Compression versus sclerotherapy for patients with isolated refluxing reticular veins and telangiectasia: a randomized trial comparing quality-of-life outcomes

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Abstract

***Objective*:** To prospectively study quality-of-life (QoL) benefits comparing compression stockings to sclerotherapy in subjects with symptomatic reticular veins and telangiectasia.
***Methods*:** Fifty-eight consecutive female patients with normal saphenous and deep venous systems and venous dysfunction score (VDS) ≥ 4 were randomized to either sclerotherapy ($N = 29$) or thigh high 20–30 mmHg compression stockings ($N = 29$). Following a trial of compression, subjects in the compression arm were eligible to crossover to the sclerotherapy arm. Patient-reported QoL data were acquired using a modified Aberdeen Varicose Vein Questionnaire in five stages, initial severity (T_0), following compression trial (T_1), after reticular vein sclerotherapy (T_2), approximately three months after sclerotherapy for telangiectasia (T_3) and the 12-month mark (T_4).
***Result*:** For patients in the compression arm, four key symptoms including aching, pain, leg cramps and restlessness were significantly reduced, while patients in the sclerotherapy arm of treatment reported broad symptom relief in all key symptoms assessed.
***Conclusion*:** Isolated refluxing reticular and telangiectatic vein disease may cause QoL impairment in select patients and represent far more than a cosmetic concern. Compression therapy offers relief of aching, pain, leg cramping and restlessness in patients with isolated refluxing reticular veins and telangiectasia. Sclerotherapy of reticular veins offers a statistically superior broad spectrum relief of symptoms, while additional sclerotherapy of residual telangiectasia in this cohort demonstrated additive relief of aching and pain. Symptom assessments at 12 months suggest ongoing symptom relief following sclerotherapy.

Keywords: varicose veins; reticular veins; telangiectasia; sclerotherapy; sodium tetradecyl sulphate

Introduction

Our hypothesis suggests that signs and symptoms of venous hypertension, such as oedema and pain, depend more upon the reflux burden of an abnormal venous network, independent of vein size or nomenclature. Many physicians believe that telangiectasia and reticular veins are 'purely cosmetic', and that only refluxing axial and saphenous tributary varices contribute to venous symptomatology.[1] Others believe that the magnitude of symptoms is not dependent on size of the refluxing vessels, and that telangiectasia and reticular veins may cause symptoms identical to gross varicose veins.[2] Large-scale epidemiology studies evaluating symptomatology caused by small cutaneous veins and chronic venous insufficiency have offered

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mixed results.[3,4] Quality-of-life (QoL) impairment has been shown to be evident in patients with concomitant venous disorders, such as presence of oedema, skin changes and ulcers.[5,6] Reflux has been identified in reticular veins of the lateral thigh.[7] Sclerotherapy of isolated dermal venous complexes has been shown to reduce symptoms such as leg pain, swelling, leg cramping, restlessness and fatigue.[8–10]

The purpose of this study was to prospectively identify and compare QoL parameters between compression therapy and sclerotherapy in patients with isolated symptomatic surface disease and well-established symptoms suggestive of venous hypertension.

Methods

Patients

Over a 16-month period, over 900 consecutive patients presented to three well-established phlebology specialty practices. Patients with a venous dysfunction score (VDS) $\geq$4, isolated dilated and ectatic reticular veins and telangiectasia, without deep, axial or saphenous tributary reflux, which nevertheless had symptoms suggestive of venous hypertension were considered for inclusion. Exclusion criteria were age less than 18, allergy to Sotradecol™, presence of overlapping pain syndromes and prospective pregnancy during the study period. Sclerotherapy in the preceding two years and recent therapeutic compression therapy were additional exclusion criteria. Fifty-eight patients (6%) met the entry criteria. Risks, benefits, study details and alternative treatment options were described and written consent obtained prior to randomization.

Procedure

Detailed venous history and physical exam were obtained, and bilateral whole leg venous mapping was performed at the time of consultation.[11] Particular attention was paid to the ultrasound scanning, assuring the absence of deep venous or saphenous vein reflux. All duplex scans were performed by credentialled vascular ultrasound personnel. Each practice site was exclusively dedicated to managing the spectrum of venous diseases and highly accomplished in providing sclerotherapy services. Identical sclerotherapy training minimized potential variation in treatment technique or clinical outcomes.

