (28.17)		
No	28 (56.00)	51 (71.83)		

Note: BMI, body mass index.

from both groups and then centrifuged to collect serum to quantify interleukin (IL)-6, tumor necrosis factor (TNF)-α, and C-reactive protein (CRP) using enzyme-linked immunosorbent assays (ELISAs). The operation process was carried out strictly following the corresponding ELISAs kit (Amyjet Scientific Inc., RD194015200R, 3512-1HP-DP-1, and 3512-1HP-DP-1).

Clinical efficacy, ulcer area, pain level, and serum inflammation were the primary outcome measures of this study, while the incidence of adverse events and rehabilitation indicators were secondary measures.

Statistical analysis

The mean ± standard error of mean was used for statistical description of measurement data, whose inter-group and within-group (before and after treatment) comparisons were made by independent samples t tests and paired-sample t tests, respectively. As to counting data, they were represented by the percentage (%) and compared between groups by the χ^2 test. Statistical software SPSS 18.0 was used for data analysis. P<0.05 was considered with statistical significance.

Results

General information

The research and control groups exhibited no notable differences in age, sex, disease course, body mass index (BMI), ulcer site, educational level, and history of smoking and alcoholism, indicating the two groups were clinically comparable (all P>0.05, **Table 1**).

Clinical efficacy

The clinical efficacy was assessed to compare the effects of the two treatments on the clinical effectiveness of DF patients. The analysis showed that the total effective rate was 88.73% in the research group and 74.00% the control group, suggesting markedly higher clinical effectiveness of skin flap grafting plus VSD versus skin flap grafting alone (P = 0.035). On the other hand, we analyzed the success of skin flap grafting through calculating the survival rate of the grafted flap. The data showed a markedly higher overall survival rate of the grafted flap in the research group versus the control group (92.96% vs. 70.00%, P<0.001; **Tables 2**, **3**).

Table 2. Clinical efficacy of the two groups

	Cure	Significant effectiveness	Effectiveness	Ineffectiveness	Total effective rate
Control group (n = 50)	6 (12.00)	16 (32.00)	15 (30.00)	13 (26.00)	37 (74.00)
Research group (n = 71)	15 (21.13)	30 (42.25)	18 (25.35)	8 (11.27)	63 (88.73)
χ^2					4.440
P value					0.035

Table 3. Survival rate of the grafted flaps in both groups

	Complete survival	Partial survival	Complete necrosis	Total
Control group (n = 50)	8 (16.00)	27 (54.00)	15 (30.00)	35 (70.00)
Research group (n = 71)	21 (29.58)	45 (63.38)	5 (7.04)	66 (92.96)
χ^2				11.210
P value				<0.001

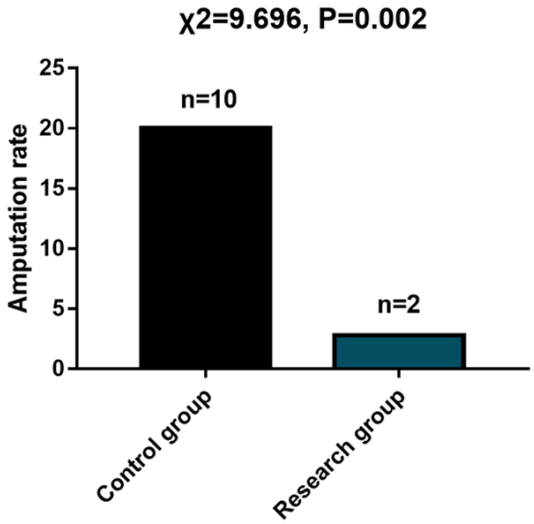

Figure 2. Comparison of the amputation rate between two groups.

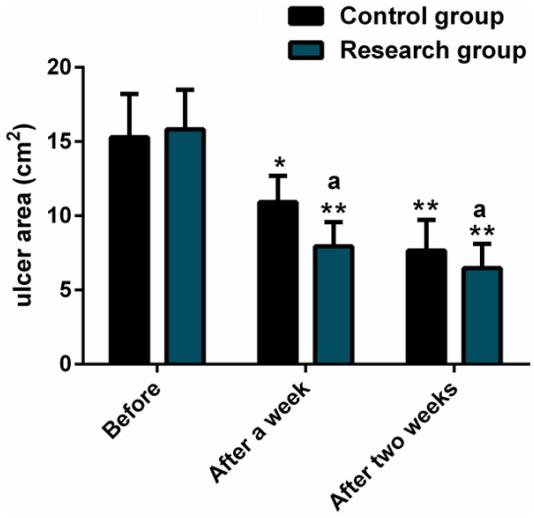

Figure 3. Ulcer area of two groups. *P<0.05 and **P<0.01 vs. before treatment; [a]P<0.05 vs. control group.

