

Vacuum-assisted accelerated healing of postphlebotic ulcer

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Background

Chronic leg ulcers affect ~1% of the adult population in developed countries. The cornerstones of these regimens are compression therapy and resolution of the cause. Topical negative pressure has been used to promote the healing of tissue defects. The aim of our study is to evaluate the efficacy of vacuum assisted compression (VAC) in ulcer healing.

Patients and methods

After the ethics committee's institutional review board (IRB) under number MS.17.06.09, this prospective randomized controlled study was conducted on 30 patients presented to the Vascular Surgery Department between June 2017 and October 2018. The patient was randomly allocated into three groups; each group contained 10 patients: one group underwent conventional therapy, the second group underwent VAC therapy, and the third underwent combined VAC and conventional therapies. These groups were compared regarding ulcer size, presence of granulation tissue, and presence of infection. The VAC system was placed in situ for 3 weeks, and the dressing was changed every 5 days. Patients were evaluated clinically through follow-up clinic visits at first week, the second week, 1 month, and 3 months after the procedure, regarding depth, width, and breadth and ulcer closure percentage.

Results

The current study shows that compression plus VAC group had a statistically significant faster closure duration than other compression groups ($P < 0.05$). Approximately 50% of the studied cases in the compression plus VAC group had complete closure within 1 week of the procedure, and only 20% had total closure after 3 months. The compression group showed the worst wound closure rate after the procedure, as 80.0% of the studied group had complete closure after 3 months of operation. There was no statistically significant difference in sociodemographic characteristics between the studied techniques, except for occupation number of parity and bodyweight of the studied groups, which showed a nonstatistically significant difference ($P > 0.05$). Cases that were lost to follow-up were 10, 20, and 20% in the compression group, VAC group, and combined group.

Conclusion

Healing of venous ulcers is a complex process attributed to several elements. Although various parameters proved to positively affect the healing of venous ulcers in our study, large prospective multicenter studies are needed to provide well-defined outcomes.

Keywords:

postphlebotic syndrome, postphlebotic ulcer, vacuum-assisted therapy

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Introduction

Chronic leg ulcers (CLUs) affect up to 1% of the adult population in developed countries [1]. The prevalence is increasing with age and is reported to be 4–5% in the 80-year population. Patients with leg ulcer course and prognosis differ according to the underlying pathogenesis; a venous disease is seen in up to 80% [2]. The prevalence of C1 disease, according to the CEAP classification, is seen in ~80% of the population, especially in the developed countries. C2 class is seen in ~20–60%, whereas C5 and C6 prevalence is ~1–2%. Different treatment modalities and protocols have been documented to date, mainly

focusing on ambulatory management of venous ulcers; these regimens' cornerstones are compression therapy and resolution of the cause [3]. A long-standing nonhealing leg ulcer is a daily challenge. Debridement of nonviable tissue and unhealthy, mainly superficial yellow slough can facilitate wound healing [4]. Several wound debridement methods are available today, such as autolytic, chemical,

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mechanical, and surgical; however, these options have been stated in multiple papers as not successful [5]. Topical negative pressure had been used to promote healing of tissue defects as the constant suction on the wound surface stimulates the formation of granulation tissue [6]. Vacuum assisted compression (VAC) (vacuum-assisted closure) is a procedure designed to help wound healing through the creation of continuous or discontinuous subatmospheric pressure with the effect of increasing blood flow to the wound and promoting granulation tissue and angiogenesis development [7]. The aim is to study the efficacy of VAC in ulcer healing compared with standard ulcer dressings in hospitalized patients with chronic venous leg ulcer (postphlebotic ulcer) and also to evaluate the effect of VAC therapy in recurrence rate, pain release, and quality of life of patients.

Patients and methods

After the approval of ethics committee's institutional review board under number MS.17.06.09, this prospective randomized controlled longitudinal study was conducted on 30 patients who presented to the Vascular Surgery Department between June 2017 and October 2018. They were selected for managing postphlebotic ulcers and gave written informed consent before participation in the study. Randomization was done using the opaque envelope method. Allocation concealment was maintained to ensure no selection bias. Consent was verbally taken and documented on the patient file with the patient signature during the clinic appointment and again was reviewed with the patient immediately before the procedure.

