Study of Effect of Four Layer Compression Bandage versus Four Layer Compression Bandage with Negative Pressure Wound Therapy in Treatment of Chronic Venous Ulcer

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Introduction: In order to improve wound healing conditions, negative pressure wound therapy (NPWT) was introduced as an alternative to conventional.

Aim of work: Assessing effectiveness of adjuvant Negative Pressure Wound Therapy (NPWT) in conjunction with compression bandages in accelerating chronic venous ulcers healing.

Patients and methods: Patients with venous leg ulcers for at least three months were enrolled in this study. A four-layer compression bandage was used to treat the first group (compression-only group). The second group (NPWT group) was treated with adjuvant Negative Pressure Wound Therapy (NPWT) in conjunction with a four-layer compression bandage. Dressings were done twice a week, with ulcer size evaluation every two weeks.

Results: The NPWT group showed a significant reduction in ulcer size compared to the compression-only group: 6.18±2.91 cm² vs. 7.55±3.12 cm² after two weeks, and 3.37±1.45 cm² vs. 5.74±2.09 cm² after four weeks. A significant difference was observed in the reduction in cumulative ulcer surface area between NPWT group and compression-only group: 29% vs. 17% after two weeks, and 61.3% vs. 37.9% after four weeks. After six weeks, 90% healing of index ulcer was achieved in 37 ulcers (74%) in the NPWT group versus 20 ulcers (40%) in the compression-only group, with statistically significant differences between the two groups. The mean duration needed for healing in the NPWT group was significantly lower (31.5±4.18 days) compared to the compression-only group (38.14±3.53 days).

Conclusion: The combination of adjuvant NPWT and compression bandages significantly enhanced the healing of chronic venous ulcers, resulting in a shorter healing time and a higher number of healed ulcers compared to using compression bandages alone.

Key words: Chronic venous ulcer, compression bandage, NPWT.

Introduction

Chronic venous ulcers (CVUs) represent a significant challenging concern in healthcare systems worldwide, burdening both patients and health care providers with extended treatment durations, frequent hospital visits, and considerable healthcare costs.[1]

The prevalence of chronic venous ulcers is estimated to be around 1-2% of the adult population in developed countries, with the risk increasing with age. The prevalence can rise among those over 65 years to approximately 4-5%, reflecting the cumulative impact of chronic venous insufficiency (CVI) over time.[2] The pathophysiology of CVUs is complex, involving sustained venous hypertension, inflammation, and microcirculatory dysfunction, leading to tissue breakdown. Despite advancements in wound care, CVUs remain notoriously difficult to manage, with high rates of recurrence and significant impacts on patients' quality of life.[3]

Current therapeutic strategies, including compression therapy, wound dressings, and surgical interventions, offer varying degrees of success, but there is still no definitive cure.[4] Compression therapy is considered the cornerstone in management of chronic venous ulcers (CVUs). It directly addresses the pathophysiology of CVUs by improving venous return and reducing venous pressure, which are crucial for healing and preventing recurrence.[5]

In order to improve wound healing conditions, negative pressure wound therapy (NPWT) was introduced as an alternative to conventional wound care. Exudate control, oedema elimination, tissue perfusion promotion, and granulation tissue formation stimulation are some of the ways that NPWT works.[6] NPWT has shown encouraging outcomes when applied to several wound types.[7]

Aim of work: The purpose of this study is to assess how adjuvant NPWT to compression bandages aids in the healing of chronic venous ulcers.

Patients and methods

This study was approved by Menoufia University's Ethics Review Board and conducted as a single center randomized controlled trial in the department of general surgery.

Inclusion criteria: This research included patients who had a single venous leg ulcer (VLU) that had persisted for three months or longer. Clinical signs of primary or secondary venous illness served as the basis for the diagnosis of VLU, which was verified by duplex ultrasonography.

Exclusion criteria: Patients who had reflux at the

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saphenofemoral junction, great saphenous vein, or sapheno-popliteal junction, had multiple venous ulcers, had no discernible pedal pulse, had poorly controlled diabetes mellitus, were younger than eighteen, had recently received chemotherapy, or had active cancer were excluded. Furthermore, patients with immunocompromised conditions, hypoalbuminemia, or severe anaemia were not included.