Randomization

The random number series developed by Microsoft Excel for windows (Microsoft Inc, Redmond, WA, USA) facilitated treatment arm allocation using the sealed envelope technique. Each envelope was numbered sequentially and sealed with the contents of random assignment. The treatment arm became known to the patient and provider simultaneously, following a discussion on protocol and compliance requirements of each treatment arm. The study design and treatment methods represent accepted care for this element of disease. Formal Institutional Review Board (IRB) review was not conducted.

Patient flow

Patients randomized to the compression arm were fitted into thigh-high stockings (Jobst Opaque style 20–30 mmHg; BSN Medical Inc, Rutherford College, NC, USA). All hosiery was applied by nursing personnel to verify proper fitting. Each patient received education for the ease of donning and the importance of compliance during the trial. Custom garments were unnecessary. Compression therapy was implemented for a minimum of six weeks to meet an arbitrary duration consistent with many insurance carrier guidelines. The stockings were to be donned upon beginning the day and removed at bedtime. Compliance was assessed by phone interview. Subjects found non-compliant with compression were dropped from the study, although initial severity data were reserved for analysis. One hundred percent of the patients completing the compression trial crossed over to the sclerotherapy arm. Once the compression trial was complete, no further compression was utilized throughout the remainder of the trial.

Patients randomized to the sclerotherapy arm and crossover participants received staged treatment using 0.1% or 0.2% Sotradecol™ (Bioniche Pharma, Lake Forest, IL, USA) diluted from stock 3% solution in 0.9% sodium chloride solution. The specific concentration employed was dependent on the size of the vessels and skin type. Liquid sclerotherapy was performed exclusively. A proximal to distal approach was implemented, treating refluxing vessels of the thigh before those below the knee. Initial sclerotherapy sessions addressed refluxing reticular vein complexes only. Every attempt was made to avoid direct injection of telangiectasia and manipulation of chemical into adjacent telangiectasia during this first sclerotherapy phase. Following the completion of reticular vein management and resolution of bruising, residual

telangiectasia were treated with additional sclerotherapy. Patients were monitored for 12 months following the initial enrollment date.

Outcome assessment

QoL parameters were sequentially recorded using the modified Aberdeen Varicose Vein Questionnaire (AVVQ) (Figure 1). Patients were instructed to answer the questionnaires judging the interval severity and prevalence of symptoms following each stage of therapy. The severity ranges in the questionnaires were as follows: 1 – rarely; 2 – occasionally; 3 – common symptoms; 4 – severe; and 5 – critically severe. Limbs without symptoms were recorded as 0 or none. QoL parameters were assessed before and after compression therapy and after each stage of the sclerotherapy protocol to yield five potential data points.

Statistical analysis

Descriptive statistics were utilized to assess demographic variables and subgroup analyses using SAS software (SAS Institute Inc, Cary, NC, USA). Matched pair, Student's *t*-tests were applied for testing the mean difference between paired observations to determine variability between treatment

Patient Health Questionnaire - Modified AVVQ

This evaluation is about you and how your physical condition affects the quality of your life. It is a very important component of this study and greatly helps us determine the degree of symptoms you have related to your venous problems. Please check only the most appropriate response for each question. Thank you.

Patient Name: _____ Date: _____

Clinic Location: _____ Physician: _____

Please indicate whether you have any of these symptoms. If no, please write 'no' next to the appropriate boxes if yes, please rank how severe the symptoms have been for you over the past week.

Rankings: ***None = 0, Rarely = 1, Occasionally = 2, Common = 3, Severe = 4, Critically Severe = 5***

Symptom/Concern	*If Yes, Please Rank*
Itching	1 2 3 4 5
Swelling (Ankles and/or Legs)	1 2 3 4 5
Dissatisfaction with Appearance of Legs	1 2 3 4 5
Skin Discoloration	1 2 3 4 5
Aching	1 2 3 4 5
Skin Rash/Eczema	1 2 3 4 5
Night Cramps	1 2 3 4 5
Phlebitis (Tender, Red, Hard, Painful Veins)	1 2 3 4 5
Pain	1 2 3 4 5
Do your legs give you problems when you are at rest? (restlessness sensation)	1 2 3 4 5

Office Use Only

Patient # _____

Figure 1 Modified Aberdeen Varicose Vein Questionnaire

groups as patients progressed through advancing stages of treatment. All statistical analyses were performed independently by a third-party consultant.