We noted the preoperative chronic venous insufficiency (CVI) and recent deep venous thrombosis (DVT) and superficial vein varicosity and leg monitoring with the duplex scan. Patients were regularly followed up in the department. The data included the patient's demographics, underlying medical conditions, any previous varicose vein operation or another operation, the anatomical site of ulcer, operative procedure details, time to become functionally closed, comorbidities, hemoglobin levels, morbidity, and mortality. The study included 30 patients with CLU. The patients were randomized into three groups. Each group contained 10 patients, where one group underwent conventional therapy, the second group underwent VAC therapy, and the third underwent combined VAC and conventional therapies. These groups were compared regarding ulcer size, presence of granulation tissue, and presence of infection.

Inclusion and exclusion criteria

All patients were aged from 18 to 70 years. Patients with nonhealed CLU for more than 3 months on conventional therapy, with Ankle Brachial pressure index (ABPI) above 0.8, were included. We excluded patients with allergy to the dressings used in the study, untreated osteomyelitis, tumor tissue present in the wound, primary varicose vein, and underwent salvage procedures to improve the vein competence. Those who did not give consent (unconscious) or those with mental or behavioral disorders were excluded. The patients' demographics, underlying medical conditions, previous varicose vein operation, and other associated morbidity were reported. All patients had been examined regarding arterial assessments, which included pulse examination, ABPI measurement, and venous assessments, including examining the limb with CLU regarding infection state and granulation tissue formation. Size, shape, depth of ulcer, active DVT or recanalized leg perforator and CVI presence were recorded. The following laboratory results were documented: blood picture, blood sugar level, kidney functions, liver functions, and coagulation profile. Duplex ultrasonographic examination was done to assess diameter and the veins' compressibility, including leg perforators deep to the ulcer, DVT, arterial assessment, and included patency.

Procedure

The VAC (Smith & Nephew PLC, London, United Kingdom) system was placed in situ for 3 weeks, and the dressing was changed every 5 days. The same device was used for all patients treated. Photographs of the wounds were taken every week. The wound was evaluated by the percentages of fibrin (yellow), granulation (red), and necrosis (black) in the wound every week. The periwound skin was also examined for signs of maceration or eczema. Patients were evaluated clinically through follow-up clinic visits at first week, second week, 1 month, and 3 months after the procedure regarding depth, width, and breadth and the percentage of ulcer closure.

Statistical analysis and data interpretation

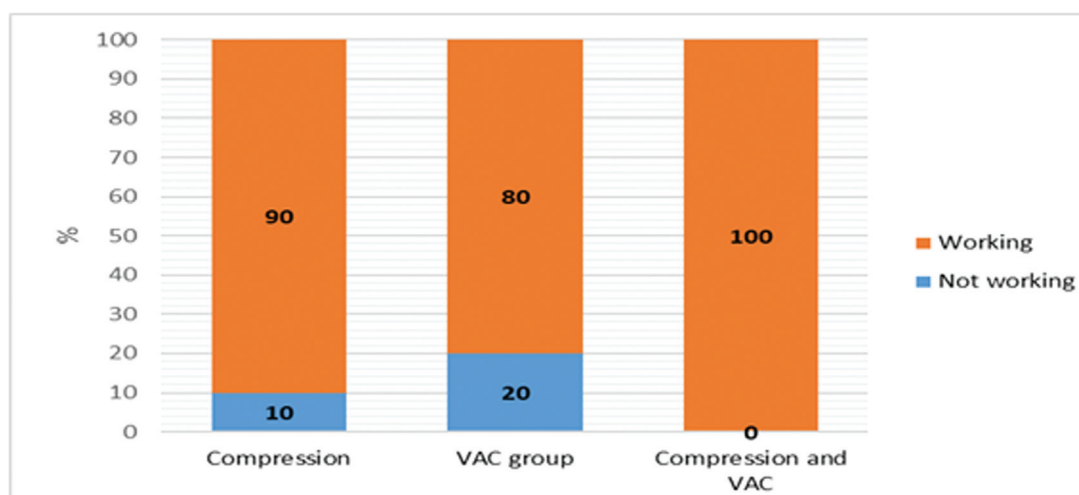
All statistics were performed using IBM Corp. (Released in 2012. IBM SPSS Statistics for Windows, Version 21.0.; IBM Corp., Armonk, New York, USA). Qualitative data were described using number and percent. Quantitative data were described using median (minimum and maximum) and interquartile range for nonparametric data and mean and SD for parametric data after testing normality using Shapiro-Wilk test. The significance of the obtained results was judged at the 0.05 level.