Incidence of adverse events

As shown in **Figure 2**, statistics on amputation and complications revealed a lower amputation rate in the research group compared with the control group (2.82% vs. 20.00%, P = 0.002); while neither group of patients experienced significant complications during treatment.

Ulcer area

The ulcer area of both groups before and one and two weeks after treatment were detected to comparatively analyze the influence of the two treatments on the ulcer area of DF patients. The ulcer area of the control group before treatment as well as one week and two weeks after treatment was (15.15±3.0) cm^2, (10.92±1.77) cm^2, and (7.66±2.06) cm^2, respectively, compared with (15.84±2.7) cm^2, (7.94±1.64) cm^2, and (6.48±1.62) cm^2 respectively in the research group. The analysis showed no significant inter-group difference in the ulcer area prior to treatment (P>0.05). Significantly reduced ulcer areas were observed in both groups at one and two weeks after treatment (all P<0.05), with an even smaller ulcer area in the research group (P<0.05), see **Figure 3**.

Rehabilitation

By detecting the granulation tissue formation time and ulcer wound healing time, the effects

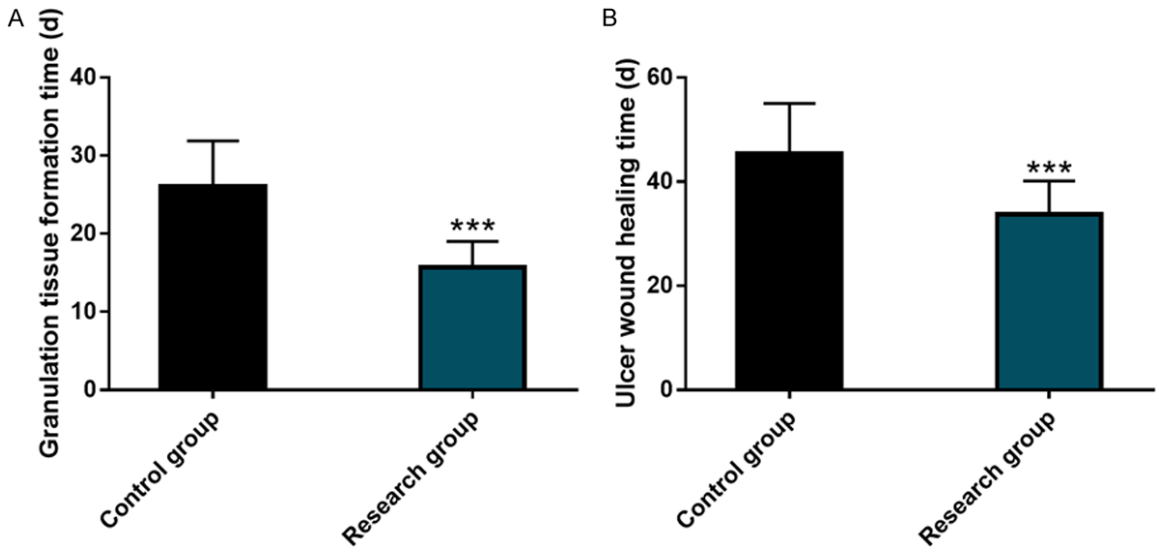

Figure 4. Rehabilitation of the two groups. A. The research group had significantly shorter granulation tissue formation time than the control group after treatment. B. The research group had significantly shorter ulcer wound healing time than the control group after treatment. Note: ***P<0.001 vs. before treatment.

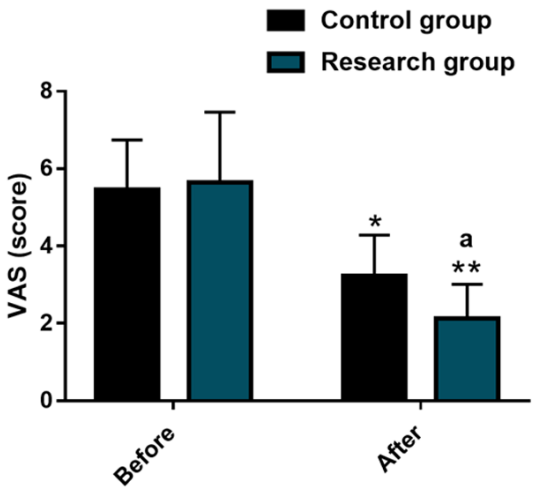

Figure 5. Pain levels of the two groups. *P<0.05 and **P<0.01 vs. before treatment; [a]P<0.05 vs. control group. VAS, Visual Analogue Scale.

of two treatments on DF patients' rehabilitation were analyzed. In the control and research groups, the granulation tissue formation time was (26.04±5.83) d and (15.69±3.34) d, respectively, and the ulcer wound healing time was (45.34±9.66) d and (33.72±6.42) d, respectively. The analysis showed the research group experienced shorter granulation tissue formation time and wound healing time than the control group (both P<0.001, **Figure 4**).

