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Comparison of 1% and 3% Polidocanol Foam in Ultrasound Guided Sclerotherapy of the Great Saphenous Vein: A Randomised, Double-Blind Trial with 2 Year-Follow-up. ''The 3/1 Study''

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Objectives. *To compare 1% and 3% POL foam in treating the great saphenous vein (GSV) by ultrasound guided sclerotherapy.*
Design. *Multicentre, prospective, randomised, double-blind trial with 2 year-follow-up.*
Patients and methods. *148 patients with GSV reflux (saphenous trunk diameter 4–8 mm) were randomised to undergo ultrasound guided foam sclerotherapy using either 1% or 3% POL foam in a single session. Foam production was standardised using a sterile disposable syringe kit including sterile air and the Turbofoam® machine. Duplex ultrasonography was used to assess the outcome at 3 weeks, 6 months, 1 year, 18 months and 2 years. The main criterion of success was the disappearance of the venous reflux. The length of occlusion of the vein (only measured at 3 week-echography assessment) was a secondary criterion. Side effects were assessed.*
Results. *74 patients were included in each group.*
The mean volume of foam injected was 4.4 ml for the 3% group and 4.6 ml for the 1% group. After 3 weeks, reflux was abolished in 96% (71 patients) of the 3% group and 88% (68 patients) of the 1% group (NS). The mean occlusion length of the vein was 38 cm for the 3% group and 34 for the 1% group (NS). After 2-years, reflux was absent in 69% of the 3% group and 68% of the 1% group (NS). 14 patients were lost to follow-up at 2 years.
Conclusion. *This study demonstrates equivalent efficacy for 1% POL and 3% POL foam in sclerotherapy of the GSV where the trunk is less than 8 mm in diameter. These data obtained two years of follow-up confirm our previously reported 6 month-follow-up data published in 2005.*
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Keywords: Varicose veins; Sclerotherapy; Foam sclerotherapy; Foam sclerosant; Ultrasound guided sclerotherapy; Polidocanol.

Introduction

Limited clinical evidence supports the use of sclerotherapy in clinical practice.[1,2] Recent enhancements of this technique including ultrasound-guided sclerotherapy (UGS)[3,4] and foam sclerosant agents[5,6] have contributed greatly to the efficacy of this method.[7] As a result UGS is becoming established as a technique in its own right for the treatment of incompetent saphenous veins. A shortage of well-conducted clinical trials and the absence of standardised procedures for sclerotherapy and foam production continue to hinder the process of obtaining a higher-grade recommendation.

In 2003 we published data demonstrating considerable superiority of foam compared to liquid 3% polidocanol (POL) in sclerotherapy of the great saphenous vein (GSV). We observed 85% success rate for a single injection of foam compared to 35% for liquid in abolishing reflux in the GSV.[7,8] These results were confirmed by a Japanese study in 2004.[9] We used the same volume of foam and liquid, but the quantity of active substance was 5 times less for the foam compared to the liquid. Efficacy in obliterating the vein with foam was twice that for the liquid sclerosant.

Compared to liquid sclerosants, the doses of foamed sclerosants should be reduced in volume[10]

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and in concentration. Histological studies performed on human endothelial cells placed in contact with various concentrations of sclerosing liquid and foam concord with this.[11] Endothelial destruction was identical in appearance for concentrations of 0.5% POL foam and 3% POL liquid (1.5 seconds' contact).

The aim of this study is to compare the efficacy of foams made from 1% and 3% POL since this has not been studied systematically. To ensure comparability between sclerotherapists, foam was prepared using the Turbofoam® machine, which was available in each of the 5 investigative centres. A detailed protocol for this randomised trial as well as early results after 6 months of follow-up were published in 2005.[12]

Photograph 1. Numbered ampoules of Aethoxysklerol®.

Methods

This multicentre, prospective, randomised, double-blind trial was sponsored by the Société Française de Phlébologie and carried out in 5 centres. One additional independent centre was responsible for overall data collection and statistics. The study was approved by the Normandy Ethics Committee (registered on 15.05.2003 under No. 2003/015). It complies with the Declaration of Helsinki (1964) according to its latest version (Hong Kong 1989). Patients who gave informed written consent were considered for inclusion in the study.

