



## CLINICAL OUTCOMES OF COMPRESSION ALONG WITH ULTRASOUND GUIDED FOAM SCLEROTHERAPY IN THE MANAGEMENT OF VENOUS ULCERS: A PROSPECTIVE STUDY AT TERTIARY CARE HOSPITAL, PESHAWAR.

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### ABSTRACT

**BACKGROUND:** Ultrasound-guided foam sclerotherapy UGFS has been demonstrated to be as successful as open surgery in the management of venous ulcers. **OBJECTIVE** This study aimed to evaluate the clinical outcomes of compression along with ultrasound guided foam sclerotherapy in the management of venous ulcers. **MATERIAL AND METHODS:** This eighteen-month prospective observational study was conducted from July 2022 to December 2023 with a follow up period of one year at a Tertiary Care Hospital in Peshawar. Patients were recruited through non-probability convenience sampling. Prospective assessments were conducted on patients with superficial truncal venous incompetence and active venous leg ulcers CEAP clinical class C6 diagnosed through clinical evaluation and findings from doppler ultrasound. Baseline clinical, imaging, and demographic data were gathered before the the standard procedure of compression therapy and ultrasound guided foam sclerotherapy. The time frame from the intervention to the complete healing of the ulcer and the rate of ulcer recurrence throughout the one-year follow-up period were the main outcome measures **RESULTS:** The study included 33 individuals aged 40-50, with a mean age of  $43 \pm 5$  years. The gender distribution was 19 men 57.6% and 14 women 42.4%. By the end of the one-year follow-up period, 26 patients 78.8% had fully healed ulcers, three patients 9.1% had incomplete healing, with ulcers showing moderate improvement but not fully healing. Four patients 12.1% had unhealed ulcers, indicating no progress during the research period. Ulcer recurrence was reported in one patient 4% who had previously healed ulcers. The healed ulcers had an average size reduction of  $80\% \pm 5\%$ . The average time for healing was  $14 \pm 3$  weeks **CONCLUSION:** The results of this study concluded that, treating venous ulcers with compression therapy and ultrasound-guided foam sclerotherapy together significantly improves healing rates, reduces ulcer size, and enhances patient quality of life. The beneficial result of this study encourages the use of this combination therapy strategy in clinical settings for improved patient care.

**KEYWORDS:** Compression, Foam Sclerotherapy, Ultrasound guided, Venous Ulcers

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## INTRODUCTION

Venous leg ulcer VLU is a clinical entity characterized by full-thickness skin defect, usually in the lower leg and ankle region, that is sustained by venous hypertension as a result of chronic venous illness and does not heal naturally as defined by the 2004 revision of the CEAP classification.<sup>1</sup> The majority of venous leg ulcers VLU's are considered chronic leg ulcers CLUs, which are prolonged leg wounds that do not heal after three months of proper care or do not heal completely after one year.<sup>2</sup> The most serious complication brought on by the progression of chronic venous insufficiency CVI is venous leg ulcers VLUs.<sup>3,4</sup> Approximately, 70–90% of all chronic leg ulcers are formed due to CVI.<sup>5</sup> 40% of individuals with VLUs have underlying deep vein thrombosis DVT, and the prevalence increases with age, with women suffering three times more than males.<sup>6</sup> According to population-based studies, the prevalence rate of venous ulcer ranges from 0.7% to 2.7%.<sup>7</sup> Venous Ulcers have a poor tendency to heal, thus treatment is still challenging. Concomitant risk factors include advanced age, obesity, the size of the ulcer, the length of the ulcer, and inadequate adherence to treatment. Standard wound care, compression therapy, and surgical or interventional management are the treatment options for VUs.<sup>8,9</sup> The most accepted treatment option for chronic venous disorder is graduated compression therapy. The deep and superficial venous systems are intended to be compressed by