Eligible patients were randomly assigned to two groups using a computerized list following the acquisition of written informed permission. Four layers of compression therapy (A cotton padding layer, a crepe bandage layer, an elastic bandage layer, and an outside layer composed of an elastic cohesive bandage) were used to treat the first group, which was the compression-only group. Four-layer compression therapy combined with adjuvant Negative Pressure Wound Therapy (NPWT) was used to treat the second group. The wound cavity was filled with a sterile, open-cell foam dressing. A fenestrated evacuation tube was inserted into the foam and attached to a vacuum pump that had a fluid collecting canister. After that, an airtight adhesive drape was used to seal the wound site. After applying intermittent negative pressure of -100 to -150 mmHg, four-layer compression treatment was provided, which is comparable to what was done in the Compression-Only group.

Before starting therapy and during follow-up, the size of the ulcer was measured. At the vascular surgery outpatient clinic, dressings were done twice a week, and every two weeks, the size of the ulcer and the decrease in its surface area were measured. The wounds were measured using the mathematical calculations presented by Johnson,[9] and the elliptical approach given by Shaw et al.[8] For both groups, the ulcer healing rate—which is the total area healed each day—was noted. With either 90% healing of the index ulcer or six weeks of therapy as the research endpoint, ulcer healing was the main outcome of interest in this investigation.

Statistical analysis: SPSS version 24.0 was used for the statistical analysis (IBM Corp., Armonk, New York, USA). Continuous data were shown as averages and standard deviations (SD), whereas discrete variables were given as counts and percentages. Quantitative variables of regularly distributed data were compared using the Student's t-test, and quantitative variables of non-normally distributed data were compared between the two groups using the Mann Whitney test. To investigate the relationship between qualitative variables, the chi-square test ($\chi 2$) was employed. Fischer's Exact test was applied if any of the anticipated cells were fewer than five. Two-tailed probabilities were used to quote significant test results. The results' significance was assessed at the 5% level ($P > 0.05$).

Results

One hundred patients out of 671 with chronic venous ulcers were eligible to take part in this study, which ran from July 2019 to January 2024. They were divided into two groups of 50 patients each at random. As shown in Table 1, the patients' baseline characteristics, ulcer size, and chronicity were similar in the two groups.

The evaluation of mean ulcer size, reduction in ulcer surface area (S/A), and healing rate was conducted at three intervals: after 2, 4, and 6 weeks of treatment (Table 2). Assessment of ulcer size after two weeks revealed a reduction from 9.1±4.07 cm^2 to 7.55±3.12 cm^2 in the compression-only group, and from 8.72±3.86 cm^2 to 6.18±2.91 cm^2 in the NPWT group, with statistically significant differences between the two groups. Significant difference was also detected in proportion of reduction in cumulative ulcer surface area (17% vs 29%), and ulcer healing rate (11.07 mm2 Vs 18.64 mm2) per day in compression only group and NPWT group respectively.

After four weeks, the NPWT group demonstrated a greater reduction in cumulative ulcer surface area (61.3% vs. 37.9%) and a higher ulcer healing rate (19.1 mm^2 vs. 12 mm^2 per day) compared to the compression-only group. Ulcer size decreased from 9.1±4.07 cm^2 to 5.74±2.09 cm^2 in the compression-only group and from 8.72±3.86 cm^2 to 3.37±1.45 cm^2 in the NPWT group, showing statistically significant differences between the groups.

The primary study outcome, defined as 90% healing of the index ulcer, was assessed after six weeks of treatment and showed healing in 20 ulcers (40%) in the compression-only group versus 37 ulcers (74%) in the NPWT group, with statistically significant differences between the two groups. The mean duration needed for healing within healed ulcer of both groups was significantly lower in NPWT group (31.5±4.18 Vs 38.14±3.53 days) compared to compression-only group.

The variations in the mean ulcer size and the cumulative ulcer surface area for both groups over the duration of the study were illustrated in **(Figs. 1,2).**

Photographic documentation of ulcers before and after treatment in both groups was depicted in **(Figs. 3-8).**

Subgroup analysis of healed ulcer in both groups in relation to initial ulcer size revealed that ulcers with surface area of 10 cm2 or less have more tendency to reach 90% healing in comparison to ulcers with larger surface area that showed reduction of ulcer size. Adjuvant NPWT not only resulted in higher healing rate but also improved the granulation tissue of ulcer in large ulcers.