Pre-calculation of required sample size was undertaken using a Casagrande/Pike calculation formula on the basis of a unilateral superiority trial where 3% would have a success rate of 85% and that 1% would be inferior by at least 20%. This resulted in a minimum sample of 140 patients with alpha = 0.05 and Beta = 0.10. In each centre, a randomization list was created by the statistician and a series of numbered ampoules of Aethoxysklerol® (concentration not indicated) was provided by Kreussler Laboratories (Photo 1). Each treatment was assigned to the patients according to the randomisation list. Statistical analysis was conducted on blinded data and the unblinding was done after writing of the statistical report.

Patients considered for inclusion in this study were of either sex presenting with varices arising from incompetence of the GSV, with or without saphenofemoral junction (SFJ) incompetence. The size of the GSV was limited to those with a diameter of between 4 and 8 mm, measured below the SFJ while the patient was standing. All CEAP classes between C2 and C6 (Ep, As2, Pr) were allowed. Patients presenting a contraindication to sclerotherapy in general and/or to POL in particular were not included. Inclusion and exclusion criteria are shown in Table 1.

The success of treatment was assessed by duplex ultrasonography. Patients were evaluated in the standing position according to the authors' usual practice. Flow was elicited by manual compression of the calf, followed by release. Reflux was considered to be present if reverse flow persisted for 1 or more seconds.

The primary outcome criterion was abolition of venous reflux at 2 years. Interim assessments were undertaken at 3 weeks and absence of recurrence of reflux was checked at 6 months, 1 year and 18 months. The secondary outcome criterion was the length of occluded vein assessed by duplex ultrasonography. This was only measured at the 3 week assessment. The local and systemic complication rates were also recorded as part of the study, including visual disturbance and chest symptoms.

Patients who were found to have residual incompetence of the GSV at the 3-week assessment were allowed to withdraw from further study assessments and resume management of their clinical varices. These were considered to be treatment failures and counted as a treatment failure when analysing the study data.

Foam production

Foam production was obtained using a sterile disposable syringe kit including sterile air and the TURBOFOAM® system (Kreussler Pharma, Wiesbaden, Germany) Photo 2. This machine includes a microprocessor, which standardises the pressure, the speed and the number of movements of the syringes used to produce sclerosant foam.[13] One of the syringes was filled with 2 ml Aethoxysklerol® and 8 ml sterile air giving

Table 1. Inclusion and exclusion criteria − 3/1 Study

Inclusion criteria	Exclusion criteria
➢ Patient of either sex or any ethnic group. ➢ Age between 18 and 80 years, inclusive. ➢ Agreeing to take part in the study and having given written informed consent. ➢ Presenting with incompetence of the GSV: reflux of SFJ + trunk or reflux of trunk of the GSV in the thigh, with or without incompetence below the knee, with a diameter below the SFJ of between 4 and 8 mm inclusive (patient standing). Reflux measured on Doppler ultrasound must be greater than or equal to 1 second. ➢ CEAP classifications authorised: C2 to C6, Ep, AS2, Pr.	➢ Patient presenting a state or history of mental or psychiatric disorder or any factor limiting the ability to take part in the study in an informed and compliant way. ➢ Informed consent not signed. ➢ Patient with incompetence of SFJ of the GSV without trunk incompetence of the GSV at the thigh or trunk incompetence below the knee without trunk incompetence of the GSV at the thigh. ➢ Patient with chronic liver disease. ➢ Renal impairment (creatininemia > 150 micromol/l). ➢ Women who are pregnant or breastfeeding. ➢ Women with a risk of becoming pregnant during the course of treatment (absence of effective contraception). ➢ Material or geographical impossibility of taking part in the study. ➢ Patient with a known progressive malignant disease. ➢ Patient with uncontrolled hypertension. ➢ Patient with cardiac or respiratory failure. ➢ Patient with a personal history of deep vein thrombosis. ➢ Patient with known acquired or constitutional coagulopathy. ➢ Patient intolerant to alcohol or having taken, in the past month, a product blocking the metabolisation of ethyl alcohol (e.g. Esperal). ➢ Patient with a known allergy to Lauromacrogol 400 or Polidocanol.