Results

The present study was carried out on 30 patients, where 10 underwent compression technique, 10 cases underwent VAC technique, and 10 patients underwent compression plus VAC group. All cases were followed up after the procedure to detect complication rate, response, and wound closure rate. There was no statistically significant difference in sociodemographic characteristics among the studied techniques except for occupation (Fig. 1). Mean age among the studied groups was 43.9, 46.0, and 44.85 years for compression group, VAC group, and combined compression and VAC group, respectively. A statistically significant difference was found regarding occupation between the VAC and the two other techniques. The number of parity and BMI

among the studied groups showed a nonstatistically significant difference ($P>0.05$) (Table 1). Moreover, there was no statistically significant difference among the studied groups regarding medical and smoking history. Among the studied cases in each technique (compression, VAC group, and combined compression and VAC group), smokers represented 40.0, 30.0, and 20%, respectively; diabetic represented 30.0, 10.0, and 10%, respectively; hypertensive represented 30.0, 20.0, and 20%, respectively; and allergy to drugs represented 10.0, 10.0, and 10%, respectively (Table 2). Presence of comorbidities represented 10.0, 10.0, and 10% of compression, VAC group, and combined compression and VAC group, respectively, without statistically significant difference among the studied groups. Only platelet count in laboratory results (hemoglobin, total leukocyte count, international

Figure 1



Occupation distribution between studied groups.

Table 1 Statistical significance between compression group and VAC group of sociodemographic characteristics of the studied groups

	Compression (N=10) [n (%)]	VAC group (N=10) [n (%)]	Compression and VAC (N=10) [n (%)]	P value
Age (years)				
Mean±SD	43.90±15.36	46.0±13.05	44.85±13.4	0.95
Sex				
Female	2 (20.0)	5 (50.0)	3 (30)	0.26
Male	8 (80.0)	5 (50.0)	7 (70)	
Marital status				
Not married	1 (10.0)	2 (20.0)	0	0.25
Married	9 (90.0)	8 (80.0)	10 (100.0)	
Occupation				
Not working	2 (20.0)	7 (70.0)	0	0.016*†
Working	8 (80.0)	3 (30.0)	10 (100)	
Number of parity				
Weight (kg)	1.0 (0.0–5.0)	3.0 (0.0–5.0)	3.0 (0.0–4.0)	0.38
Mean±SD	78.5±25.41	82.20±27.87	81.77±12.71	0.9

VAC, vacuum assisted compression. *P value is < 0.05%.

normalized ratio, serum creatinine, serum albumin, and RBG) showed a statistical difference in the studied groups.

Compression plus VAC technique showed a statistically significant higher mean platelet count than the other studied groups (284.31 vs. 280.0 and 220.60 for the compression and VAC groups, respectively) (Table 3). Regarding ulcer characteristics, median ulcer width was 3.0, 7.5, and 4 and median ulcer duration per month was 33.0, 36.0, and 240 for compression group, VAC group, and combined compression and VAC group, respectively, with no statistical significance.

Severe calcification was higher among cases with the VAC technique. The medial ulcer was more frequent than the lateral ulcer (Table 4). There was no statistically significant difference among the studied groups regarding family history, operation history, and history of similar conditions (Table 5). Regarding venous insufficiency, leg perforator, and DVT distribution among the studied groups, the highest

frequencies for venous insufficiency were among compression plus VAC group, whereas the presence of leg perforators deep to the ulcer was higher among the compression group. The presence of DVT was higher among the compression plus VAC group. Recanalized DVT was higher among the compression group.

All groups had ABPI more than 0.9. Only one case with osteomyelitis and primary varicose vein was in the compression plus VAC group. None of the studied groups had a history of malignancy.

Cases lost to follow-up were 10, 20, and 20% in the compression group, VAC group (Fig. 2), and combined compression plus VAC group, without statistically significant difference among them. The highest rate of hemorrhage was detected for the compression group, whereas the compression plus VAC group had the lowest complication rate (Fig. 3).

