

Original Article

The management of venous leg ulcers: Effects of four-layer bandage system

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Abstract:

Aim: Chronic Venous Ulcer (CVU) accounts for nearly 70% of all chronic leg ulcers (CLU), seriously impacting the quality of life and creating a heavy economic burden. Here, we present CVU therapy with a four-layer bandage system in 113 patients retrospectively treated by the General Surgery Chronic Wound Unit and Cardiovascular Surgery Department.

Material and Methods: From January 2022 to January 2023, 113 patients with CVU were evaluated retrospectively. All patients were documented by color Doppler ultrasonography (CDUS), ulcer size, and demographics. If there were multiple ulcers, the largest one was assessed. Immobile patients and patients with an Ankle Brachial Index (ABI) of <0.7 were excluded. Debridement, exercise, venoactive drugs, and a four-layer bandage system were performed for all patients. The primary outcome was to assess the ulcer healing, and the secondary outcome was to obtain the recurrence rate and the treatment compatibility of patients.

Results: The mean age of the patients was 60.73±11.3 (28-91) years and 77.9% were male. Body Mass Index (BMI) was 30.4±7.7 kg/m² (min:18-max:51 kg/m²). The mean follow-up period was 18.82±13.4 weeks. *Pseudomonas aeruginosa* (38%) and *Staphylococcus aureus* (31.8%) were the most identified microorganisms. Four patients experienced recurrence of the CVU (3.5%). The older patients had larger ulcers than the younger patients. Female patients had larger-sized ulcers (p=0.001). Completely healed ulcers were 26.5% of the total. The four-layer compression bandage was applied 12 times for per patient. The mean healing period was 23.2±13.8 weeks. The mean healing rate was 4.17±3.78% for a week. The multivariate analysis revealed that age and pain had negatively affected the ulcer healing.

Conclusion: The management of CVU is challenging and needs a multidisciplinary approach. Compression is the main goal of the treatment. Surgical or endovenous therapies may be beneficial for decreasing ulcer recurrence. For patients with slow ulcer healing, adjuvant treatment modalities such as patient education, smoking cessation, diet and lifestyle modification, and exercise should be recommended.

Keywords: Venous ulcer, varicose, compression bandages, venous hypertension, wound healing

INTRODUCTION

Chronic venous disease (CVD) is a widespread disease in adult populations, and chronic venous ulcer (CVU) accounts for nearly 70% of all chronic leg ulcers as a progressed stage of this disease [1]. CVU is defined as an open skin lesion of the leg or foot that

occurs in an area affected by venous hypertension. CVU seriously impacts the quality of life with a heavy economic burden and it is a complex clinical problem that requires multidisciplinary wound-care teams. Venous hypertension due to chronic venous insufficiency (CVI) or obstruction is considered the primary underlying mechanism for CVU [2].

CITATION

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The mainstay treatment for CVU is surgery and compression therapy for which there is strong evidence of their role in wound healing and reduction of the recurrence. CVI is estimated to affect 10-35% of the entire US population, and 4% of people over 65 years old have active venous ulcers [3]. The prevalence of venous leg ulcers is estimated to be within a range of 0.06-2%. The high prevalence of the disease results in a heavy economic burden on the health care system annually for all countries [4]. A recent study from Germany demonstrated that the average cost was nearly 10000 euros per patient/year [5].

Concerning compression bandage therapy, some statements are accepted: Compression improves ulcer healing; multicomponent compression systems are more effective; higher compression is better; and healed CVU has a high recurrence rate in the absence of ongoing treatment. The four-layer bandage application comprises a high compression system defined as ankle-subbandage pressure with 35-40 mmHg. The therapeutic impact of these bandages may vary or depend upon the applicators' experience or skill level.

We conducted our study retrospectively with patients with active CVU who were treated with the four-layer bandage therapy and a combination of medical treatments in the Chronic Wound Unit working closely with the Cardiovascular Surgery Department.

MATERIAL AND METHODS

The study protocol was approved by the Ankara City Hospital Clinical Research Ethics Committee (date/no: 08.23.2023/E2-23-4760) and complied with the Helsinki Declaration. From January 2022 to January 2023, 113 patients with active venous ulcers treated in the Chronic Wound Unit were admitted.