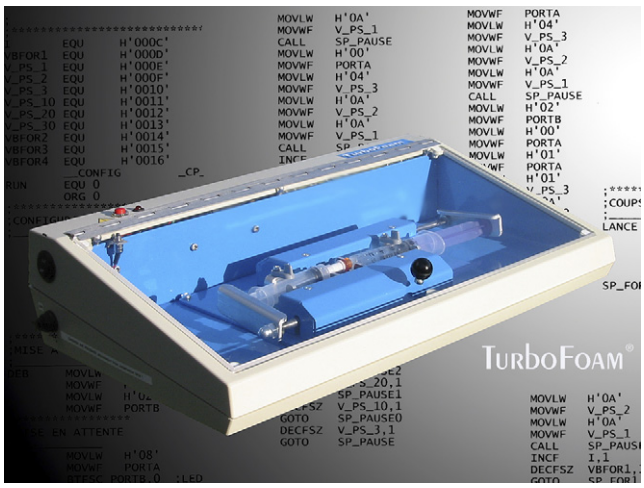
GSV: Great Saphenous Vein.
SFJ: Sapheno-Femoral Junction.

a sclerosant liquid−air mixture of 1 + 4. The characteristics of the foam obtained were assessed in an independent laboratory* using diffuse transmission spectroscopy and the range of bubble size was:

- Aethoxysklerol® 1% and 3%: 70−100 μm 20 seconds after preparing the foam.
- Aethoxysklerol® 1% and 3%: 100−140 μm 40 seconds after preparing the foam.

Treatment

One treatment session with sclerosant foam was carried out, and no further injection of the GSV was allowed during the follow-up period of 2 years. This contrasts with our standard practice of obliterating all varices by a course of sclerotherapy but allows objective assessment of the efficacy of the two strengths of foam. Patients lay supine during treatment. All injections were given under ultrasound guidance and performed using the direct puncture technique.[7,12,13] The first injection (2.5 ml foam) was given at the junction between the upper and middle-third of the thigh. If necessary, up to 2 more injections were allowed into the GSV in the thigh (total foam volume not exceeding 7.5 ml). The development of venospasm in the treated vein and the observation that the vein was completely filled by foam on the ultrasound image was used to judge satisfactory completion of the treatment session. No concomitant treatment was carried out to other varices or saphenous trunks. No special precaution was taken after the injections to prevent foam entering the deep veins or to protect the limb from deep vein thrombosis. No leg elevation, no compression of the SFJ and no ankle dorsiflexion was used. Patients received no special post-operative instructions regarding



Photograph 2. TurboFoam® device.

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exercise or walking. Compression bandages or stockings were not applied to the limb following treatment, in keeping with our usual practice for saphenous trunks. Elastic compression, analgesic or anti-inflammatory drugs were only prescribed if secondary inflammation or painful reactions occurred.

After the initial treatment session, all investigators were invited to provide their own impression of the concentration of the sclerosant which they had injected by completing an item on the report form for each patient. This was an assessment of whether there were any clearly obvious differences of the immediate effects of treatment with 1% or 3% POL foam.

Follow up

Patients were reviewed after 3 weeks for clinical and duplex ultrasound examination. Further clinical and duplex ultrasound examinations were performed every 6 months thereafter for 2 years, unless the patient was withdrawn from further follow-up assessments if the treatment failed to close the GSV. These patients remained in the study as far as the assessment of treatment efficacy was concerned with the outcome recorded in the results as a failure. Additional or alternative treatment was offered to patients in whom the single treatment session failed to obliterate the GSV. At each assessment the presence of venous reflux in the GSV was sought on ultrasonography. We recorded disappearance of the successfully treated GSV when it could no longer be visualised in the thigh by B mode imaging. The diameter of incompetent veins was measured.

Statistics

Data were described by the number of veins or limbs and percentage and quantitative data by mean and standard deviation. Contingency tables were analysed using a Chi squared test and comparison of means anova. The level of statistical significance was taken as 0.05. Data were analysed using SAS software V. 8.2.