Results

Fifty-eight patients were randomized (Figure 2), 29 to the sclerotherapy arm and 29 to the compression arm. Seven patients in the compression arm were lost over the duration of the study, three due to poor compliance with compression and one for personal reasons prior to completing the compression trial. Three additional patients in the compression arm were lost to follow-up after sclerotherapy had been initiated. Two patients in the sclerotherapy arm were lost to follow-up after initiating treatment for reticular veins. One subject was specifically lost due to extreme intolerance to

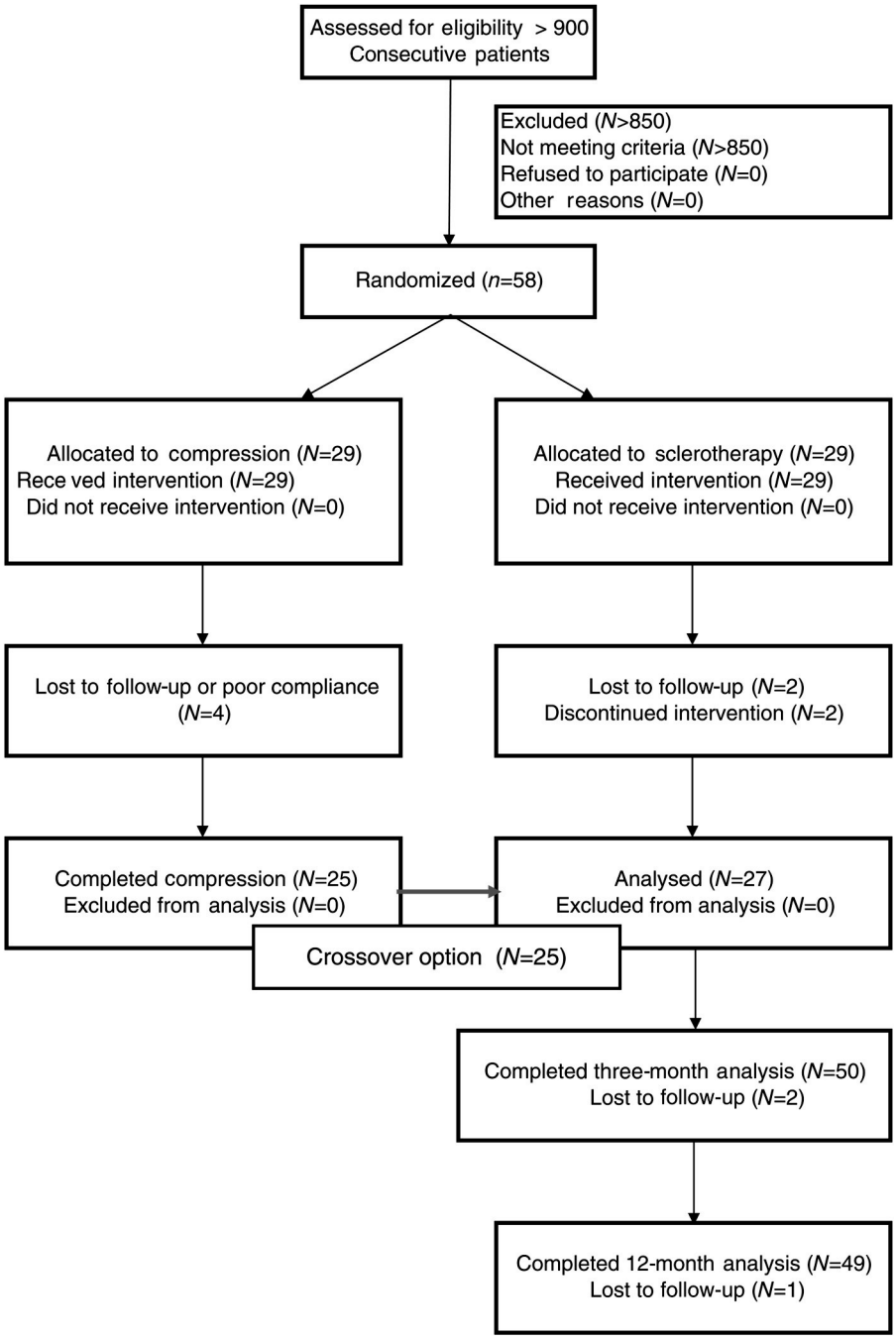

Figure 2 Consort diagram

Table 1 Patient retention chart

	T_0	T_1	T_2	T_3	T_4
Compression arm	29 (100%)	25 (86%)	25 (86%)	23 (79%)	22 (76%)
Sclerotherapy arm	29 (100%)		27 (93%)	27 (93%)	27 (93%)
Pooled data	58 (100%)	25	52 (90%)	50 (86%)	49 (84%)

needles. The patient retention chart (Table 1) demonstrates steady subject commitment in each treatment arm over the course of the study.

Demographic variables between groups are shared in Table 2. All patients were women, Caucasian, and their average age, height, weight and venous dysfunction scores were without significant differences. Similarly, the severity of initial symptomatology between the groups demonstrated homogeneity of the populations under study (Table 3). Initial venous dysfunction scores ranged from four to seven, and a breakdown of the VDS statistics is displayed in Table 4. Over-the-counter analgesic use was documented in nearly 90% of all participants, and the physical finding of oedema was identified in over 40% in each treatment arm. The presence