Compression plus VAC group had the best operation results, as 30% had total closure, 50% had near-total

Table 2 Smoking status and medical history between studied groups

	Compression (N=10) [n (%)]	VAC group (N=10) [n (%)]	Compression and VAC (N=10) [n (%)]	P value
Smoking status				
Nonsmoker	6 (60.0)	6 (60.0)	8 (80)	0.53
Smoker	4 (40.0)	3 (30.0)	2 (20.0)	
Passive smoker	0	1 (10.0)	0	
DM				
Non-DM	7 (70.0)	9 (90.0)	9 (90)	0.48
DM	3 (30.0)	1 (10.0)	1 (10)	
Hypertension				
Normotensive	7 (70.0)	8 (80.0)	8 (80)	0.38
Hypertensive	3 (30.0)	2 (20.0)	2 (20)	
Allergy to drugs				
Negative	9 (90.0)	9 (90.0)	9 (90)	0.97
Positive	1 (10.0)	1 (10.0)	1 (10)	
Comorbidities				
Absent	9 (90.0)	9 (90.0)	9 (90)	0.89
Present	1 (10.0)	1 (10.0)	1 (10)	

DM, diabetes mellitus; VAC, vacuum assisted compression.

Table 3 Laboratory results between studied groups

Laboratory results	Compression N=10	VAC group N=10	Compression and VAC N=10	P value
HB (g/dl)	12.95±1.76	12.07±1.85	11.88±1.42	0.29
TLC	8.63±1.5	8.81±1.84	8.42±1.16	0.82
PLT	280.0±62.7	220.60±57.10	284.31±63.95	0.042 [†]
INR	1.21±0.26	220.60±57.1	284.31±62.95	0.87
S.Cr	0.91±0.17	0.95±0.15	0.95±0.16	0.46
S.Alb	4.2±0.41	4.15±0.43	4.24±0.22	0.84
RBG	135.90±62.1	116.80±55.56	137.31±72.01	0.72

HB, hemoglobin; INR, international normalized ratio; PLT, platelet; S.Alb, serum albumin; S.Cr, serum creatinine; TLC, total leukocyte count; VAC, vacuum assisted compression. [†]P value is < 0.05%.

Table 4 Ulcer characteristics between the studied groups

	Compression (N=10) [n (%)]	VAC group (N=10) [n (%)]	Compression and VAC (N=10) [n (%)]	P value
Ulcer size width	3.0 (1.0–12.0)	7.5 (2.0–15.0)	4.0 (1.0–15.0)	0.19
Ulcer duration (months)	33.0 (5.0–84.0)	36.0 (2.0–240)	240 (1.0–120.0)	0.86
Calcification of arterial limb				
Non	0	0	1 (7.7)	0.42
Mild	2 (20.0)	1 (10.0)	0	
Moderate	3 (30.0)	6 (60.0)	6 (61.5)	
Severe	5 (50.0)	3 (30.0)	3 (30.8)	
Ulcer side				
Right lower limb	4 (40.0)	7 (70.0)	6 (60)	0.42
Left lower limb	6 (60.0)	3 (30.0)	3 (30)	
Both	0	0	1 (10)	
Site of ulcer				
Medial	8 (80.0)	5 (50.0)	8 (80)	0.35
Lateral	2 (20.0)	5 (50.0)	2 (20)	

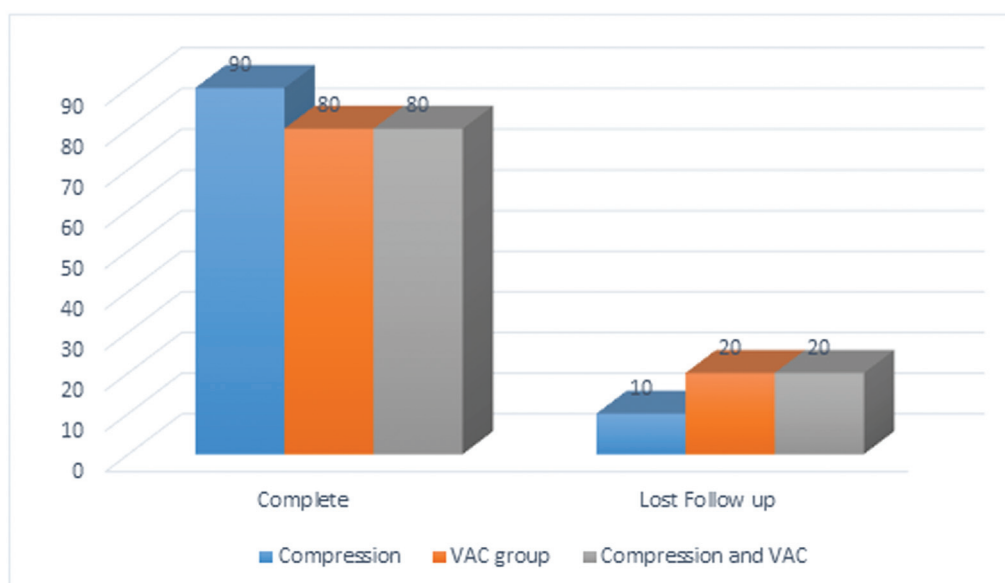
VAC, vacuum assisted compression.