Results

Between September 2003 to January 2004, 148 patients were included in the study and were randomly allocated to the treatment groups. Patient characteristics were similar in the two groups (Table 2). 38% of patients presented with isolated truncal reflux and 62% presented with truncal + SFJ reflux and these were evenly distributed in the two study groups. Most patients were treated by one or two injections with only 16% of patients requiring a third injection. Venous spasm was obtained in 99% of cases. One patient experienced flushing and a sensation of tightening in the throat, which resolved spontaneously within a few minutes. No other adverse event was observed.

Table 2. General inclusion data − 3/1 Study

	3% Group ($N = 74$)	1% Group ($N = 74$)
Sex	Women 80% ($n = 59$)	Women 78% (58)
Chi: 0.04 p: N.S.	Men 20% ($n = 15$)	Men 22% (16)
Mean age	53 years S.D. 15	56 years S.D. 14
Anova: 1.82 p: N.S.		
Mean saphenous vein diameter	6.1 mm S.D. 1.3	6.1 mm S.D. 1.3
Anova: 0.06 p: N.S.		
Isolated truncal reflux	39%	36%
Truncal + SFJ reflux	61%	64%
Chi: 0.73 p: N.S.		
Mean injected volumes	4.4 ml S.D. 1.8	4.6 ml S.D. 1.6
Anova: 0.52 p: N.S.		

The investigators' assessment of the strength of sclerosant foam was evaluated after 2 years when unblinding was done. In 71% of cases, the investigators failed to identify the solution which had been used. In 50% of cases the answer was ''no idea'' and in 21% of cases the answer was wrong. The authors are confident that the sclerotherapists were effectively blinded to the treatment that they had given.

All 148 patients were seen again at the 3-week review. Five patients came for an intermediate visit (before follow-up at 3 weeks) for the following reasons:

- pain in the lower limb: 2 cases
- ecchymosis: 1
- inflammation and pain in the thigh: 1 (DVT on D19, discussed below)
- inflammation in the leg with lump (thrombectomy was performed): 1

At 3 weeks, a few minor secondary effects were present (Table 3). Minor ecchymoses persisted in 2 cases. In 3 cases, skin inflammation was more painful, with lumps (thrombophlebitis): for 2 of them a thrombectomy was performed (one at an intermediate visit, cf).

There were also 3 undesirable events which were probably not linked to treatment (1 lower back pain, 1 localised pain 24 h after the session, 1 asthenia for 8 days after the session), but another more serious event − segmental thrombosis of the common femoral vein (CFV) − occurred in the 3% group. This thrombosis was a parietal, non-obstructive clot that extended from the ipsilateral GSV as an extension of thrombus from the GSV into the SFJ. Thrombus dimension in the CFV was 4 mm maximum thickness with a length of about 2 cm. It was fixed to the anterior wall of the

Table 3. Side effects (local complications and systemic complications) – 3/1 Study

IMMEDIATE SIDE EFFECTS (DAY 0)	FLUSHING AND A SENSATION OF TIGHTENING IN THE THROAT	CHEST SYMPTOMS, COUGH	NEUROLOGICAL COMPLICATIONS (INCLUDING VISUAL DISTURBANCE, MIGRAINE…)	MALAISE	PAIN	ALLERGY
	1	0	0	0	0	0
Secondary side effects (from D0 to W3)	Minor ecchymosis	Haematoma	Minor pain or skin inflammation	Skin inflammation with lumps (thrombophlebitis)	Pigmentation	SVT DVT
	2	0	9 (adjuvant treatments: 2)	3 (thrombectomy: 2)	3	0 1
Events with unlikely relation to treatment	Lower back pain	Other pain	Asthenia			
	1	1	1			

On inclusion: 148 patients, no patient was lost to follow-up at week 3.
SVT = Superficial Vein Thrombosis.
DVT = Deep Vein Thrombosis.

CFV. The GSV was obliterated throughout its entire length (75 cm). The episode was diagnosed on day 19, after the patient had sought advice for pain in the thigh. This patient had received a total of 7.5 ml of foam for a GSV measuring 7 mm in diameter. At the time of inclusion, he had reported 2 previous episodes of spontaneous superficial venous thrombosis (SVT). He was managed by elastic compression, full anticoagulation with low molecular weight heparin and oral anticoagulants for 3 months. Other authors suggest treating non-occlusive thrombosis by elastic compression only.[14] The thrombus disappeared completely after 3 weeks and the GSV remained obliterated at 2 years. Thrombophilia screening showed a high factor VIII level (225%) combined with hyperhomocysteinaemia.

