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Effects of negative pressure wound therapy on graft success in patients with diabetic foot ulcers: A retrospective study

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Abstract

Aim: One of the technological advances in wound healing is negative pressure wound therapy (NPWT). NPWT is frequently used in acute and chronic wound care. However, few studies in the literature have investigated the effects of NPWT on the graft in patients with diabetic foot ulcers. In this study, we aimed to assess the effects of applying negative pressure wound closure on grafts and its influence on. The healing time indiabetic foot ulcers and thus contribute to the literature by sharing our experience.

Materials and Methods: We retrospectively evaluated patients who had received treatment for diabetic foot ulcers in the chronic wound care unit of our hospital between February 2018 and October 2021 and underwent split-thickness skin grafting. The patients were categorized into two groups: those who did and did not receive NPWT to provide support for the graft. The patients were compared in terms of wound healing rates and healing times.

Results: The study included 34 men (56.7%) and 26 women (43.3%) (n = 60). The mean age of the patients was 62.07 ± 11.5 years. Supportive NPWT was performed on the graft in 19 (31.7%) patients, whereas 41 (68.3%) patients were treated with grafting and conventional therapy. The treatment duration was shorter in the NPWT group (29.63 ± 19.6 days) than in the non-NPWT group (34.05 ± 17.5 days); however, this difference was not significant ($p > 0.05$). A significant weak positive correlation ($r = 0.28$) was observed between the Wagner stage and treatment duration.

Conclusion: The treatment of diabetic foot ulcers is affected by several factors, including the presence of infection, vascularization status, wound size, and glycemic control. In this study, we examined a general patient population with diabetic foot ulcers and identified no significant difference in terms of treatment times and healing rates between NPWT and conventional methods as graft-supporting measures.

Prospective studies investigating patient populations comprising subgroups may yield varying results, which emphasizes the need for further research in this direction.

Introduction

Diabetic foot ulcers are a common complication of diabetes, with an annual incidence of approximately 2.0%–2.5% in Western countries [1]. Diabetic foot ulcers and infections are the long-term complications of diabetes responsible for most hospitalizations, accounting for approximately half of all diabetes-related hospitalizations [2]. Up to 25% of the annual expenditure on diabetic patient care is directly attributable to complications such as foot ulcers, infections, and amputations [3].

The use of negative pressure to aid wound closure was described in the 1990s. Subatmospheric pressures applied to the wound are known to reduce edema, enhance local blood flow, and increase granulation tissue [4]. Negative pressure can be used for acute, chronic, and subacute wounds; additionally, negative pressure wound therapy (NPWT) accelerates healing and reduces complications in chronic wounds [5,6].

The use of various treatments, including drainage, debridement, revascularization, NPWT, growth factors, platelet-rich plasma, and skin grafting, has been reported in the management of diabetic foot ulcers [7–11]. Although the standard treatment of diabetic foot ulcers includes establishing glycemic control, wound debridement, and the use of topical agents to combat infections, many authors have

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reported relatively better healing rates and shorter healing times with split-thickness skin grafting [12–14]. NPWT is effective, safe, and economical in the treatment of diabetic foot ulcers [15]. The application of NPWT on the graft has been investigated in various patient populations (patients with burns and traumatic wounds) [15,16]. However, studies specific to the population of patients with diabetic foot ulcers are limited [17].

This study aimed to examine the impact of applying NBMT on grafts and its effect on the healing time in patients with diabetic foot ulcers, an area that has been sparsely explored in the existing literature. Additionally, we sought to share our experience in this regard.

Materials and Methods

The approval of the local ethics committee (Kahramanmaraş Sütçü İmam University Medical Research Ethics Committee, Date: 17.5.2022, session no: 2022/16, Decision no: 07) was obtained for this study. Subsequently, data were obtained from hospital digital records, patient files, and operation books by conducting a retrospective analysis of patients who underwent split-thickness grafting for diabetic foot ulcers between February 2018 and October 2021.