of worsening symptoms with activity suggests an extensive burden of venous disease, and upon regression analysis, VDS severity was shown to directly correlate with the volume of sclerosant required in the reticular vein management portion of the study ($P \leq 0.005$).

The most burdensome symptoms affecting QoL are identified as aching, pain, swelling, leg cramping and symptoms at rest. Figures 3–7 reveal interval changes between each stage of treatment for the major symptoms.

Aching (Figure 3): Compression therapy is shown to offer significant relief ($P < 0.0001$), while sclerotherapy resulted in dramatic relief following the management of reticular veins and the trend was noted through the 12-month assessment (e.g. $P < 0.0001$ and <0.05, respectively).

Table 2 Comparison of group demographics

Demographic variables	Sclerotherapy arm	Compression arm
N	29	29
Age, mean (range)	46.9 (18–71)	43.6 (24–60)
BMI, mean (range)	27.0 (18.8–43.3)	24.9 (17.2–45.8)
Mean VDS (range)	4.7 (4–7)	4.6 (4–7)
Analgesic use (%)	26 (90.0)	25 (86.2)
Oedema (%)	13 (44.8)	12 (41.4)
Pigmentation (%)	2 (6.9)	3 (10.3)

BMI, body mass index; VDS, venous dysfunction score

Table 3 Initial symptom severity

	Compression arm	Sclerotherapy arm	*P*
Itching	1.2	1.3	0.86
Swelling	2.4	2.5	0.81
Appearance	4.2	4.1	0.89
Discolouration	2.9	2.1	0.11
Aching	4.4	3.9	0.15
Leg cramps	2.8	2.7	0.83
Pain	3.4	3.6	0.50
Rest symptoms	3.3	3.1	0.80

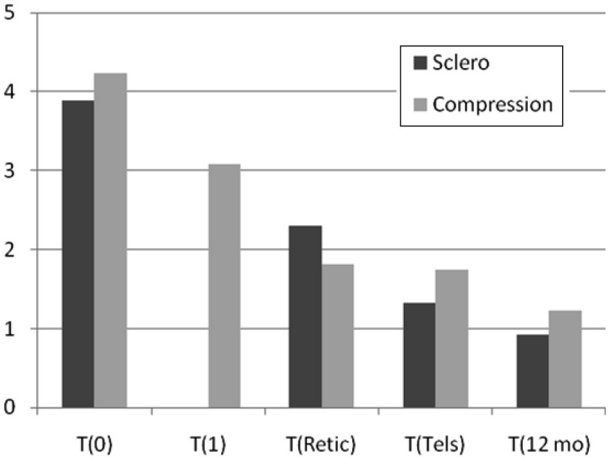

Figure 3 Symptom of aching. This chart demonstrates the stepwise reduction in the symptom of aching, sharing benefits of compression and sclerotherapy from symptoms of severe to rare at the 12-month mark