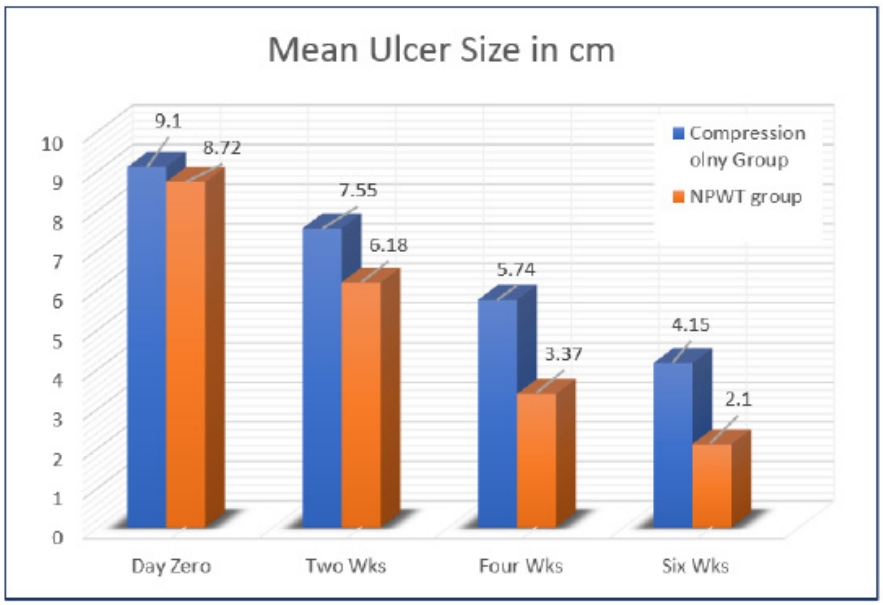

Fig 1: Mean ulcer size in both groups along study period.

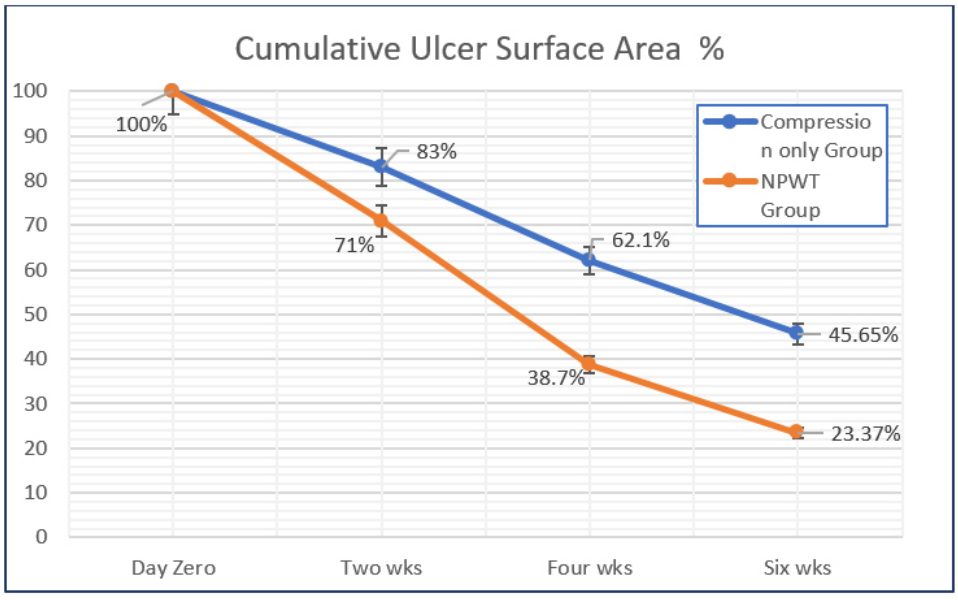

Fig 2: Cumulative reduction of ulcer surface area along study period.

Fig 3: Venous ulcer before and after treatment (NPWT group).

Fig 4: Venous ulcer before and after treatment (NPWT group).

Fig 5: Venous ulcer before and after treatment (NPWT group).

Fig 6: Venous ulcer before and after treatment (Compression only group).