Pain level

The pain level was detected by the VAS to evaluate the influence of two treatment modalities on the pain degree of DF patients. The pre- and post-treatment VAS scores of the control group were (5.46±1.28) points and (3.22±1.06) points, respectively, versus (5.65±1.81) points and (2.13±0.88) points in the research group, respectively. The analysis showed no significant difference in pre-treatment VAS scores between the two groups (P>0.05); but the VAS score of both groups decreased significantly after treatment (both P<0.05), with an even lower score in the research group (P<0.05), as shown in **Figure 5**.

Serum inflammation

Serum inflammatory factors, such as IL-6, TNF-α, and CRP, were detected by ELISA to evaluate the effects of two treatments on serum inflammation in DF patients. The pre-treatment IL-6 levels of the control and research groups were (46.06±7.75) ng/L and (48.06±7.43) ng/L, respectively, while the IL-6 post-treatment levels were (27.24±4.97) ng/L and (17.96±3.75) ng/L, respectively. The pre- and post-treatment TNF-α of the control group were (56.24±7.05) ng/L and (29.01±5.93) ng/L, respectively, versus (57.36±9.4) ng/L and (21.90±3.81) ng/L in the research group, respectively. The pre-

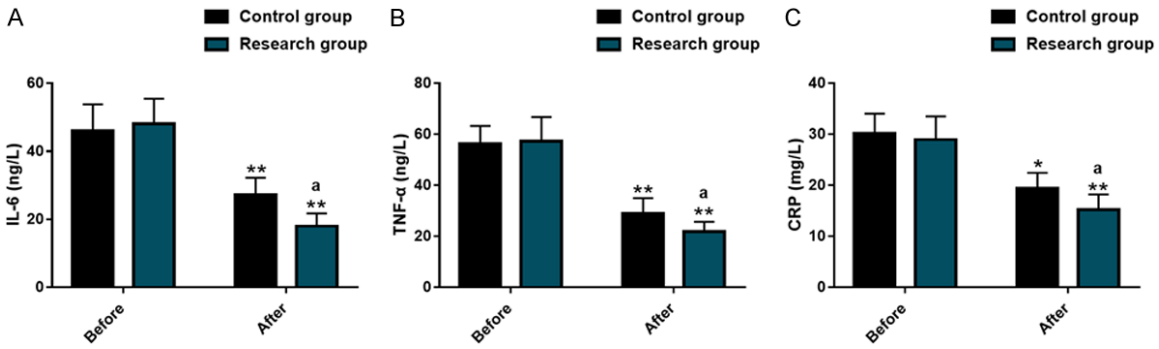

Figure 6. Serum inflammation in two groups. A. The research group had markedly lower IL-6 than the control group after treatment. B. The research group had markedly lower TNF-α than the control group after treatment. C. The research group had markedly lower CRP than the control group after treatment. Note: *P<0.05 and **P<0.01 vs. before treatment; [a]P<0.05 vs. control group. IL-6, interleukin-6; TNF-α, tumor necrosis factor-α; CRP, C-reactive protein.

Table 4. Univariate analysis of factors affecting treatment effectiveness

	Effectiveness (n = 100)	Ineffectiveness (n = 21)	χ^2/t value	*P* value
Age (years)	54.61±8.93	54.43±10.58	0.081	0.935
Sex				
Male	56 (56.00)	14 (66.67)	0.810	0.368
Female	44 (44.00)	7 (33.33)		
Disease course (year)	2.89±0.74	2.95±0.74	0.338	0.736
BMI (kg/m^2)	22.39±2.59	22.80±3.17	0.633	0.528
Ulcer site			0.808	0.668
Pelma	53 (53.00)	10 (47.62)		
Toe	24 (24.00)	7 (33.33)		
Acrotarsium	23 (23.00)	4 (19.05)		
Ulcer area before surgery (cm^2)	15.37±2.76	16.69±2.62	2.009	0.047
Surgical approach			4.440	0.035
Skin flap grafting	37 (37.00)	13 (61.90)		
Skin flap grafting + VSD	63 (63.00)	8 (38.10)		

Note: BMI, body mass index; VSD, vacuum sealing drainage.

treatment CRP levels were (30.18±3.86) mg/L and (28.94±4.57) mg/L respectively in the control group and the research group, and (19.41±3.04) mg/L and (15.22±3.00) mg/L after treatment. No statistical inter-group differences were found in these indexes before treatment (all P>0.05). All these indexes were inhibited to varying degrees after treatment (all P<0.05), with even lower levels of them in the research group (all P<0.05), as shown in **Figure 6**.