Table 5 Family history, operation history, and types of distribution among studied groups

	Compression (N=10) [n (%)]	VAC group (N=10) [n (%)]	Compression and VAC (N=10) [n (%)]	P value
Family history				
Negative	10 (100.0)	7 (70)	9 (90)	0.17
Positive	0	3 (30)	1 (10)	
History of varicose veins operation				
Negative	7 (70)	8 (80)	8 (80)	0.87
Positive	3 (30)	2 (20)	2 (20)	
History of other operation				
Negative	10 (100)	9 (90)	7 (70)	0.04*
Positive	0	1 (10)	3 (30)	
Operation types				
Varicose vein	10 (100)	7 (70)	9 (90)	0.17
Stripping	0	3 (30)	1 (10)	
History of similar condition				
Negative	8 (80)	9 (90)	7 (70)	0.48
Positive	2 (20.0)	1 (10)	3 (30)	

VAC, vacuum assisted compression.

Figure 2



Follow up among studied groups.

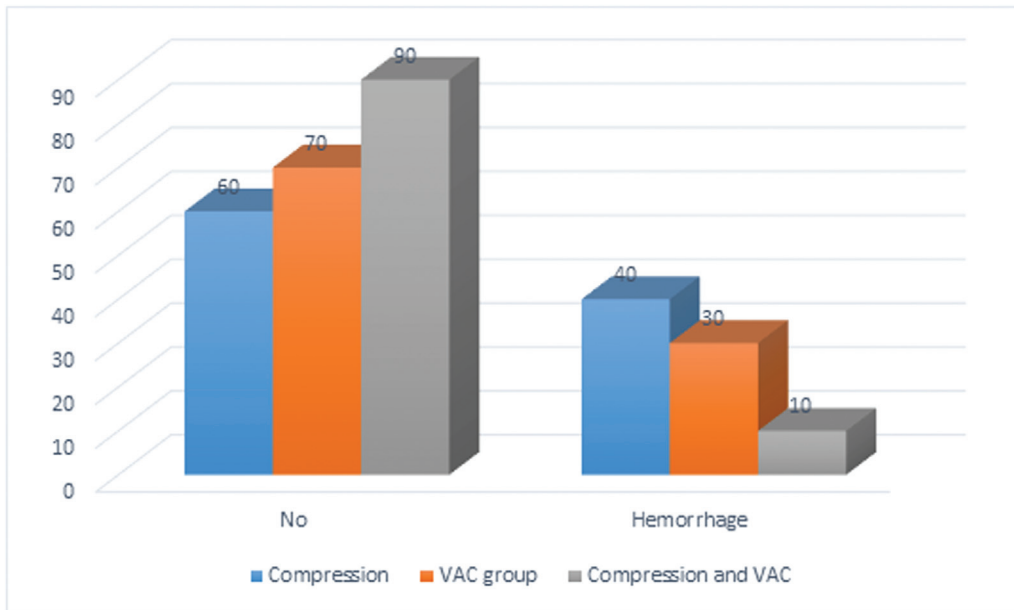
closure, and none of the studied cases had no closure. The compression plus VAC group had a statistically significant faster closure duration than other compression groups ($P<0.05$) (Fig. 4). Approximately 50% of the studied cases in compression plus VAC group had complete closure within 1 week of operation, and only 20% of them had total closure after 3 months. The compression group showed the worst wound closure rate after the

operation, as 80.0% of the studied group had complete closure after 3 months of the procedure (Fig. 5) (Table 6).