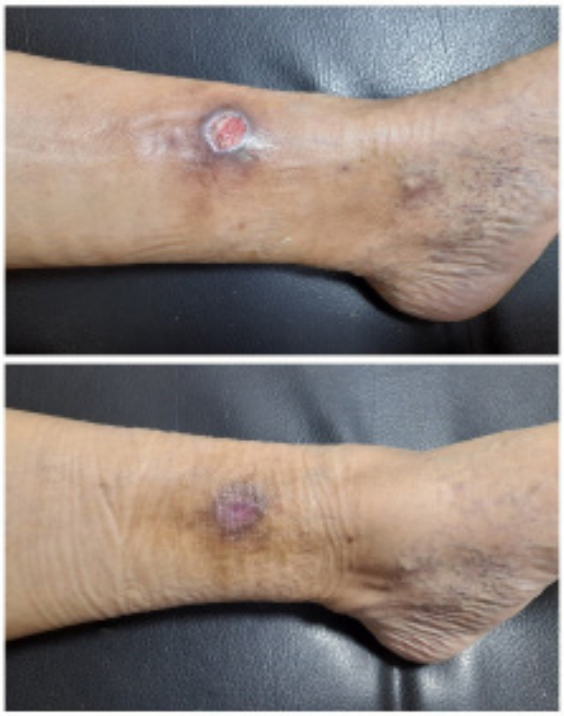

Fig 7: Venous ulcer before and after treatment (Compression only group).

Fig 8: Venous ulcer before and after treatment (Compression only group).

Table 1: Baseline Characteristics of Studied Groups

	Compression only group (N=50)	NPWT group (N=50)	Test of significance (X^2)	P-value
Age (years)				
Mean ±SD	39.94±8.42	42.45±11.29	t= 0.697	0.488
Range	26- 61	31- 58		
Female/Male	13/37	6/44	2.33	0.13
Smoking	20	14	0.819	0.29
Diabetes Mellites	5	11	0.05	0.17
History of DVT	29	37	2.18	0.139
Prolonged standing occupation	26	29	0.29	0.59
BMI (kg /m^2)				
Mean ±SD	31.08±2.66	32.47±5.53	t= 4.197	0.11
Range	25-37	25-43		
Duration of ulcer (Months)				
Mean ±SD	10.14±5.54	9.22±4.81	U= 1.353	0.27
Range	3-17	5-19		
Size of ulcer (cm)				
Mean ±SD	9.1± 4.07	8.72± 3.86	U= 3.566	0.63
Range	2.75 -29.53	3.16-34.40		

DVT: Deep Venous Thrombosis. SD: Standard Deviation. BMI: Body Mass Index.

Table 2: Healing of the ulcer in both groups

	Compression only group (N=50)	NPWT group (N=50)	P-value
Ulcer size after two weeks (mean± SD) (cm^2)	7.55±3.12	6.18±2.91	0.025
Reduction of cumulative ulcer S/A after two weeks (%)	17%	29%	0.01
Healing rate at two weeks (mm^2 /day)	11.07	18.64	0.001
Ulcer size after four weeks (mean± SD) (cm^2)	5.74 ±2.09	3.37 ±1.45	0.001
Reduction of cumulative ulcer S/A after four weeks (%)	37.9 %	61.3 %	0.012
Healing rate at four weeks (mm^2 /day)	12	19.1	0.007
Ulcer size after six weeks (mean± SD) (cm^2)	4.15±1.88	2.1±1.06	0.001
Reduction of cumulative ulcer S/A after six weeks (%)	54.35%	76.63%	0.03
Number of healed ulcer (90% healing) after six weeks (%)	20 (40 %)	37 (74 %)	0.002
Days needed for 90% healing (mean ±SD) days	38.14±3.53	31.5±4.18	0.001

Discussion

Venous leg ulcers (VLUs) are a prevalent and challenging condition that significantly impacts patients' quality of life and pose a substantial burden on healthcare systems. The underlying etiology of venous insufficiency and venous ulceration is mainly venous hypertension; However, its pathogenesis remains unclear.[10]