Diagram 1 summarises the findings during the 2-year follow-up period. The outcome of treatment was the same at each treatment point as far as disappearance of reflux was concerned. At 2 years, the success rates were 68% for 1% Aethoxysklerol®, and 69% for 3% Aethoxysklerol® (NS). (14 lost to follow-up: 9 for the 1% group and 5 for the 3% group).

In recanalised GSVs with recurrence of reflux, the mean diameter of the new channel was 2.8 mm – compared to the initial mean diameter of 6.1 mm, i.e. the diameter was reduced by more than half. This problem was readily resolved by a further sclerotherapy session.

For the 1% group, in the case of isolated truncal reflux, the success rate at 3 weeks was 76%, whereas it was 63% in the case of truncal + SFJ reflux (NS Chi-square 0.27).

For the 3% group, the respective success rates were 78% and 64% (NS Chi-square 0.22).

Diagram 1. Elimination of reflux (E.R) in the great saphenous vein and disappearance of the GSV or image of an echogenic string (at the thigh level) in B mode – 3/1 Study.

At the 2 year-follow-up interval, the situation was unchanged within each group (NS). The rate of recanalisation was not significantly lower for the 3% group than for the 1% group in GSVs with an incompetent SFJ (37% recanalisation for the 1% group and 36% for the 3% group; Chi-square 0.96).

Discussion

The outcome of ultrasound guided foam sclerotherapy has been reported in several clinical series but few randomised trials. Clinical series report good results for sclerotherapy of saphenous trunks.[5–9,14–22] Some authors, including Barrett,[19] have also reported excellent levels of satisfaction and improvement in patients' quality of life. Some series have included detailed analysis of the incidence of side effects to treatment.[19,23] Our present study is a "dose-finding" study, seeking only to answer the question whether 1% or 3% POL foam is the more effective.

We treated only the GSV in the thigh, ignoring varices, perforators and other saphenous veins.

The main outcome variable, abolition of venous reflux assessed by duplex ultrasonography, reflects a pure indicator of success or failure. This cannot be judged reliably on clinical criteria since a clinical recurrence of varicose veins may not be obvious for several years following sclerotherapy.[24]

Each practitioner assessed the results of his own treatment, but since he was unaware of the strength of foam injected into each patient, his conclusions about the outcome were unbiased.

In the course of the study we showed that it was not possible to identify the strength of the injected foam from the response of the saphenous trunk and therefore the investigators were blinded to the treatment that they were giving. Clinical criteria were taken into account by each practitioner at each consultation but were not used to evaluate outcome.

We standardised the method of preparing foam as far as was possible, since Tessari's three-way tap-method[25] yields foam with variable physical characteristics[26] even though this is a very widely used technique. Each centre used the Turbofoam system ensuring that the sclerosant was the same in each of the 5 centres.

In a comparative study of 80 cases of GSV treatments, Ceulen showed no statistical difference in efficacy (occlusion) for 1% and 3% POL foams at 1 year follow-up.[27] Despite this he is convinced that 3% should be a more efficient concentration with a larger study required to demonstrate this. Our own results at 2 years, with almost double number of patients, confirm equivalent efficacy for the two treatments. In a large series with 3 years follow-up, Myers reports better efficacy for 1.5% and 1% concentrations compared to lower concentrations or to 3% sclerosant.[28] We acknowledge that long-term outcomes (e.g. 5 years) may be different but no clinical trial of foam sclerotherapy has been published with such a long period of follow-up.