Discussion

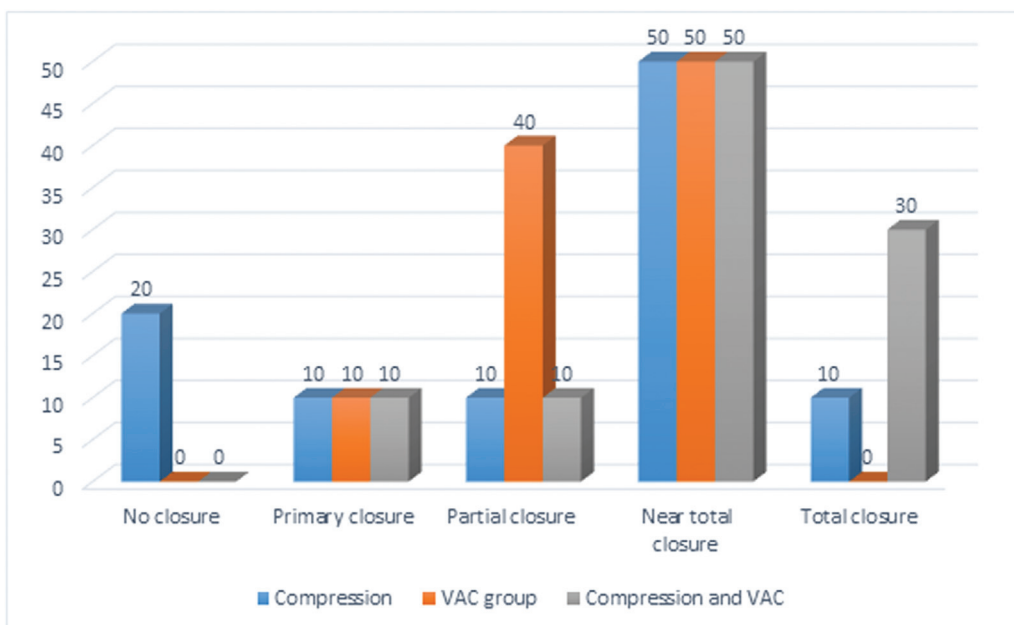
A venous leg ulcer is common, debilitating, and costly. It appears in up to 3% of people over 60 years of age and 5% over 80 years of age. Australians aged over 65 years

Figure 3



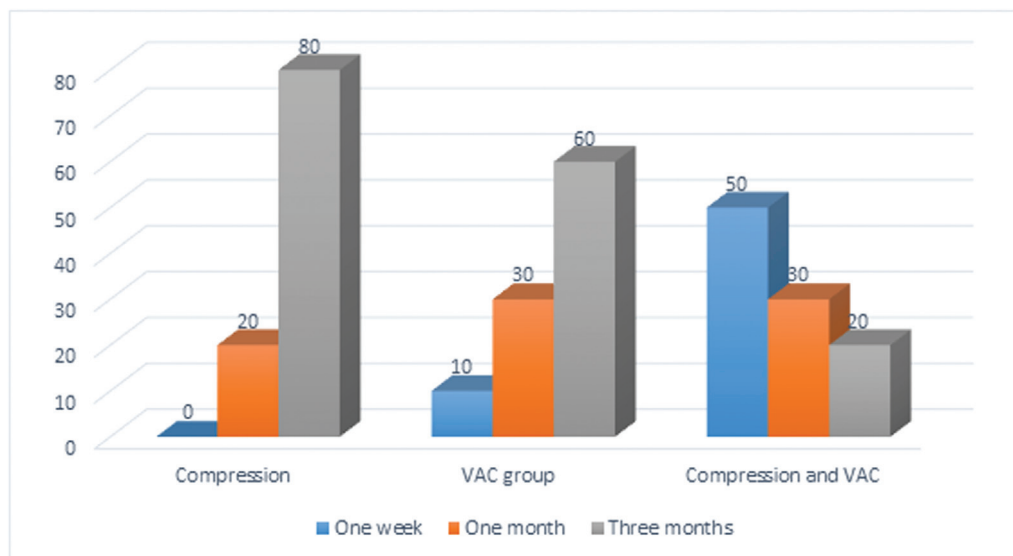
Complications distribution among studied groups.