Micro-lymphangiopathy, capillary dilatation, capillary blockage by microthrombi or white blood cells, decreased capillary function, increased capillary permeability, and plasma protein leakage are among the alterations that take place at the microvascular level. Mast cell degranulation, leukocyte recruitment, elevated matrix metalloproteinase inhibitors, and prostacyclin synthesis are all seen at the cellular level. M1 macrophages contribute to the proinflammatory microenvironment by releasing TGF-β1, IFN-γ, and IL-1α. Ulcers and resistance to healing occur from these microvascular changes and the inflammatory cascade that follows, which impedes the healing process.[11]

The most significant development in wound care this century has likely been negative pressure wound treatment (NPWT), which was created in 1997 as an alternative to conventional wound care.[12] NPWT facilitates wound healing by establishing a wet,

airtight environment. It improves blood flow to the area of the wound, eliminates healing inhibitors, decreases inflammatory marker levels, and reduces oedema through macro-deformations. Furthermore, by encouraging the migration and proliferation of tissue-repairing cells and bolstering angiogenesis, NPWT promotes the development of granulation tissue.[13]

Compression therapy is widely recognized as the cornerstone of VLU management, providing a non-invasive and effective approach to enhance venous return, reduce edema, and promote ulcer healing.[14] The adjunctive role of NPWT in management of venous leg ulcer is still undervalued, and only a limited number of studies have assessed its effectiveness in these types of wounds.

The purpose of this randomized controlled trial was to assess the effectiveness of adjuvant NPWT in treating chronic venous ulcers when combined with compression treatment. The findings showed that adjunctive NPWT was superior in terms of the quantity of ulcers that were cured at the study's conclusion.

This study evaluated the efficacy of NPWT in treating big ulcers that would not heal completely during the study's anticipated follow-up period using two additional parameters: cumulative ulcer surface area and healing rate. During the planned follow-up visits, the supplementary use of NPWT showed a substantial decrease in cumulative ulcer surface area. Additionally, individuals receiving supplementary NPWT had a noticeably improved healing rate.

Analysis of patients who achieved complete ulcer healing revealed that initial ulcer size was a significant factor. Ulcers smaller than 10 cm^2 were more likely to reach complete healing in both groups. However, among those whose ulcers healed, patients treated with adjunctive NPWT experienced a significantly shorter mean healing time.

In patients with incomplete ulcer healing, adjunctive NPWT not only significantly reduced the cumulative ulcer surface area but also appeared to improve granulation tissue formation in the ulcer bed. However, this improvement in granulation tissue was a clinical observation and could not be statistically validated.

Upon reviewing the published evidence, many studies have evaluated the role of NPWT in the management of venous ulcers, either as a type of chronic leg ulcers or in venous ulcer-specific patients, but with different study designs.

The first set of research was planned as a prospective or retrospective single-arm study. Twelve patients (15 VLUs) received treatment in a pilot research by Wang et al. for a median of 20 days (Range: 7–42 days). The ulcers' surface area decreased from 2.1 cm^2 to 0.8 cm^2 (P=0.022) and their depth decreased from 3.0 mm to 0 mm (P=0.005). They found that adding NPWT shortened the recovery period from 6.3 weeks to 4.3 weeks (P=0.024) when compared to a historical group with comparable characteristics that just underwent compression treatment.[15]

Tekin et al. conducted a study on 14 infected venous ulcers, demonstrating that NPWT helped reduce the need for antibiotics by decreasing the biological burden. Compared to baseline, the mean reduction in ulcer size was 46.4% after the first six applications and 72.8% after additional treatments.[16]

The average ulcer surface area dropped by 24.28% to 27.4% in the first three weeks and then by 6.7% to 10% in the following weeks in a different trial including 15 patients. Ten of the patients recovered in six weeks, while the other five took 10, 12, 14, 16, and 20 weeks to recover.[17]

In the second set of research, NPWT was utilized as an adjuvant therapy for venous ulcers either before to or following split-thickness grafting. According to these investigations, the use of NPWT in the treatment of venous ulcers led to excellent graft success and quick wound bed preparation.[18–23]

Another cluster of studies focused on ulcer changes that occur with NPWT as discharge control or macro and micro changed of ulcer bed., Orlov et al., noted that NPWT provided effective management of wound exudate, preventing wound irritation, inflammation, and maceration, which could otherwise compromise patients' quality of life.[24]