All patients were evaluated with color Doppler ultrasonography (CDUS). All varicose ulcers were active and categorized as stage-6 regarding CEAP classification. All patients had leg ulcers of venous etiology, documented by CDUS. The ulcer size was measured and recorded before the treatment; all were above 1 cm². If a patient had multiple ulcers, the largest was measured, and the features were included (Figure 1: Measurement of wound size). Immobile patients and patients with an Ankle Brachial Index (ABI) of <0.7 were excluded. Measurements and before-after photographs were documented for all patients (Figure 2a,2b,2c: Wound bed preparation, wound care follow-up in 0, 1st, and 12th weeks). Arterial CDUS was conducted for all patients without arterial distal pulse or those having lower ABI levels as an indicator for peripheric arterial disease.

We examined all patients and followed them after the CVU therapy for recurrence and treatment compatibility. The primary outcome was the CVU healing, and the secondary outcome was the recurrence and the treatment compatibility of the patient.



Figure 1. Measurement of wound size



Figure 2. Wound bed preparation, wound care follow-up(0, 1, 12. weeks)

Wound Care and Technical Details of Four-Layer Bandage Application

All therapies were carried out with a multidisciplinary approach between the Cardiovascular Surgery Department and the Chronic Wound Unit. The same team performed all four-layer bandage applications during the treatment.

All patients received a four-layer bandage system after wound bed preparation. Deep tissue cultures were taken at the first examination of all patients. Biofilms, infected and necrotic tissues were washed out, debrided, and the wound bed was prepared for optimal healing under local anesthesia. The debridement techniques were surgical, mechanical, enzymatic, or combined. Wound care products were used under the four-layer bandage system. Systemic antibiotics were administered according to wound cultures. Venoactive drugs were combined. Micronized purified flavonoid fraction (MPFF) and other medications that the Cardiovascular Surgery Department advised were continued. Acetylsalicylic acid (ASA) and pentoxifylline were combined if necessary. In case the patient was under warfarin or novel oral anticoagulants (NOAC) therapy, surgical or mechanical debridement was performed more gently. Enzymatic debridement was preferred wisely in these cases.

Different wound care products were used for wound dressing after debridement. The wound care product was decided according to the condition of the patient and the wound. A hydrophilic, hydrofiber wound dressing (AquacellAg, ConvaTec, Princeton, NJ, USA) made of silver sodium carboxy methyl cellulose and foam dressing containing ibuprofen (BiatainIbu Non-Adhesive, Coloplast, Tatabanya, Hungary) were the most commonly used wound care products. In cases with prominent pain, a foam dressing containing ibuprofen was preferred. The four-layer bandage system was changed every 4-7 days during the first weeks of treatment. Discharging advice was expressed for patients to open the four-layer bandage at home, take shower, and wear compression stockings before coming to the wound unit. The patient was controlled at the chronic wound unit on the 4th to 7th day. After the first weeks, the treatment continued weekly until the ulcer had healed. No operation or endovenous procedure was performed during the therapy. An exercise program and medical treatments were initiated for all patients.

Statistical Analysis

All statistical analyses were conducted using SPSS for Windows (version 20.0, SPSS Inc., Chicago, Illinois). The demographics, the features of ulcers, and comorbidities were given. Categorical variables were given as count and percentile and compared using χ^2 or Fisher Exact χ^2 . Mean and standard deviation (SD) were used to demonstrate continuous variables if data had normality of distribution. Regarding the ulcer size, the patients were divided into two groups according to ulcer size of <10 cm or ≥ 10 cm. An Independent sample t-test was performed to compare

the continuous data and presented graphically by box-plot. To determine the ulcer healing rate (UHR), the data was calculated as ratio of the ulcer healing percentile and the ulcer healing time. A threshold of UHR was calculated by receiver operating characteristic (ROC) curve analysis. The graphical expressions of sensitivity-specificity curves were given. According to the cut-off value, the slow wound healing predictors were investigated by using binary logistic regression analysis with forward stepwise. All prediction values were reported with 95% confidence intervals (CIs). A p-value of <0.05 was accepted to determine statistical significance.

RESULTS

From January 2022 to January 2023, 113 patients with active venous ulcers were treated in the Chronic Wound Unit. A multicomponent four-layer compression system was performed on all patients except one who experienced allergic reactions.