the fabric's mechanical qualities, which then counteracts the underlying pathophysiologic venous hypertension. Endovenous methods such as radiofrequency ablation RFA, endovenous laser therapy EVLT, and ultrasound-guided foam sclerotherapy UGFS have been demonstrated to be as successful as open surgery in the management of venous ulcers and varicose veins.<sup>10</sup> Ultrasound-guided foam sclerotherapy UGFS, high ligation and stripping, endovenous thermal or non-thermal ablation, and skin grafting of the ulcer are the interventions used to treat pathological epifascial reflux.<sup>11</sup> Minimally invasive endovenous procedures including foam sclerotherapy have gained more attention recently as they don't require open surgical incisions and can be performed safely.<sup>12</sup> Foam sclerotherapy reduces the superficial incompetent vein's ability to contribute to chronic venous hypertension by the occluding the vein which is believed to be a significant cause of venous ulcers.<sup>13</sup> In a group of 116 patients, Cabrera et al reported an 83% ulcer healing rate after six months of foam sclerotherapy.<sup>14</sup> Work done by Bergan et al and colleagues showed a group of 12 patients in which ulcers did not heal following compression treatment while after receiving foam sclerotherapy, nine of these patients recovered in two weeks and all of the patients recovered in six weeks indicating the potential of improved outcomes after utilizing foam sclerotherapy.<sup>15</sup> According to a research conducted by O'Hare et al., foam

sclerotherapy FST was successful in 75% of the 185 limbs with venous ulcers and severe venous illness. As a result, the authors concluded that FST was equally effective for both complicated and uncomplicated venous disease.<sup>16</sup>

This study aimed to evaluate the clinical outcomes of compression along with ultrasound guided foam sclerotherapy in the management of venous ulcers.

## **MATERIAL AND METHODS STUDY**

**DESIGN/SETTING/DURATION:** This eighteen-month prospective observational study was conducted from July 2022 to December 2023 with follow up period of one year at a Tertiary Care Hospital in Peshawar. Data was collected from patients after the ethical approval was granted from the institutional review board. Informed consent was obtained from each participant. Non-probability convenience sampling was used.

**PATIENT SELECTION CRITERIA:** Prospective assessments were conducted on patients with superficial truncal venous incompetence and active venous leg ulcers CEAP clinical class C6 diagnosed through clinical evaluation and findings from doppler ultrasound.

**INCLUSION CRITERIA:** The inclusion criteria of the study were as follow:

- The great saphenous vein GSV, small saphenous vein SSV, anterior accessory saphenous vein AASV, or any other big superficial vein with a considerable proximal deep venous connection must have >1 s retrograde flow on venous duplex imaging.
- No complete incompetence of the deep veins.

## **EXCLUSION CRITERIA**

The following participants were excluded from the study:

- 0.8 or less on the ankle brachial pressure index ABPI.

- Past history of pulmonary embolism PE or deep vein thrombosis DVT.
- Inadequately managed diabetes mellitus.
- Rheumatoid arthritis
- Malignancy
- Current use of anticoagulants

## **PRE-INTERVENTION DATA COLLECTION:**

Baseline clinical, imaging, and demographic data were gathered before the intervention. The location, size, length, and indications of infection of the ulcer were noted together with demographic information such as age, gender, and medical history. Measurements of the Ankle Brachial Pressure Index ABPI was carried out to rule out peripheral artery disease. Past DVT or PE, diabetic management, rheumatoid arthritis, cancer, immobility, and current anticoagulant use were all included in the medical history.

## **INTERVENTION COMPRESSION AND ULTRASOUND GUIDED FOAM SCLEROTHERAPY**

Patient was first examined in standing position and all visible varicosities were marked. In lying position, affected limb was cleaned with pyodine. Varicosities were cannulated using butterfly G-19 needles and fixed. After cannulating all varicosities under ultrasound guidance, limb was elevated. Maximum upto 20cc of foam using sodium tetradecyl sulphate was used. Sodium tetradecyl sulphate was mixed with air in 1:4 using tessari method. Prophylactic use of enoxaparin was given post sclerotherapy and compression dressings were applied.