The H0 hypothesis was accepted when there was no difference in treatment duration between patients who underwent NBMT and those who did not, and the H1 hypothesis was accepted when there was a difference in treatment duration between patients who underwent NBMT and those who did not. The independent variable in this study was the status of NBMT on the graft, whereas the dependent variable was the duration of treatment. Patients with diabetes mellitus who had lower extremity wounds requiring surgical intervention and underwent grafting were included in the study. A nonsampling approach was employed in our study, and all patients who underwent split-thickness grafting for diabetic foot ulcers in the specified period were consecutively enrolled. Patients aged <18 years who underwent previous surgical interventions, such as grafting or flap surgery, and those with missing data were excluded. Based on the study conducted by Petkar et al., an effect size of 1.6 was calculated using the G Power 3.1.9.7 program, which indicated a large effect size. Considering an α error of 0.05 and a power of 0.80 with a smaller effect size of 0.94 compared with the reference study (where n1 + n2 = 19 + 19), the estimated sample size was determined to be 38 [18].

Demographic data, such as age, sex, and laboratory values (hemoglobin, white blood cell (WBC) count, albumin, glycated hemoglobin, C reactive protein (CRP), and erythrocyte sedimentation rate), were recorded on admission. The wounds were evaluated in terms of size, presence of infection, Wagner stage, presence of flow in the dorsalis pedis artery on Doppler ultrasonography (DUSG), and healing time. The healed wound was defined as re-epithelialized skin that did not require dressing. Wound size, healing times, and healing rates were determined according to clinical notes and clinical images. Wound healing was classified as poor if graft uptake was <50%, as moderate if it was 50%–75%, and as good if it was >75%. Patients who required debridement at diagnosis underwent the process, revascularization procedures were performed when deemed necessary, and all patients with an infection and discharge underwent NPWT before grafting. The treatment period was considered as the time from graft application to healing. All patients underwent grafting. NPWT was performed by applying 80 mmHg negative pressure on the graft, which was checked every 4 days. The procedure was performed by a single surgeon, and the subsequent healing process was monitored by the same surgeon. Some of the patients received NPWT to support the graft, whereas others underwent dressing using conventional dressing materials without the application of negative pressure.

Patients were categorized into two groups: those who underwent NPWT over the graft (NPWT+) and those who were treated with conventional dressing materials without performing NPWT over the graft (NPWT−).

Statistical analysis

For statistical analysis of the study data, the trial version of the Statistical Package for Social Sciences (SPSS Inc., Chicago, IL, version 25.0) was utilized. umerical data were expressed as mean ± standard deviation (minimum–maximum data), and categorical data were expressed as number (n) and percentage (%). The conformity of the patients' data to normal distribution was evaluated using the Kolmogorov–Smirnov test. Student's t-test was used to analyze numerical data with normal distribution, and Mann–Whitney U test was used to analyze data without normal distribution. Chi-square test or Fisher's exact test was used to compare categorical data; chi-square trend analysis was used to evaluate the relationship between the wound size and the tendency to use NPWT. The relationship between the Wagner stage and the treatment duration was tested via correlation analysis. In the evaluation of statistical difference, $p<0.05$ indicated statistical significance.

Results

The study included 34 men (56.7%) and 26 women (43.3%) (n = 60). The mean age of the patients was 62.07 ± 11.5 years. Supportive NPWT was performed over the graft in 19 (31.7%) patients, whereas 41 (68.3%) patients underwent grafting and received conventional wound dressing.

Hypertension was the most common comorbidity, and five patients had a history of previous amputation owing to diabetic foot ulcer. The distribution of patient demographic data and response levels to the treatment are summarized in Table 1.

The classification of the wounds according to the Wagner classification is presented in Table 2, and the most populated group with a rate of 46.6% was Wagner Grade 3 patients.

Duration of diabetes, onset of complaints, duration of treatment, and wound sizes are summarized in Table 3, and the mean follow-up period was 6.0 ± 3.3 weeks.

The laboratory values of the patients on admission are summarized in Table 4.

In terms of the response to therapy, the healing was good in 35% (21) and moderate in 65% (39) of the patients. No complications related to NPWT occurred.

Table 1. Distribution of patient demographic data and response levels to the treatment.

Data		Number (n)	Percentage (%)
Men Women Total	Men	34	56.7
	Women	26	43.3
	Total	60	100
Comorbidity	Hypertension	28	46.7
	Coronary artery disease	14	23.3
	Chronic renal failure	6	10.0
	Congestive heart failure	1	1.7
	Chronic obstructive pulmonary disease	5	8.3
	History of amputation	5	8.3
	Cigarette smoking	7	11.7
Response to therapy	Good	21	35
	Moderate	39	65
	Poor	0	0
	Total	60	100
NPWT group	NPWT +	19	31.6
	NPWT−	41	68.3
	Total	60	100

Table 2. Classification of patients according to Wagner classification and lateralization.