Univariate and multivariate analyses of factors affecting the treatment effectiveness

Univariate analysis showed that ineffective patients had larger preoperative ulcers (with 15.4 cm^2, the median preoperative ulcer area, as the threshold), and there was a significant difference the surgical approach (**Table 4**). These two items were included in the multifactorial analysis. Logistic multivariate analysis showed that the surgical approach was an independent predictor of treatment efficacy and the use of skin flap grafting + VSD was a protective factor for treatment effectiveness (**Table 5**).

Discussion

This study comparatively analyzes the clinical effects of skin flap grafting + VSD versus simple skin flap grafting in DF, confirming that the combination therapy has more significant clinical advantages in DF treatment.

Table 5. Multivariate analysis of factors affecting treatment effectiveness

	Assignment	β	SE	Wald	*P* value	HR	95% CI
Constant		1.761	0.403	19.111	0.000	5.821	-
Ulcer area before surgery	0 = ≤15.4 cm^2; 1 = >15.4 cm^2	0.883	0.522	2.868	0.090	2.419	0.870~6.725
Surgical approach	0 = Skin flap; 1 = Skin flap grafting + VSD	-1.220	0.519	5.532	0.019	0.295	0.107~0.816

Note: VSD, vacuum sealing drainage.

In this study, the total effective rate and the survival rate of the grafted flap were significantly higher in the research group than the control group (88.73% vs. 74.00%, 92.96% vs. 70.00%), suggesting that skin flap grafting + VSD is more effective than skin flap grafting alone in treating DF, actively accelerating the formation of fresh granulation tissue. The skin flap grafting plus VSD scheme has the following advantages: 1) It isolates the wound from the outside by means of the semi-permeable biofilm sealing, reducing the risk of external bacterial infections; 2) The continuous negative pressure suction can remove tiny necrotic tissues and exudates generated on the wound surface, which is conducive to keeping the wound surface clean, and exerting a certain inhibitory effect on the reabsorption of toxic products [19, 20]. In the research of Shi L et al. [21], anterolateral thigh perforator flap plus VSD has achieved 100% skin flap survival in 12 patients with DF ulcers and successfully achieved wound repair, with higher appearance satisfaction among patients, which is similar to our findings.

In the analysis of the incidence of amputation and complications in the two groups, it was found that the amputation rate was significantly lower the research group compared with the control group (2.82% vs. 20.00%), with significant complications found in neither groups during treatment, suggesting that skin flap grafting + VSD has certain safety and can significantly reduce the risk of amputation in patients.

By comparing the ulcer area, it was found that the area was markedly reduced in the research group at one and two weeks after treatment, smaller than the pre-treatment area and that of the control group, suggesting the high efficacy of skin flap grafting plus VSD in reducing the ulcer area.

Furthermore, significantly shorter granulation tissue formation time and ulcer healing time were observed in the research group, indicating the ability of skin flap grafting plus VSD to effectively accelerate granulation tissue formation and promote ulcer wound healing in DF patients. This may be related to the active drainage of the wound exudate with vacuum sealing drainage, which promotes local blood circulation and stimulates wound tissue regeneration, thus facilitating the formation of fresh granulation tissue and promoting ulcer wound healing [22, 23]. Dong B et al. [24] also pointed out that VSD intervention is beneficial to accelerate ulcer healing in patients with ischemic DF ulcers, consistent with our observations.

The VAS score results suggested that the skin flap grafting plus VSD protocol used in the research group had a significant advantage in pain relief, which is mainly reflected in markedly lower post-treatment VAS scores than the control group. This may be attributed partially to the prolonged dressing change time under the combined treatment, which avoids the influence of frequent dressing changes on the formation of fresh granulation tissue, thus relieving pain to a certain extent [25]. Qiu L et al. [26] also confirmed that VSD significantly reduced patient pain in the treatment of acute suppurative mastitis, which supports our research results.

After ELISA quantification of serum inflammatory factors, IL-6, TNF-α and CRP levels were found to be markedly reduced in the research group after treatment, lower than those of the control group, suggesting that skin flap grafting + VSD has a more significant inhibitory effect on serum inflammatory responses than skin flap grafting alone, similar to the research results of Shi X et al. [27].

There are several limitations of this study that need to be further considered and addressed. First, this study is a single centered study with a relatively limited sample range, which may result in information collection bias. Second, studies on the long-term efficacy and prognosis

have not been carried out. Subsequent analysis of this aspect will be conducive to exploring the potential value of skin flap grafting plus VSD in the clinical application of DF for long-term efficacy and prognosis improvement. These are also the key research directions in the future and will be gradually improved.

Collectively, skin flap grafting combined with VSD is more effective than simple skin flap grafting intervention in treating DF patients, which can effectively reduce the amputation risk, pain, and ulcer area and accelerate granulation tissue formation and ulcer wound healing while significantly inhibiting serum inflammation, with clinical promotion value.

Disclosure of conflict of interest

None.

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