**FOLLOW UP:** For a period of one years, patients were followed up at regular intervals of 1 month, 6 month and 1 year. Treatment complications, ulcer recurrence, ulcer healing status, and any adverse events were noted during follow-up visits. The Doppler ultrasonography test was conducted again at predetermined intervals

to evaluate venous reflux and track the effectiveness of treatment.

**OUTCOME MEASURES PRIMARY OUTCOMES:** The time frame from the intervention to the complete healing of the ulcer and the rate of ulcer recurrence throughout the one-year follow-up period were the main outcome measures.

**SECONDARY OUTCOMES:** Reduction in the size of the ulcer, improvement in venous insufficiency, and patient-reported quality of life outcomes were the secondary outcome measures of our study.

**DATA ANALYSIS:** SPSS version 26 was used for the statistical analysis. The categorical demographic variables were reported using frequency and percentages while continuous variables were assessed by reporting means and standard deviation. Shapiro Wilk test was utilized to determine the normality of continuous variables. The association between categorical demographic variables and primary outcome were determined using chi square test. A p value of less than 0.05 was considered as statistically significant.

## RESULTS

**PATIENT DEMOGRAPHICS:** The study included 33 individuals aged 40-50, with a mean age of  $43 \pm 5$  years. The gender distribution was 19 men 57.6% and 14 women 42.4%. Manual labourers 15 patients, 45.5%, office workers 10 patients, 30.3%, and other jobs 8 patients, 24.2% were among the occupations reported by patients. The BMI categories were as follows: normal weight BMI 18.5-24.9 in 10 patients 30.3%, overweight BMI 25-29.9 in 15 patients 45.5%, and obese BMI  $\geq 30$  in 8 patients 24.2%. Before intervention, the ulcers mean duration was of  $10 \pm 4$  months. The lower leg was the most prevalent ulcer site 20 patients, 60.6%, followed by the ankle 10 patients, 30.3% and the foot 3 patients, 9.1%. Sixteen ulcers 48.5% were placed

laterally, whereas seventeen 51.5% were located medially.

**Table 1: Patient Demographics**

Demographics	Frequency and Percentage
<b>Gender</b>	
Male	19 57.6%
Female	14 42.4%
<b>Occupation</b>	
Manual Laborer	15 45.5%
Office Worker	10 30.3%
Other Occupations	8 24.2%
<b>BMI Categories</b>	
Normal Weight	10 30.3%
Overweight	15 45.5%
Obese	8 24.2%

## ULCER CHARACTERISTICS:

Before therapy, ulcers lasted an average of  $10 \pm 4$  months. The ulcers were primarily found on the lower leg 60.6% and ankle 30.3%. 48.5% of the ulcers were laterally situated, while 51.5% were medially positioned. Ulcers averaged  $4 \pm 1$  cm in diameter.

**Table 2: Distribution of Ulcer Characteristics:**

Ulcer Characteristics	Frequency and Percentage
<b>Duration months</b>	$10 \pm 4$
<b>Location Site</b>	
Lower Leg	20 60.6%
Ankle	10 30.3%
Lateral	16 48.5%
Medial	17 51.5%
Mean Diameter cm	$4 \pm 1$

## IMPROVEMENT IN VENOUS ULCER

By the end of the one-year follow-up period, 26 patients 78.8% had fully healed, indicating a significant improvement in ulcer status. Three patients 9.1% had incomplete healing, with ulcers showing moderate improvement but not fully healing. Four patients 12.1% had unhealed ulcers, indicating no progress during the research period. Ulcer recurrence was reported in one patient 4% who had

previously healed ulcers. The healed ulcers had an average size reduction of  $80\% \pm 5\%$ . The average time for healing was  $14 \pm 3$  weeks.

Patient-reported outcomes showed a significant improvement in quality of life ratings, with an average increase from 40.5 to 75.2 on the quality of life questionnaire, emphasizing the treatment approach's overall value.