Table 4 Venous dysfunction score analysis and comparison with the total volume of sclerosant used over the study

VDS severity	*N*	BMI	Age	Analgesic use (%)	Oedema (%)	Venous claudication (%)	Pigmentation (%)	Volume of sclerosant (cc)
4	32	26	43.4	28 (87.5)	3 (9.4)	0%	0%	158
5	20	26.7	47.6	17 (85.0)	17 (85.0)	1 (5.0)	1 (5.0)	158
6	2	26.3	46.5	2 (100)	2 (100)	0%	1 (50.0)	197
7	4	22.6	51	4 (100)	4 (100)	4 (100)	2 (50.0)	208

BMI, body mass index; VDS, venous dysfunction score

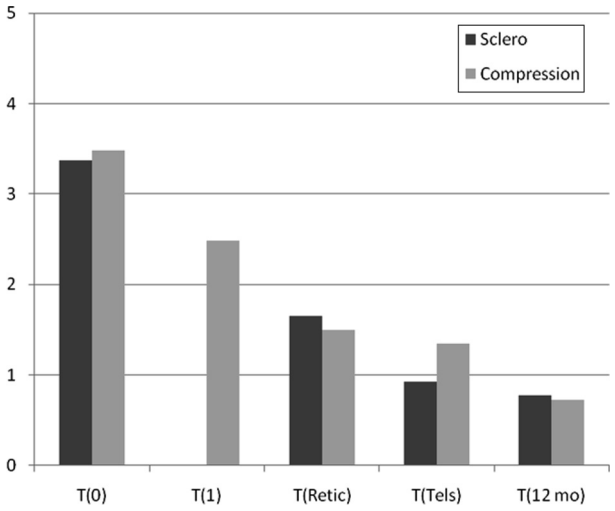

Figure 4 Symptom of pain. This graph demonstrates the stepwise reduction in the symptom of pain from common to severe at initial severity assessment to rare at the end of 12-months

Pain (Figure 4): Patients reported reduction in the severity of pain with compression and sclerotherapy of reticular veins in each treatment arm, ($P = 0.002$ and <0.0001, respectively). Further reduction trends of pain are noted, yet without statistical significance.

Swelling (Figure 5): Although slight improvement was observed, statistical significance was not established with compression alone. In each arm, however, substantial reduction in the symptom of swelling was noted ($P < 0.001$) following sclerotherapy of reticular veins. The three-month trend demonstrated a slight worsening, and yet this was shown to be resolved by the 12-month mark ($P < 0.001$ in each treatment arm).

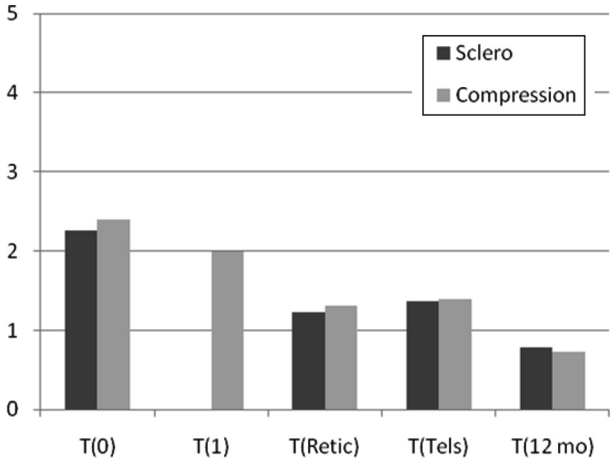

Figure 5 Symptom of swelling. This graph demonstrates the stepwise reduction in the symptom of swelling from occasional to common at initial severity to rare at the end of 12 months

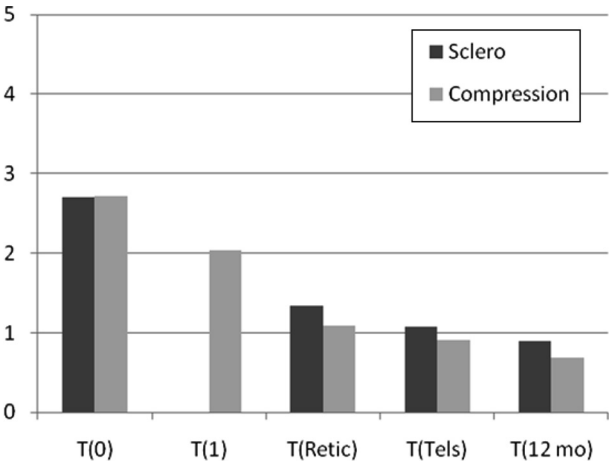

Figure 6 Symptom of leg. cramping. Leg cramping was dramatically reduced early in this trial. Reduction in this symptom continued through the 12-month assessment