Wagner stage and lateralization	Number (n)	Percentage (%)
Grade 1	1	1.7
Grade 2	21	35
Grade 3	28	46.7
Grade 4	9	15.0
Grade 5	1	1.7
Right	25	41.7
Left	31	51.7
Bilateral	4	6.7

Table 3. Duration of illness and wound dimensions.

	Mean	Standard deviation
Duration of diabetes mellitus (Years)	14.1	7.7
Duration of diabetic foot ulcer (Weeks)	7.5	8.9
Treatment duration (Days)	33.0	18.1
Wound size (cm²)	5.3	2.7

The mean duration of therapy was non-significantly longer in those who did not receive NPWT than in those who did ($p = 0.387$). Similarly, no statistical difference was noted in terms of the response to therapy ($p = 0.123$). A comparison of the wound size between those who did and did not undergo NPWT revealed that there was no significant difference ($p = 0.353$). Chi-square trend analysis was performed to answer the question "Does the rate of NPWT increase as the wound stage increases?" and no significant difference was observed ($p = 0.353$). The results of DUSG performed as part of the preoperative evaluation of the patients showed that the flow was present in those who did not undergo NPWT and absent in those who underwent NPWT; a significant intergroup difference was noted ($p = 0.006$). The CRP levels and WBC counts showed no significant intergroup difference ($p = 0.899$). A significant weak positive correlation ($r = 0.28$) was observed between the Wagner stage and treatment duration ($p = 0.029$). The duration of treatment was not significantly different between patients with flow in the dorsalis pedis artery and those without the flow ($p = 0.789$) (Table 5).

Table 4. Patients' laboratory values on admission.

	Mean	Standard deviation
C reactive protein	59.4	60.5
Hemoglobin	12.1	2.0
Albumin	36.3	5.0
Erythrocyte sedimentation rate	61.54	35.7
White blood cell count	10.2	4.1
Glycated hemoglobin	9.9	2.3

Discussion

Split-thickness skin grafting is frequently used in diabetic foot ulcers as in many other non-healing wounds. To support the graft, the graft area is closed and stabilized using conventional methods. However, because the extremity is a mobile organ, problems such as graft slippage, seroma formation, and exudate accumulation is encountered; therefore, a more effective closure method to support the graft is needed. For this purpose, Petkar et al. investigated the effect of NPWT on the graft in 40 burn wounds in a retrospective randomized study and reported that NPWT improved the graft uptake [18]. An international panel has recommended the use of NPWT in traumatic wounds and reconstructive surgery for the fixation of ST skin grafts with the highest level of evidence [19]. Similarly, in a meta-analysis of 10 randomized controlled trials involving 488 patients, Jiang et al. reported that NPWT increased the graft uptake [20]. However, these studies were conducted in different patient groups and not in a diabetic patient population. Studies investigating the effects of NPWT on the graft in a patient population with diabetic foot ulcers are limited. In a study by Gkotsoulias et al. involving a relatively small number of patients ($n = 10$ patients), the researchers reported complete graft uptake except for one patient and recommended the use of NPWT [17]. In this study, we observed no significant difference in terms of the presence of infection (osteomyelitis, WBC count, and CRP level) and wound characteristics (Wagner stage and wound dimensions); this finding suggested that the compared groups exhibited similar characteristics. In our study, 21.1% of the patients who underwent NPWT showed good healing and 78.9% showed moderate healing, whereas 41.5% of those who underwent closure with conventional methods showed good healing and 58.5% showed moderate healing; furthermore. No significant difference was noted between the two methods ($p>0.05$) Although the treatment duration was shorter in the NPWT group (29.63 days ± 19.6 days) than that in

Table 5. Results of statistical analysis.