**Table 3: Improvement in Venous Ulcer**

Improvement Parameters	Frequency and Percentage / Average Value
Complete Healing	26 78.8%
Incomplete Healing	3 9.1%
Unhealed Ulcers	4 12.1%
Recurrence	14%
Percentage Reduction in Ulcer Size	$80\% \pm 5\%$
Time to Healing weeks	$14 \pm 3$
Quality of Life Score	Mean increase from 40.5 to 75.2

### COMPLICATIONS AND SIDE EFFECTS

Minor allergic reactions 2 patients, 6.1%, superficial thrombophlebitis 1 patient,

3.0%, and changes in skin pigmentation 1 patient, 3.0% were among the complications. All issues were treated conservatively, with no serious negative consequences.

**Table 4: Complications and Side Effects**

Complications and Side Effects	Frequency and Percentage
Minor Allergic Reactions	2 6.1%
Superficial Thrombophlebitis	1 3.0%
Skin Pigmentation Changes	1 3.0%

### ASSOCIATION OF ULCER HEALING TIME WITH DIFFERENT VARIABLES

Older patients  $>45$  years had substantially longer healing durations for ulcers, with an average of  $16 \pm 4$  weeks compared to  $12 \pm 2$  weeks in younger patients  $p < 0.05$ . Large ulcers  $\geq 5$  cm took  $18 \pm 5$  weeks to heal, while tiny ulcers  $<5$  cm took  $10 \pm 2$  weeks  $p < 0.01$ . Higher BMI categories overweight and obese also led to delayed healing. While manual labourers had longer recovery periods than office workers and other occupations, the difference was not statistically significant.

**Table 5: Association of Ulcer Healing Time with Different Variables**

Variables	Subcategories	Mean Healing Time weeks	P-value
Age	$<45$ years	$12 \pm 2$	0.03
	$>45$ years	$16 \pm 4$	
BMI Category	Normal Weight	$10 \pm 2$	0.001
	Overweight/Obese	$18 \pm 5$	
Ulcer Size	Small $<5$ cm	$10 \pm 2$	0.005
	Large $\geq 5$ cm	$18 \pm 5$	
Occupation	Manual Laborer	$14 \pm 7$	0.75
	Office Worker	$12 \pm 2$	

### DISCUSSION

This two-year prospective study evaluated the clinical effects of compression therapy combined with ultrasound-guided foam

sclerotherapy in the treatment of venous ulcers. Our study included 33 patients, with an average age of  $43 \pm 5$  years. The majority of ulcers were seen on the lower

leg, and on medial side. The findings show a considerable increase in ulcer healing, with 78.8% of ulcers fully healed at the end of the follow-up period, a significant reduction in ulcer size, and an improvement in patient quality of life.

Our findings showed that 78.8% of patients had completely healed their venous ulcers at the conclusion of the one-year follow-up period, which is consistent with earlier research demonstrating the efficacy of compression therapy combined with ultrasound-guided foam sclerotherapy. A study conducted by Toni Pihlaja and colleagues assessed the outcomes of foam sclerotherapy at three different intervals, the results of which demonstrated that the completely healed ulcers at one month post treatment were 108 patients 81% ,131 98% at one year follow up while 12392% patients had completely healed ulces when assessed at two years post intervention .<sup>17</sup> A much higher rate of healing in 3085.7% was reported by weber et al in a comparative study between the outcomes of endovenous laser ablation and ultrasound guided foam sclerotherapy.<sup>18</sup> Our study found an average healing duration of  $14 \pm 3$  weeks, which is comparatively higher than the 10-weeks average reported by Zeyada et al. 2022.<sup>19</sup> Another study conducted in Finland 2020 also reported the median time of healing to be 2.3 months approximately 10 weeks.<sup>20</sup> Differences in ulcer severity, the type of sclerosing agent utilized, and the post-procedure care could all be contributing factors to variations in healing rates and healing duration among different studies. These consistent positive findings demonstrate the efficacy of foam sclerotherapy guided by ultrasonography in the management of venous leg ulcers. In consistent with our findings of ulcer recurrence rate 1 4% ,Pang et al 2010 and Zhu et al 2020 also reported similar recurrence rates of 4% and 3%.<sup>21,22</sup>