Figure 4



Procedure results among studied groups.

Figure 5



Closure time during follow up among studied groups.

Table 6 Statistical differences of different variables between groups

	Compression (N=10) [n (%)]	VAC group (N=10) [n (%)]	Compression and VAC (N=10) [n (%)]	P value
Presence of venous insufficiency	7 (70)	7 (70)	8 (80)	0.31
Leg perforator deep to the ulcer	3 (30)	2 (20)	2 (20)	0.87
Presence of DVT				
No	1 (10.0)	0	1 (10)	
Yes	3 (30.0)	5 (50)	6 (60)	
Recanalized	6 (60.0)	5 (50)	3 (30)	0.26
ABI >0.9	10 (100)	10 (100)	10 (100)	–
Osteomyelitis				
Negative	10 (100)	10 (100)	9 (90)	
Positive	0	0	1 (10)	0.45
Tumor negative	10 (100)	10 (100)	10 (100)	–
Primary varicose veins				
Negative	10 (100)	10 (100)	9 (90)	
Positive	0	0	1 (10)	0.45
Complete	9 (90)	8 (80)	8 (80)	
Lost follow-up	1 (10)	2 (20)	2 (20)	0.71
No	6 (60)	7 (70)	9 (90)	
Hemorrhage	4 (40)	3 (30)	1 (10)	0.17
No closure	2 (20)	0	0	
Primary closure	1 (10)	1 (10)	1 (10)	
Partial closure	1 (10)	4 (40)	1 (10)	
Near-total closure	5 (50)	5 (50)	5 (50)	
Total closure	1 (10)	0	3 (30)	0.09
Closure after 1 week	0	1 (10)	5 (50)	
Closure after 1 month	2 (20.0)	3 (30)	3 (30)	0.03#
Closure after 3 months	8 (80.0)	6 (60)	2 (20)	

DVT, deep venous thrombosis; VAC, vacuum assisted compression.

currently account for 14.2% of all population affected, and a corresponding rise in venous leg ulcer can be anticipated. Therefore, there is continual research into improving the treatment of VLU. Reducing time to heal of VLU will improve patients' physical and social functioning and ulcer pain, allow early mobilization, and reduce VLU. Healing time will also reduce clinic and nursing time, the number of admissions, length of stay, and ultimately health-related costs. The present study was carried out on 10 patients with a compression technique, 10 cases with VAC technique, and 10 patients with compression plus VAC group. All cases were followed up after an operation to detect complication response and wound closure rate. The current study shows no statistically significant difference among the studied groups regarding history (medical and smoking history). Among the studied cases in each technique (compression group, VAC group, and combined compression and VAC group), smokers represented 40.0, 30.0, and 20%, respectively; diabetic represented 30.0, 10.0, and 10%, respectively; hypertensive represented 30.0, 20.0, and 20%, respectively; and allergy to drugs represented 10.0, 10.0, and 10%, respectively. The presence of comorbidities represented 10.0, 10.0, and 10% of compression group, VAC group, and combined compression and VAC group, respectively, without statistically significant difference among the studied groups. There is no statistically significant difference among the studied groups regarding laboratory results (hemoglobin, total leukocyte count, international normalized ratio, serum creatinine, serum albumin, and RBG), except for platelet count. Compression plus VAC technique shows a statistically significant higher mean platelet count than the other studied groups (284.31 vs. 280.0 and 220.60 for the compression and VAC groups, respectively). The study also shows no statistically significant difference among the studied groups regarding ulcer characteristics ($P > 0.05$). Median ulcer width was 3.0, 7.5, and 4 and median ulcer duration/months was 33.0, 36.0, and 240 for compression group, VAC group, and combined compression and VAC group, respectively. Severe calcification was higher among cases with the VAC technique. A medial ulcer was more frequent than a lateral ulcer.