Leg cramping (Figure 6): The frequency of leg cramping was reduced with the use of compression ($P = 0.003$). Reticular vein management offered further relief in each treatment arm ($P < 0.05$). Although trend line suggests further reduction in leg cramping, clinical significance is not established in either treatment arm in subsequent stages of therapy.

Symptoms at rest (Figure 7): Restlessness sensations were reduced with the use of compression therapy ($P < 0.05$). Reticular vein management offered further interval relief ($P < 0.05$ in each treatment arm). Favourable interval trends were noted with the management of telangiectasia, with 12-month improvement sustained at a level of significance ($P < 0.05$ in each treatment arm).

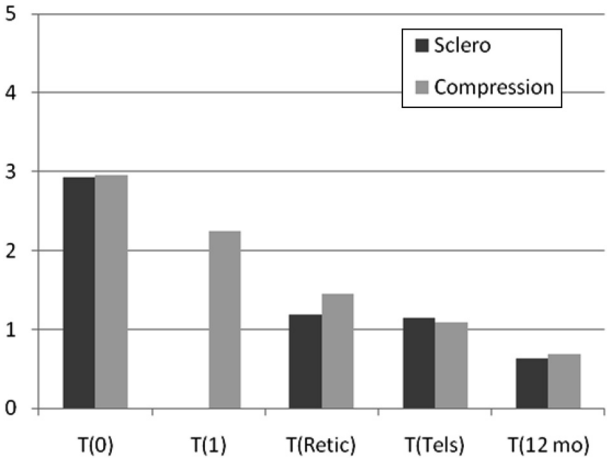

Figure 7 Symptom of restlessness. Sensations of restlessness were shown to progressively improve in each treatment arm over the 12-month period

Pooled data

Similarities between the treatment arms permit pooling of data for a combined cohort receiving sclerotherapy services (Table 5). Reticular vein sclerotherapy offered broad symptom relief when compared with compression therapy (P values each <0.0001). Further treatment of telangiectasia demonstrated additional improvement noted at three months in symptoms of aching, pain and leg cramps ($P < 0.5$). Of the 49 patients completing the sclerotherapy protocol, each major symptom affecting QoL was significantly reduced in severity to non-existent or rare ($P < 0.5$). No major complications were observed.

Discussion

Haemodynamic pathology of venous reflux is identical whether it affects the large saphenous veins or multiple smaller reticular veins and telangiectasia. Venous symptoms adversely affecting QoL parameters may be more common than previously suspected, and severity may not correlate to the size or type of refluxing vessels. This study demonstrates that patients with symptoms suggestive of venous hypertension and presence of isolated refluxing dermal complexes benefit from compression therapy and sclerotherapy. It is known that venous reflux causes an array of well-identified symptoms, and proper therapy to obliterate the responsible refluxing veins is appropriate. The specific aetiology of symptoms is unknown, and yet activation of nociceptors in the microcirculation remains a plausible aetiology.[12]

A patient's perception of pain, pruritis and frequency of leg cramps, or symptoms at rest are subjective in nature. This is the weakness found in any patient questionnaire addressing symptoms that cannot be objectively tested. Initial severity assessment incorporated objective findings including the clinical presence of oedema, focal pigmentation and use of analgesics for leg pain suggestive of symptoms of venous hypertension. Although the global clearance of vessels is an objective measure, a cosmetic outcome was not the focus of this study.