The mean age of the patients was 60.73 ± 11.3 (min:28-max: 91) years, and 88 were (77.9%) male. Body Mass Index (BMI) was 30.4 ± 7.7 kg/m² (min:18-max:51). Patient data were given in Table 1. The mean follow-up period was 18.82 ± 13.4 weeks (3-68 weeks). *Pseudomonas aeruginosa* (38%) and *Staphylococcus aureus* (31.8%) were the most identified microorganisms. Four patients experienced a recurrence of CVU after complete healing (3.5%). Older patients had larger ulcers than the younger ones ($p=0.012$). Female patients had larger ulcers (all>10cm) ($p=0.001$) (Figure 3a,b: The 1st and 26th week of the 58 year-old-female patient's follow-up). BMI was 33.4 ± 6.2 and 29.5 ± 7.9 kg/m² for females and males, respectively ($p=0.025$).

Table 1. Showing demographic datas an comorbidities predicting slow wound healing

	n, % or mean, SD	Univariate			Multivariate		
		OR	95% CI	p-value	OR	95% CI	p-value
Age	64.66 \pm 8.7	1.057	1.015-1.101	0.007*	1.059	1.015-1.105	0.009*
Gender (male)	88, (77.8%)	0.431	0.174-1.064	0.068*	0.470	0.175-1.261	0.134
Body mass index	30.78 \pm 7.3	1.010	0.962-1.062	0.684			
Smoking	69, (61%)	1.629	0.724-3.648	0.236			
Diabetes mellitus	29, (25.6%)	1.1	0.460-2.633	0.831			
Chronic heart failure	6, (5.3%)	0.872	0.153-4.979	0.877			
Chronic kidney disease	3, (2.65%)	0.875	0.077-9.956	0.914			
Trombosis	21, (18.5%)	0.853	0.313-2.321	0.756			
Wound necrosis	56, (49%)	1.294	0.600-2.791	0.511			
Pain	76, (67.2%)	2.782	1.126-6.874	2.782*	3.737	1.403-9.952	0.008*
<i>Pseudomonas aeruginosa</i>	43, (38%)	0.65	0.29-1.458	0.296			

The four-layer compression bandage was applied 12 times for per patient. After the treatment, the ulcer healing status was documented, and the CVU healing rate per week was calculated (Figure 4a,b: The 2nd and 18th week of the 61 year-old-male patient's follow-up). The mean healing rate was $4.17 \pm 3.78\%$ for a week. The ulcer healing was achieved in a mean period of 23.2 ± 13.8 weeks. The four-layer bandage treatment was effective in healing ulcers for all patients. However, total ulcer

healing could be achieved in 30 patients. The weekly healing rate was $6.43 \pm 4.86\%$ healing per week in the totally healed ulcer group, whereas it was $3.36 \pm 4.86\%$ healing in the rest ($p<0.001$, 95% CI (1.57-4.57%)). Ulcers smaller than 10 cm necessitated a minimum of 4 weeks, whereas ulcers larger than 10 cm necessitated at least 11 weeks for total ulcer healing. The mean healing period was higher in larger ulcers (32 weeks) than in smaller ones (12 weeks) ($p<0.001$). (Figure 5: Box-plot graphics

demonstrating CVU healing rate and time requirement).

ROC analysis was conducted to assess a threshold healing rate for total ulcer healing, and a value of weekly healing rate higher than 2.5% was calculated (AUC:0.769; Sensitivity: 86% and Specificity: 56%) (Figure 6: Determining a threshold value for CVU healing). According to this cut-off value, the patients were divided into the faster and slower-healed groups. Parameters were analyzed with Univariate and Multivariate logistic regression to predict factors on slower ulcer healing. The factors mitigating the ulcer healing were determined. The results revealed that age, female gender, and pain negatively affected CVU healing. However, in multivariate analysis, only age and pain negatively affected ulcer healing (Table 1).