Chronic venous leg ulcers according to the British National Health Services (NHS) guidelines, which define venous leg ulcers as 'an open lesion between the knee and the ankle joint that remains unhealed for at least 4 weeks and occurs in the presence of venous disease,' were only included in this study when considering the use of negative pressure wound

therapy (NPWT) [8]. The guideline reports that there is insufficient evidence on which to base a recommendation for topical negative pressure/VAC in chronic venous leg ulcer. Retrieval of 12 studies in full was achieved, and four met the inclusion criteria for this review [9–12]. Description of the characteristics of the included cases is shown in Table 2. Many trials have compared the effectiveness of moderate and high compression therapy modalities [9,10]. One is published as a conference abstract only [9]. One trial assessed elastic stockings' effect in decreasing the area of lipodermatosclerosis in patients with previous venous ulceration and assessed recurrence rates with or without compression [11]. Another trial compared the effectiveness of two different brands of moderate compression stockings in leg ulcer clinics [12]. Eight studies were excluded. Nelson and Bell-Syer determined recurrence as a hole in the leg's skin constant for at least 6 weeks. Vandongen and colleagues defined any break in the skin in the area between the ankle and the knee as reulceration. Milic and colleagues and Franks and colleagues did not define this as reulceration. Three trials were planned after calculating an appropriate sample size [10–12], although Milic does not report this trial design aspect in their abstract. The current study demonstrated no statistically significant difference among the studied groups regarding family history, operation history, and history of similar conditions. It shows that all groups had ABI more than 0.9. There was only one case with osteomyelitis and primary varicose vein and was in the compression plus VAC group. None of the studied groups had been diagnosed with a malignancy. The current study shows that venous insufficiency, leg perforator, and DVT distribution between studied groups had no statistically significant difference among them, with the highest frequencies for venous insufficiency, which was among the compression plus VAC group.

In contrast, the presence of leg perforators deep to the ulcer was higher among the compression group. The presence of DVT was higher among the compression plus VAC group. Recanalized DVT was higher among the compression group. The current study shows cases that were lost to follow-up were 10.0, 20.0, and 10% in compression group, VAC group, and combined compression plus VAC group, without statistically significant difference among them. It illustrates that the highest rate of hemorrhage was detected for the compression group. In contrast, the compression plus VAC group had the lowest rate of complication. Multiple studies, with a total of 630 patients, show

different forms of autolytic debridement [13–18]; where wound debridement was their study outcome, they have used the following dressing materials; hydrogel, dextranomer beads, E.U.S.O.L., B.W.D., non-adherent dressing and paraffin gauze.

The Groenewald study in 1980 showed that 40/50 (80%) patients treated with dextranomer beads and 7/50 (14%) patients treated using EUSOL achieved complete debridement after 1 week of treatment. The current study showed that compression plus VAC group had the best results of procedure, as 38.5% of the cases had total closure and 46.2% had near-total closure, and none of the studied cases had no closure. Another study compared NPWT with standard care to treat hard-to-heal leg ulcers of various etiologies. All ulcers in the study underwent a punch skin-graft transplantation, and trial treatments before and after the grafting were used. NPWT was used for 4 days postoperatively. There was a decrease in the time to healing in the NPWT group with an increase in the chance of healing. The study's follow-up time was undetermined, but it shows that most participants were followed up for a minimum of 1 year – no difference in the number of ulcers complete cure during follow-up. Moreover, there was evidence of a difference in wound preparation for grafting in the NPWT-treated group. There was no evidence of a difference in the EQ-5D utility measure or pain scores at 8 weeks between the study groups, although some estimates were imprecise [8]. The current study shows that combined compression plus VAC group had a statistically significant faster closure duration than other compression groups ($P < 0.05$). Approximately 50% of the studied cases in the compression plus VAC group had complete closure within 1 week of study, and only 20% of them had total closure after 3 months. The compression group showed the worst rate of wound closure after the study as 80.0% of the studied group had complete closure after 3 months of procedure.

Conclusion

The current study shows that compression plus VAC group had a statistically significant faster closure duration than other compression groups ($P < 0.05$). Approximately 50% of the studied cases in the compression plus VAC group had complete closure within 1 week of the procedure, and only 20% had total closure after 3 months. The compression group showed the worst wound closure rate after the procedure, as 80.0% of the studied group had complete closure after 3

months of operation. This paper should serve as a guide for further studies, as well as an up-to-date review of published evidence. In light of conflicting evidence and lack of studies with a large volume of patients, we recommend multicenter randomized control trials to see the effect of using VAC on the healing of the venous ulcers.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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