The venous dysfunction scoring system was utilized to identify the most severe cases with isolated refluxing dermal complexes. This score assesses anatomic, clinical and disability parameters. The anatomic score was by design identical in each participant. The clinical component identified those subjects with substantial symptoms and physical findings accompanying this isolated element of venous disease. Many patients may complain of symptoms attributed to reticular veins and telangiectasia, but a VDS score ≥ 4 identify the use of analgesics, and objective findings of oedema, focal pigmentation and disability score. Although venous severity scoring may be used to follow clinical improvement, the range we were using offered limited ongoing utility beyond the initial assessment of venous severity.[13] As patients found substantial relief of pain, swelling and cosmetic appearance following treatment, it is logical to believe that the VDS would approach zero. As symptom resolution was the primary focus of the study, a truncated AVVQ was exclusively implemented to follow sequential symptom severity. Given the broad spectrum of subjective QoL parameters a full AVVQ captures, it was felt that the comprehensive questionnaire was not necessary and that sequential assessment of the symptom component alone would prove more useful. There are a number of different validated systems that follow features of venous disease that change with treatment.[14,15] Arguably the study of reticular veins and telangiectasia is more difficult to objectively follow symptomatic versus cosmetic resolution following treatment.[16] The strength in the tools we employed lies in the fact that we were able to identify patients with substantial symptom severity and physical findings. Although data may be weakened by the use of a subjective questionnaire, the absence of ongoing analgesic use and resolution of swelling substantiates the value of sclerotherapy in managing this element of disease.

Table 5 Pooled symptom severity table and response to sclerotherapy

	Initial severity	Compression therapy	Reticular veins	three-month	12-month
Aching	4.1	3.1**	2.1**	1.5*	1.1*
Pain	3.4	2.5*	1.6**	1.1*	0.8*
Swelling	2.3	2.0	1.3**	1.4	0.8**
Leg cramping	2.7	2.0*	1.2**	1.0*	0.8*
Symptoms at rest	2.9	2.2*	1.3**	1.1	0.7*

The values shown reflects the pooled mean severity for each symptom on a 0–5 scale
*$P < 0.5$, **$P < 0.0001$

There is ongoing discussion about guidelines for clinical studies when studying the effects of compression devices for venous disease.[17] Compliance with compression was a critical component to this study, and yet there is no device to follow compliance in the patients who were randomized to the compression arm. These subjects were followed by telephone to assure that donning was not a problem and emphasized the importance of compliance for participation in the study. Our study population comprised all women with isolated surface disease, predominately vessels that involved the Albanese complexes of the lateral thigh. In order to address symptom benefits from compression, 20–30 mmHg thigh-high garments were employed to provide the greatest benefit if symptoms were truly attributed to isolated refluxing dermal complexes. This is the first study to show symptom relief for this element of disease, and further study may indicate that greater compression may yield proportionately greater symptom control.

Nearly 90% of the selected patients reported significant leg discomfort of such severity that routine over-the-counter analgesics were utilized. Habitual abuse of analgesics may lead to other complications that are often reported and compliance with gradient compression stockings is historically poor.[18,19] These patients have meaningful and consequential symptoms even though they have not developed gross saphenous axial or tributary incompetence. Patients with symptoms and without axial reflux or bulging varicose veins often express dissatisfaction after consultation with a physician who tells them that they only have a cosmetic problem. This preliminary investigation shows that patients with only small-surface reticular veins and telangiectasia may suffer significant deterioration of their QoL and they may abuse over-the-counter analgesics and face frustration in search for palliative treatment. This group of patients may gain temporary improvement of several key symptoms with the use of graduated compression stockings, and longer-term, broad-spectrum benefit may be delivered with definitive sclerotherapy treatment.

Conclusion

Venous reflux causes an array of symptoms, and traditional therapy for this element of disease offers statistically proven symptom relief. Compression stockings can offer relief of aching, pain and cramping in patients with isolated refluxing reticular veins and telangiectasia. Sclerotherapy of these smaller vessels offers superior relief of aching, pain, swelling, leg cramps and presence of symptoms at rest. Sclerotherapy of residual telangiectasia demonstrated even further relief of aching and pain.

Reticular veins and telangiectasia represent a significant part of many Phlebology practices, and may cause QoL impairment in select patients representing far more than a simple cosmetic concern.

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Conflicts of interest: Bioniche Pharma USA (Lake Forest, IL, USA) provided all of the Sotradecol™ stock 3% solution; BSN Medical (Rutherford College, NC, USA) provided compression stocking supplies and financial support for independent statistical analysis.

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