Figure 3. The 1. and 26. week of the 58 years old female patient's follow-up



Figure 4. The 2. and 18. week of the 61 years old male patient's follow-up

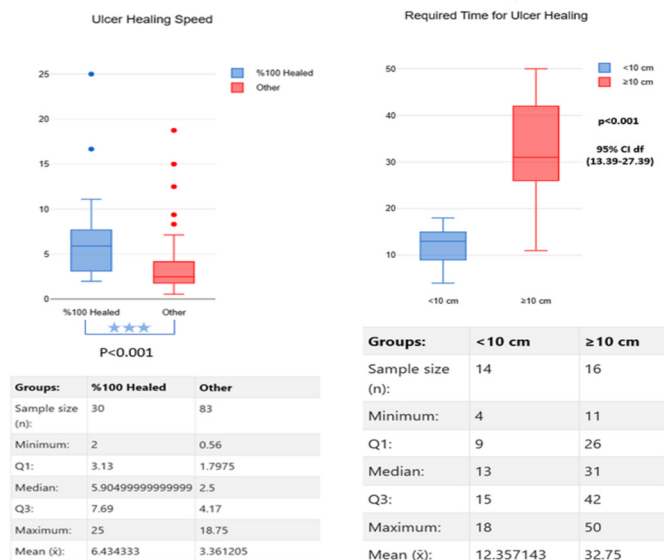


Figure 5. Box-plot graphics demonstrating CVU healing rate and time requirement

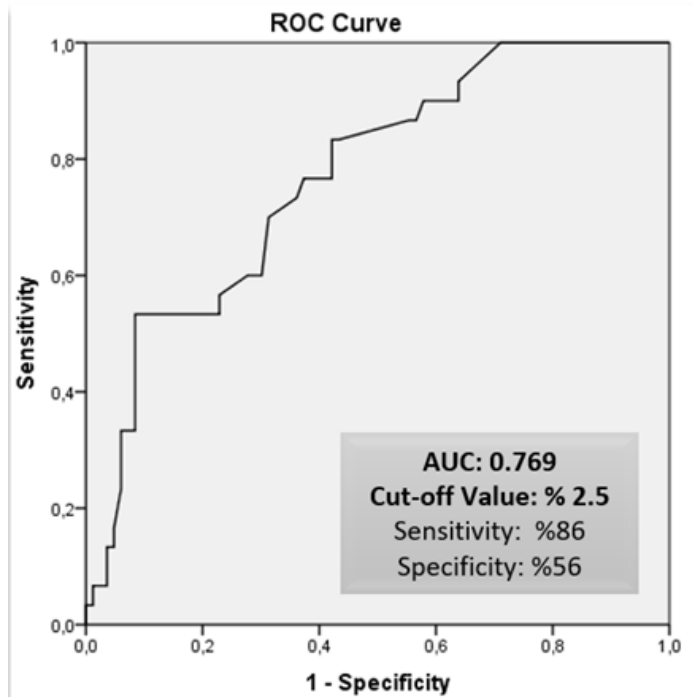


Figure 6. Determining a threshold value for CVU healing



Figure 7. a. Male patient with venous ulcer, 7b. Allergic reaction caused by the four layer bandage system

DISCUSSION

Venous leg ulcers are the most common leg ulcers with a significant socioeconomic burden due to slow wound healing [6]. Chronic venous insufficiency is considered the primary etiological cause contributing to the occurrence of venous ulcers. Compression is considered the principal therapeutic approach for managing CVU [7]. The therapy goals include reduced edema and pain, improved venous reflux, and enhanced healing. It is helpful for ulcer healing and prevention of recurrence [8].

Compression stockings, compression bandages, adjustable

compression velcro straps, and intermittent pneumatic compression pumps are the most commonly encountered compression methods in the literature. Compression bandaging systems consist of elastic compression bandages or non-elastic bandages ranging from one to four layers. Elastic bandages can be long or short stretch. The most common method of non-elastic compression therapy is the Unna boot, which contains zinc oxide, glycerin, sorbitol, gelatin, and aluminum silicate, hardens after application, and is changed weekly [9-12].

Considering the outcomes according to the analysis of reviews, compression is more effective than no compression. Nevertheless, there is low-quality evidence between the different compression methods to speculate the superiority of one method over another [13-17]. A prospective, randomized, comparative study shows that intermittent pneumatic compression systems, stockings, and multi-layer bandaging are very useful and effective in treating venous leg ulcers. The two-layer short-stretch bandages and Unna boots are inefficient [18]. According to the guidelines of the Society for Vascular Surgery (SVS) and The American Venous Forum (AVF), the use of intermittent pneumatic compression is recommended when other compression options are not available, cannot be used, or have failed to aid in venous leg ulcer healing after prolonged compression therapy. They suggest using multicomponent compression bandages over single-component bandages to treat venous leg ulcers [19].

