

## Ultrasound guided sclerotherapy injection of subulcer venous plexus for treatment of chronic venous ulcer

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### ABSTRACT

**Objectives:** Venous hypertension contribute to venous ulceration. We sought to describe patient characteristics and procedural factors that impact rates of sub ulcer venous plexus (SUV) thrombosis through injection with ultrasound-guided sclerotherapy (UGS) for the healing of venous ulcers without axial reflux. **Material and Methods:** Retrospective review of UGS of SUV injections from 2/2018–9/2018 identified 47 treated venous ulcers in 47 patients. Patients had no other superficial/axial reflux and were treated with standard wound care and compression therapy for three months. Ultrasound was used to screen for venous plexus beneath and near ulcer(s), superficial to deep fascia, and these were injected with polidocanol foam and assessed for thrombosis. Demographic data, comorbidities, treatment details and outcomes were analyzed. Univariate and multivariable modeling was performed to determine covariates predicting SUV thrombosis and ulcer healing. **Results:** 47 patients with active ulcers for an average of 8 months with compression therapy prior to subulcer plexus treatment had an average age of 44 years, were 85% male and 78.7% had a history of DVT. Ulcers were treated with SUV injections, with average successful closure rate of 85%. Of 47 ulcers, 38 patients (80.9%) healed ulcers, while 9 patients (19.1%) had non-healed ulcer(s) in mean follow-up of 3 months. Patients that healed ulcers had an SUV closure rate of 97.4 % vs. 33.3% in patients who did not heal ( $P<.001$ ). Multivariate models demonstrated initial ulcer size and ulcer duration negatively predicted thrombosis of SUV. Multivariate model for ulcer healing found complete SUV thrombosis was a positive predictor ( $P=.001$ ), while repeated injection sessions was a negative predictor ( $P=.007$ ). **Conclusions:** Thrombosis of SUV with UGS increases venous ulcer healing in a difficult patient population. Complete closure of all SUVs in an ulcerated limb was the only predictor of ulcer healing. The failure of complete closure after first session have decreased rates of SUV thrombosis with UGS.

**Keywords:** Venous ulcer, ultrasound guided, sclerotherapy injection.

### INTRODUCTION

Venous ulcers are associated with a significant disability and socioeconomic impact with a prevalence 1–1.5% of the population.<sup>(1)</sup> Compression therapy is one of the essential components for promoting ulcer healing.<sup>(2)</sup> In a systematic review of the effect of compression bandaging on venous ulcer healing, demonstrated that compression is associated with an ulcer healing rate of 60–80%.<sup>(3)</sup> However, there are other modalities when applied to the venous ulcer may have an accelerating effect on ulcer healing rate such as foam sclerotherapy of perforating veins.<sup>(4,5)</sup>

In our study, the purpose is to describe the effect of sub ulcer venous plexus (SUV) closure using ultrasound guided sclerotherapy (UGS) and how this impacts healing of venous ulcers. In addition, suggesting data on the predictors of successful UGS of SUV and its impact on ulcer healing rate.

### PATIENTS AND METHOD

Forty seven patients assessed by complete history, physical and venous duplex ultrasound (US). Patients with reflux of deep or superficial system excluded. Also, presence of acute thrombosis or patients on anticoagulation did not

included in this study. Venous plexus in the vicinity of the ulcer were considered pathologic.

#### **Ultrasound-Guided Sclerotherapy Technique**

Ultrasound-guided sclerotherapy injections were performed by vascular surgeons using Samsung C3. Foam was prepared using the Tessari method with a 4:1 air: sclerosant mixture.<sup>(6)</sup> Under direct ultrasound visualization, 3% polidocanol (POL) sclerosing agent was utilized and 23-gauge needle was inserted into the varicosities around ulcer. The skin surrounding the ulcer and injection site was massaged to move the foam into the perforator as well as into adjacent varicosities. Under dynamic imaging of ultrasound, foam sclerosant was seen filled the subulcer venous plexus, then pressure was applied at the injected area for at least 5 minutes with an ultrasound probe. The surrounding injected varicosities were imaged again to ensure complete sclerosis.

Less than 10 cc of foam sclerotherapy was used per injection session to limit the post injection complications. Patients may need more than one injection sessions scheduled to insure complete closure of SUV. Immediately following the injection, deep venous system were checked to ensure they were clear of foam. Patients injected in supine position, compression was applied at the injected area and they were allowed to ambulate for 20 minutes immediately after session. Compression left in place for 24 hours after that the ulcer care and compression therapy were resumed.

#### **Follow-up**

Patients were seen weekly after treatment by a duplex ultrasound to evaluate for thrombosis of the injected SUV, rule out deep venous thrombosis and assess for other non-closed SUV. The number of complete ulcer healing group (H)

and non-healed group (NH) within three months post injection were recorded. After complete ulcer healing of (H) group, patients were instructed to continue compression stocking.

Phone contact follow up for six months with patients to ensure that no new ulcers developed.