Several processes that address the underlying pathophysiology of chronic

venous insufficiency are responsible for the improvement of venous ulcers during foam sclerotherapy. In order to improve sclerosing agent contact and efficacy with the venous walls, foam sclerotherapy entails injecting the agent in a foamed form, usually polidocanol or sodium tetradecyl sulfate.<sup>23</sup> By displacing blood within the vein, the foam enables the sclerosant to directly target the endothelium lining. This causes endothelial damage, which is followed by an inflammatory reaction and fibrosis, which ultimately causes the treated vein to obliterate.<sup>24,25</sup> Foam sclerotherapy decreases venous hypertension and enhances venous return by sealing up incompetent veins, which is essential for halting the development and symptoms of venous ulcers. The extravasation of inflammatory mediators and proteins that aid in the development and maintenance of ulcers is reduced as a result of this drop in venous pressure. Furthermore, enhanced venous circulation facilitates wound healing by enhancing the transport of nutrients and oxygen to the injured tissues.<sup>26</sup> Together, these benefits support re-epithelialization, lessen ulcer size, and eventually aid in ulcer healing. Thus, these underlying mechanisms can account for the clinical effects we observed in our study.

Our study's complications included minor allergic reactions in 6.1% of patients, superficial thrombophlebitis in 3.0%, and changes in skin pigmentation in 3.0% of the patients. In contrast, a study by Thomasset et al. 20 that included 126 patients with UGFS showed higher problems. Skin staining occurred in 28% of cases, superficial thrombophlebitis in 18%, discomfort in 14% of cases, and skin blistering in 1% of cases.<sup>27</sup> All complications in our study were addressed conservatively with no major side effects, which is consistent with the conservative management measures indicated in the literature. The absence of serious negative

outcomes adds to the safety profile of this combined therapy strategy.

According to our research, the average healing time for venous ulcers was shown to be substantially longer in older patients >45 years than in younger patients  $12 \pm 2$  weeks;  $p < 0.05$ . Our study also showed that higher BMI categories—overweight and obese—were linked to longer healing periods. These results are consistent with earlier study by Joseph D. Raffetto 2020, which found that aging-related reductions in immune system and cellular regeneration result in longer healing durations in older people. The study also highlighted some other factors responsible for delayed healing of venous ulcers including obesity, nutritional deficiencies, cooler temperatures, previous venous disease and increased wound area.<sup>28</sup> Similar to a study conducted in 2020, the results of which illustrated that larger ulcer size is a predictor of delayed healing due to increased tissue damage and greater need for revascularization, large ulcers  $\geq 5$  cm in our study took  $18 \pm 5$  weeks to heal, whereas smaller ulcers  $< 5$  cm healed in  $10 \pm 2$  weeks  $p < 0.01$ .<sup>29</sup>

The small sample size and single-center methodology of this study could limit the generalizability of the results. Additionally, long-term outcomes like ulcer recurrence and persistent improvements in quality of life may not be sufficiently captured during the follow-up period. Potential biases could affect the outcomes, such as patient adherence to treatment plans and subjective reporting of quality of life. To confirm and build on these results, future investigations should concentrate on multicentre trials with larger and more varied populations as well as longer follow-up times. Developing advanced imaging techniques and investigating molecular and genetic markers that impact therapy response could improve individualized treatment plans for venous ulcers.

## CONCLUSION

The results of this study concluded that, treating venous ulcers with compression therapy and ultrasound-guided foam sclerotherapy together significantly improves healing rates, reduces ulcer size, and enhances patient quality of life. The beneficial result of this study encourages the use of this combination therapy strategy in clinical settings for improved patient care.

**ETHICS APPROVAL:** The ERC gave ethical review approval.

**CONSENT TO PARTICIPATE:** written and verbal consent was taken from subjects and next of kin.

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## AUTHORS' CONTRIBUTIONS:

All persons who meet authorship criteria are listed as authors, and all authors certify that they have participated in the work to take public responsibility of this manuscript. All authors read and approved the final manuscript.

**CONFLICT OF INTEREST:** No competing interest declared

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