The four-layer bandage system is an example of high compression defined as ankle-subbandage pressure of 35-40 mmHg. The clinical effect of these bandages might differ or depend on the practitioner's experience or skill in achieving the correct amount of pressure. Therefore, meta-analysis or review articles on this issue may not reflect the real-world experience [13-15]. The four-layer bandaging system provides very effective results in ulcer healing. In our experience, all our patients had wound healing with the treatment, but some had a slower healing rate. In these patients, endo-venous ablation or surgery should improve healing and decrease the recurrence rate. However, according to the quality of evidence regarding the efficacy of open surgical or endovenous interventions, there is no definitive support for the superiority of the compression therapy methods [15].

Although still incompletely understood, pathophysiological mechanisms of CVD have potential targets and strategies addressed by venoactive drugs. These roles include improved venous tone, reduced edema and inflammation, and improved microcirculation, facilitating CVU healing. In our experience, to improve CVU healing, we gave MMPF to all our patients in combination with compression therapy. Our duration of providing medical adjuvant therapy was minimally six months or maybe longer, depending on the individual healing process. Pentoxifylline was the second most used medical adjuvant therapy added when the ulcer healing rate was slower than expected. Combining with venoactive drugs to the four-layer

compression therapy could improve our outcome.

A recent meta-analysis on the effect of compression therapy reported that there was no significant difference in the distribution of payment rates among different compression methods [13-17]. O'Meara et al. found out in another meta-analysis that the four-layer bandage system seems to be much more effective than short-stretch bandaging regarding the healing period. The four-layer bandaging increases the chance of healing by around 30% when independent prognostic factors are considered [20]. In our study, a healing rate of 6.43 ± 4.86 % weekly was found in total healed ulcers, whereas a healing rate of 3.36 ± 4.86 % weekly was found in the rest ($P < 0.001$ 95% CI (1.57-4.57%)). In larger ulcers, more treatment is needed for total healing. The average healing rate was 4.17 ± 3.78 % per week. Healing under 2.5% per week was determined as a slower healing rate, and a rate of under 10 % per month can be used in clinics for the prognosis. Adjuvant therapies or other treatment modalities (surgical treatment, RF ablation) should be combined for total wound healing. In multivariate analysis, age and pain affected ulcer healing rate negatively. Pain in venous ulcers might decrease reaching adequate compression pressure due to the low treatment compatibility of the patient.

We observed that the patient's daily activity was increasing while pain and wound exudate was decreasing with the four-layer bandage system. Appropriate dressing under compression stockings may not always be possible. The four-layer bandage system relieves patients and caregivers from the obligation of daily dressing changes. The economic analysis concluded that a four-layer bandage system was the dominant treatment strategy and had lower costs with greater health benefits, including the cost of bandages, nurse, and doctor visits [20].

The choice of compression system remains at the clinicians' discretion based on evidence of effectiveness, patient tolerability, and preference. However, ulcers larger than 10 cm are recommended the four-layer bandage system if there is no sign of peripheral arterial disease and/or an ABI of < 0.7 . Only one patient was incompatible with this compression therapy because of an allergic reaction. (Figure 7a: Male patient with the venous ulcer, Figure 7b: Allergic reaction caused by the four-layer bandage system)

Cardiovascular Surgery Clinics should build up a vascular and/or venous subclinic in this patient cohort to overcome treatment efficacy limitations. Clinical practice guidelines are also valuable in providing quality care and decreasing economic burdens. For this reason, the Cardiovascular Surgery Community also developed and implemented a guideline for these venous diseases in 2021 [21]. The current study carries the limitations of being single-center documentation retrospectively. There was no comparison between the other compression methods.

CONCLUSION

In conclusion, the management of CVU is a therapeutic challenge

and should be multidisciplinary. Compression is the main goal of treatment. In case of failure, surgical or endovenous procedures can be considered. These interventions are also crucial for decreasing ulcer recurrence. In our experience, the ulcer healing rate is essential. If it is slow, newer treatment modalities with proper patient education regarding smoking cessation, diet, and lifestyle modification with exercise should be referred. More extended follow-up periods are necessary for recurrence issues; however, for large and problematic CVU, high compression with four-layer bandage systems should be in charge.

Ethics Committee Approval: The study protocol was approved by the Ankara City Hospital Clinical Research Ethics Committee (date/no: 08.23.2023/E2-23-4760) complied with the Helsinki Declaration.

Patient Consent for Publication: Not necessary for this manuscript.

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

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