## **RESULTS**

Analysis of UGS injections of SUV from February 2018 to August 2018 identified 47 venous ulcers in 47 patients who had compression and standard wound care for an average of three months prior to SUV ablation. The prevalence of ulcer among male more than female (85% in comparison to 15% respectively) at mean age 44 year old. In 78.7% of patients had past history of deep venous thrombosis and suffering from manifestation of venous hypertension.

Complications post injection were five cases, two with cellulitis, another two with superficial thrombophlebitis (STP) and one patient with post procedure deep vein thrombosis (DVT) presented as solitary posterior vein (PT) thrombosis. It was short occlusion posterior tibial vein thrombosis. In this patient, he was placed on 325 mg/day aspirin, with 100% recanalization of their short-occlusion thrombosis on follow-up duplex. Cellulitis and superficial thrombophlebitis (4 other injection complications) were seen in 4.1 % per each

Of 47 patients, 38 patients (80.9%) had healed ulcers (Group H), while 9 (19.1%) never healed completely (Group NH) at last follow-up visit after three months (Table I). Mean initial ulcer size was 9 cm<sup>2</sup> in Group H vs. 70 cm<sup>2</sup> in Group NH (p=.10). Mean ulcer duration before commitment of injection was 6 months in Group H vs. 16 months in Group NH. show (Table 1).

**Table 1: Distribution of the studied cases according to different parameters (n=47)**

	No. (%)
<b>Sex</b>	
Male	40 (85.1%)
Female	7 (14.9%)
<b>Age (years)</b>	
≤45	21 (44.7%)
>45	26 (55.3%)
Median (Min. – Max.)	46 (24 – 60)
Mean ± SD.	44.8 ± 8.5
<b>Post thrombotic</b>	
Negative	10 (21.3%)
Positive	37 (78.7%)
<b>Mean duration of ulcer (months)</b>	
H group	6 months
NH group	16 months
<b>Size mean (cm)</b>	
H group	9
NH group	70
<b>Healing &lt;3m duration</b>	
Healed	38 (80.9%)
Non healed	9 (19.1%)
<b>Complication</b>	
Without	42 (89.4%)
With	<b>5 (10.6)</b>
Cellulitis	2 (4.3%)
STP	1 (2.1%)
Solitary PT	2 (4.3%)
<b>No. of sessions</b>	
One session	19 (40.4%)
More than one session	28 (59.6%)
Median (Min. – Max.)	2 (1 – 3)
Mean ± SD.	1.9 ± 0.9
<b>SUV closed &gt;3m</b>	
Failed closure	7 (14.9%)
Successful closure	40 (85.1%)

### Subulcer venous plexus injection results

An average of 10 cc foam was used per session. Polidocanol was used in concentration of 3%. There was an 85.1% overall SUV closure rate after 3 month post injection. Show **Figure 1**. SUV Thrombosis occurred in 97.4% of injections for Group H vs. 33.3% of the injections for Group NH ( $p < 0.001$ ) at the end of follow-up. All cases with non-healed group (100%) need repeated session of sclerotherapy before complete SUV closure in three patients only (33.3%) out of nine. show (**Table 2**).

Half of patients (19) in H group, complete SUV thrombosis occurred after single sclerotherapy injection. Nearly the other half (47.4%) need one or two subsequent sessions to close SUV i.e. of healed ulcers, 50% required a single SUV injection. Only one case failed to close plexuses even after repeated three times of injections (2.6%). Compared to group NH, where 6 out of 9, subsequent injections were unsuccessful (66.7%) ( $p < .001$ ) as shown in **Table 3**. The mean duration time of venous ulcer before injection was 16 months in NH group in comparison to 6 months in H group.



**Fig 1:** Ulcer healed after SUV injection. (a) Before injection, (b) after injection, (c) Ultrasound guided sclerotherapy of SUV

**Table 2: Relation between healing <3m duration with No. of sessions and SUV closed >3m (n=47)**

	Healing <3m duration		χ <sup>2</sup>	FE p
	Healed (n=38)	Non healed (n=9)		
<b>No. of sessions</b>				
One session	19 (50%)	0 (0%)	7.554*	0.007*
More than one session	19 (50%)	9 (100%)		
<b>SUV closed &gt;3m</b>				
Closure failed	1 (2.6%)	6 (66.7%)	23.540*	<0.001*
Successful closure	37 (97.4%)	3 (33.3%)		

χ<sup>2</sup>: Chi square test FE: Fisher Exact

p: p value for associated healing <3m duration and two categories

\*: Statistically significant at p ≤ 0.05

**Table 3: Relation between No. of sessions and SUV closed >3m (n=47)**

	No. of sessions		χ <sup>2</sup>	FE p
	One session (n=19)	More than one session (n=28)		
<b>SUV closed &gt;3m</b>				
Closure failer	0 (0%)	7 (25%)	5.581*	0.032*
Successful closure	19 (100%)	21 (75%)		