According to a different study by Ren et al., NPWT combined with oxygen-loaded fluid irrigation can successfully raise the partial pressure of oxygen in the skin around wounds, aid in the type I to type II conversion of macrophages, and encourage the growth of granulation tissue, all of which improve epithelialization.[25]

After a week, Dini and his colleagues also found that, in comparison to the control group, all patients in the NPWT group had significantly improved, especially in angiogenesis, lymphatic vessel creation, and macrophage and lymphocyte proliferation. They suggested using NPWT in addition to the usual treatment for venous leg ulcers.[26]

According to a comprehensive study by Glass et al., NPWT promotes the deposition of granulation tissue, remodels the extracellular matrix, and stimulates angiogenesis to improve wound healing.[27]

Kieser and his associates assessed the use of compression bandaging in conjunction with adjunctive Negative Pressure Wound Therapy (NPWT) for four weeks in seven patients with a total of twelve chronic resistant venous ulcers.

They came to the conclusion that this regimen could help promote the healing of chronic venous ulcers. Nevertheless, the study had a number of shortcomings, including the absence of a control group, the use of patients as their own controls by extrapolating previous wound changes, the lack of documentation of the initial ulcer size or ulcer surface area reduction, and the emphasis on improved granulation tissue formation rather than ulcer surface area reduction.[28]

Marston et al. used either mechanically powered (MP) or electrically powered (EP) negative pressure wound therapy (NPWT) for 16 weeks or until the wound was completely closed to 40 patients with venous leg ulcers (VLUs) from 13 centers in a randomized controlled study. 52.6% (10/19) of patients treated with MP NPWT and 23.8% (5/21) of patients treated with EP NPWT at 30 days had 50% wound closure. At 90 days, 38.1% (8/21) of patients treated with EP NPWT and 57.9% (11/19) of patients treated with MP NPWT had fully closed their wounds. While ulcer healing improved in all groups, MP NPWT treatment increased the chance of full wound closure.[29]

50 patients with venous leg ulcers that had persisted for at least three months were treated in a randomized-controlled study by Alkhateep et al. with either negative pressure wound treatment (NPWT) or a traditional daily dressing made with regular saline. The NPWT group's wound healing rate was 13.1 mm^2/day, whereas the control group's was 2.8 mm^2/day. 17 ulcers (68%) in the NPWT group had 90% healing after 30 days of therapy, with a mean healing time of 24 days. After 30 days of therapy, none of the ulcers in the control group healed 90% of the way. Although this study showed how NPWT helps cure chronic venous leg ulcers (CVLU), One disadvantage is that, instead of employing normal compression therapy like the control group, it uses regular wound dressings.[30]

Fifty patients with chronic venous ulcers (VU) were randomized by Tawfic et al., to either compression therapy alone or negative pressure wound therapy (NPWT) in conjunction with compression therapy. The NPWT group saw a mean decrease in ulcer surface area of 79% after 12 weeks, whereas the compression group experienced a mean reduction of 58%. For NPWT patients, the average time to full healing was 75.4 ± 8.7 days, but for patients getting just compression treatment, it was 96.3 ± 7.2 days ($P < .001$).[31]

There is not enough evidence to support a recommendation for the use of negative pressure wound therapy (NPWT) as a treatment option for chronic venous leg ulcers (CVLU), according to the Cochrane Database of Systematic Reviews, which reviewed guideline recommendations on the topic.[32]

Additionally, according to the recommendations of the European Society for Vascular Surgery, there is no evidence from randomized controlled trials (RCTs) that negative pressure wound therapy (NPWT) is an effective primary treatment for venous leg ulcers (VLUs).[33]

The regular main use of negative pressure wound treatment (NPWT) for venous leg ulcers (VLUs) was discouraged by the American Venous Forum and the Society for Vascular Surgery's clinical practice recommendations (grade-2; level of evidence C). This advice stems from the fact that, although there is evidence that negative pressure treatment has a good impact on wound healing generally, there is insufficient research to support its primary usage for VLUs.[34]

Conclusion

Compared to utilizing compression bandages alone, the combination of adjuvant NPWT and compression bandages significantly improved the healing of chronic venous ulcers, resulting in a shorter healing period and a larger number of healed ulcers by the study's endpoint.

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