		NPWT status		
		None (n = 41)	Present (n = 19)	p
Duration of treatment (days)		34.05 ± 17.5	29.63 ± 19.6	0.387*
Response to treatment	Good	17 (41.5%)	4 (21.1%)	0.123**
	Moderate	24 (58.5%)	15 (78.9%)	
	Poor	0	0	
Wound size (cm^2)		34.05 ± 17.5	29.63 ± 19.6	0.353***
Wound stage	Grade 012	16 (72.7%)	6 (27.3%)	0.581****
	Grade 345	25 (65.8%)	13 (34.2%)	
	Total	41 (68.3%)	19 (31.7%)	
Doppler ultrasonography	Flow present	32 (78.0%)	8 (42.1%)	0.006**
	Flow absent	9 (22.0%)	11 (57.9%)	
C reactive protein		58.9 ± 57.4	60.6 ± 68.3	0.899***
White blood cell count		9.886 ± 3.758	10.917 ± 5.030	0.681***
Osteomyelitis	Present	3 (7.3%)	4 (21.1%)	0.193*****
	Absent	38 (92.7%)	15 (78.9%)	
Necrosis	Present	12 (29.3%)	9 (47.4%)	0.172**
	Absent	29 (70.7%)	10 (52.6%)	
		Flow in dorsalis pedis artery		
		Absent	Present	p
Treatment Duration (Days)		33.5 ± 19.9	32.2 ± 17.5	0.789*

NPWT (Negative pressure wound therapy).
*Student's t-test, **Chi-square test, ***Mann–Whitney U test, ****Chi-square trend analysis, *****Fisher's exact test.

the non-NPWT group (34.05 days ±17.5 days), the difference was not significant (p>0.05). This result does not appear to be consistent with other studies in the literature [18–20]. The reason for this discrepancy was examined, and statistical evaluation was performed to answer the question "Do practitioners tend to apply NPWT to clinically worse wounds?" No intergroup difference was found in terms of wound characteristics or infection parameters. However, we statistically determined that the practitioners tended to perform NPWT at a higher rate in the group with no flow in the dorsalis pedis artery on DUSG (p = 0.006). Hence, no difference was observed between the groups in terms of healing times and healing rates even if they underwent recanalization procedures, and the healing time was prolonged in the NPWT arm. Özkayın et al. reported that the disadvantage of NPWT is that it cannot be used in patients with peripheral artery disease [21]. Although recanalization procedures were performed in our patients, the microvascular system is affected in patients with diabetes. In our study, no difference was observed in treatment duration and response to treatment when compared with conventional therapies; this observation was made after taking all diabetic patient populations, all Wagner stages, and different wound sizes into consideration. The efficacy of NPWT reported in the literature might not have been observed in our study because of the tendency to apply it on the side with accompanying vascular insufficiency and the tendency of the operator to use NPWT. Notably, a significantly weak positive correlation was found between the Wagner stage of the disease and the duration of treatment (r = 0.28, p = 0.029), which supports the data reported in the literature. This finding suggests that treatment is related to the Wagner stage.

Although NPWT has shown excellent effects in promoting wound healing, there have been reports of associated complications, such as bleeding, infection, pain, cardiac rupture, and even short-term mortality [22]. Prolonged use of NPWT may lead to reduced quality of life, increased anxiety, and malnutrition [22]. Bleeding can occur when NPWT is applied directly over a heart or a blood vessel [23]. Right ventricular rupture, although rare, is a life-threatening complication that has been linked to NPWT. In patients with post-sternotomy mediastinitis, the high negative pressure from NPWT can potentially cause the heart to be pulled toward the sharp edges of the sternum, which results in damage to the right ventricle [24]. However, it is important to note that in our study, no bleeding or fatal complications were observed.

Limitations

The limitations of the study are that it was a retrospective study, the comparison groups were not homogenous owing to reasons such as DUSG results, and the operator was a single surgeon.

Conclusion

The treatment of diabetic foot ulcers is affected by several factors, such as the presence of infection, vascularization status, wound size, and glycemic control. Our study examined a general patient population with diabetic foot ulcers and found no significant difference in terms of treatment times and healing rates between the use of NPWT and conventional methods as graft-supporting measures. The favorable effects of NPWT as a supportive measure for graft uptake have been reported in many studies. Studies examining subgroups of patient populations in those with diabetic foot ulcers may produce different results; hence, investigations in this direction are warranted.

Ethical approval

Approval for this study was obtained from the Medical Research Ethics Committee of Kahramanmaraş Sütçü İmam University (Date: 17.5.2022, session no: 2022/16, Decision no: 07)

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