χ<sup>2</sup>: Chi square test FE: Fisher Exact

p: p value for associated No. of sessions and SUV closed >3m

\*: Statistically significant at p ≤ 0.05

## DISCUSSION

In spite of the efficacy of compression therapy for treatment of venous ulcer has been proven, a sector of treated patients failed to heal these ulcers completely.<sup>(7-11)</sup> For ulcers that persist more than three months, minimally invasive elimination of plexus of veins near the ulcer increases healing rates with few wound complications and high rates of technical success. In comparison to ablation of venous ulcer perforators that need instrumentation into or near the ulcer, this procedure is difficult to master and does not close the surrounding varicosities fed by perforator.<sup>(12-14)</sup>

Recently, percutaneous ablation of incompetent perforator veins associated with venous ulcer has been advocated by ultrasound-guided sclerotherapy (UGS). Masuda et al demonstrated good results with low rates of complications by using UGS for IPV treatment.<sup>(15)</sup>

Perforators thermal ablation has a high closure rate (approximately 80– 90%).<sup>(16-18)</sup> Guex et al demonstrate a comparable 90% occlusion rate after three or fewer sessions of sclerotherapy.<sup>(19)</sup> Ultrasound-guided subulcer venous plexus injection is attractive in this therapy and can be used to eliminate multiple perforators and their associated varicosities in one sitting. It is rapidly performed and is technically straightforward. Unlike perforator ablative techniques, SUV sclerotherapy is able to be performed virtually 100% of the time. Many series of perforator ablation techniques appear to report that not all attempts at cannulation and ablation of pathological perforators has been successfully completed. Additionally, USG sclerotherapy is less expensive. Previous studies of UGS have demonstrated thrombosis rates after 3 months varying from 69% to 96%, while follow-up studies at 1 to 2 years demonstrated rates of 53% to 80% in great saphenous veins and varicose veins.<sup>(20)</sup> Little work has been done to illustrate the effect of UGS on ulcer healing when performed on patients without other venous pathologies.

Our study population consisted of patients who had failed compression therapy for at least three months, and had no superficial venous reflux. In this very difficult population, SUV thrombosis was achieved in 97.4% of H group

and 33.3% of NH group. This indicates closure of SUV has high predictive value of ulcer healing.

Previous work has demonstrated decreased thrombosis after UGS in patients with ulcer in comparison to GSV.<sup>(15)</sup> Physiologic reasons for a decrease in successful SUV thrombosis in comparison to axial veins includes that varicosities around ulcer are high-flow vessels with multiple feeding perforators and elevated venous pressure. In addition most of these patients were on anticoagulant that decrease thrombosis rate by 20%.

Each ulcer averaged 2.67 injections. Repeated injections were performed for incomplete thrombosis of initial injection. Half of patients in H group had complete SUV closure after only one UGS session in comparison to NH group through all patients need more than one session. Precisely speaking, about two thirds of NH did not closed after three UGS injections. This could be attributed to high venous pressure in this category with early recanalization. This likely reflects two potentially overlapping populations; patients with many perforators in the ulcerated limb who required several sessions to safely treat these veins, and patients who had a lower rate of perforator thrombosis. Regardless, both groups represent more severe venous and perforator disease. We found that repeated treatments had a success rate of 80%. Although this was lower than the initial injection thrombosis rate of 50% ( $p=0.007$ ), ulcer healing increased with successful thrombosis of SUV.

Thus, we endorse continued SUV injection until thrombosis is achieved, as this was the most significant predictor of ulcer healing and ulcer healing was achieved in more than 80% of patients.

Our incidence of DVT was low and comparable to other known studies.<sup>(15,21-23)</sup> Side effects of SUV include induration, and pain in the majority of cases, while cellulitis and phlebitis occur in the minority of cases (two patients each).<sup>(24,25)</sup>

However, predictably large initial ulcer area demonstrated a lower chance of ulcer healing, even with successful SUV thrombosis (cases).<sup>(26)</sup> Ulceration with long-term follow-up additionally speaks to the nature of new appearing perforating veins at-risk areas, or the occurrence of late recanalizations. This study has limitations. The most important is the largely retrospective nature

of the review. Variances in long-term follow-up have prohibited standardized healing curves. Small sample size, combined with variations in initial ulcer sizes precluded cumulative analysis of healing rates of all ulcers. Due to the inconsistency of quality of life data being collected on patients, it was not valuable in our current analysis.

It was found that there was a significant relation between duration and initial size of the ulcer. The long duration of ulcer and larger size consumed long duration to healing, there was a positive correlation between duration of ulcer and the duration of healing, also the size of ulcer effect on the duration of healing, the increasing in number of session decrease the duration of healing.

## CONCLUSIONS

In patients who fail a 3-month trial of compression therapy of venous ulcer, our experience demonstrates both the feasibility and effectiveness of sub ulcer venous plexus ablation. We recommend ultrasound-guided foam injection of subulcer venous plexus. It was found to be safe and to predict ulcer healing. Thrombosis of SUV was the most powerful predictor of ulcer healing in our analysis in addition to other factors such as initial ulcer size and ulcer duration. SUV closure may require more than one session of injection and it is associated with low complication rates.

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