The average injected volume was similar in the two groups, although we had expected that a higher volume would have been required in the 1% group. The actual mean volume of sclerosant required was small (4.4–4.6 ml) compared to that used by some authors. In the foam versus liquid study, volumes (liquid or foam) were 2 or 2.5 ml using 3% Aethoxysklerol® only, with good outcomes for foam.[7,8] These data confirm the recommendations from the Tegernsee Consensus[10] and other authors' experiences[15,27,29]: large volumes seem not to be necessary in order to close medium calibre saphenous trunks. Our study shows that the risk of recanalisation is unrelated to the concentration of sclerosant or to the coexistence of SFJ incompetence. There may be a relationship to the total injected volume but other so far unidentified factors are probably also important.

We found that the disappearance of the GSV on ultrasonography begins after 6 months following treatment in 30% of cases. However in many patients this occurs more slowly so an image of an echogenic string or disappearance of the vein sometimes occurs as late as 18 months or 2 years (63% at 1 year, 80% at 18 months, 85% at 2 years). In our trial, the concentration of the injected foam had no influence on the onset of disappearance, nor on the speed of its occurrence (no difference between the 2 groups – Chi squared: N.S.).

In our study, the modest volume of sclerosant resulted in few adverse events. The only serious problem was a non-occlusive thrombus extending into the CFV in a patient with a previously undiagnosed thrombophilia. The only clue to this in his medical history was some episodes of SVT. Since thrombophilias are common and deep vein thrombosis is uncommon following sclerotherapy, it is probably inappropriate to check each patient for thrombophilia prior to sclerotherapy.

Our direct puncture technique gives flexibility and adaptability in treating saphenous veins.

We used the development of vasospasm and filling of the vein on ultrasound imaging to judge whether a sufficient foam volume had been injected. This enabled us to minimise the volume of foam required, thus obtaining a low complication rate. This is probably the reason why we can avoid routine compression treatment after sclerotherapy of trunks. In the present study therefore, delayed elastic compression was applied only 3 times.

Conclusion

In a previous randomised trial, we have demonstrated the clear superiority of 3% POL foam compared to POL as a liquid sclerosant in treatment of GSV. We have now investigated the use of 1% and 3% POL foam in sclerotherapy of the GSV. No difference was found between these two foams in the immediate response to injection or in the rate of recanalisation after two years. These outcomes are in line with other studies evaluating the efficacy of different concentrations but no long-term trials have so far been reported.

Recanalisation was observed in about one third of saphenous veins managed in this way. However, this was a clinical research study and is not comparable with our everyday practice. We consider that the efficacy of treatment was prejudiced by not treating saphenous tributaries, perforators or other varices. In addition, we did not permit subsequent treatment sessions in which any untreated vein was addressed. This strategy was essential in order to compare the efficacy of different strengths of sclerosant foam under identical conditions.

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References

1 Traitement des varices des membres inférieurs. Rapport de l'Agence Nationale d'Accréditation et d'Evaluation en Santé. Service Evaluation en santé publique − Evaluation technologique Juin 2004.
2 Jia X, Mowatt G, Burr JM, Cassar K, Cook J, Fraser C. Systematic review of foam sclerotherapy for varicose veins. *Br J Surg* 2007; **94**:925−936.
3 Schadeck M. Doppler et échotomographie dans la sclérose des veines saphènes. *Phlébologie* 1986;**39**:697−716.
4 Knight RM, Vin F, Zygmunt JA. Ultrasonic guidance of injection into the superficial venous system. In: Davy A, Stemmer R, eds. *Phlébologie*. John Libbey Eurotext; 1989, pp. 339−341.
5 Cabrera Garrido JR. Elargissement des limites de la sclérothérapie: nouveaux produits sclérosants. *Phlébologie* 1997;**50**:181−188.
6 Monfreux A. Traitement sclérosant des troncs saphèniens et leurs collatérales de gros calibre par la méthode MUS. *Phlébologie* 1997;**50**:351−353.
7 Hamel-Desnos C, Desnos P, Wollmann JC, Ouvry P, Mako S, Allaert FA. Evaluation of the efficacy of polidocanol in the form of foam compared with liquid form in sclerotherapy of the greater saphenous vein: initial results. *Dermatol Surg* 2003;**29**:1170−1175.
8 Ouvry P, Hamel-Desnos C. Evaluation de l'efficacité du Lauromacrogol sous forme mousse versus forme liquide dans la sclérothérapie de la grande veine saphène. Résultats après 2 ans de suivi. Société Française de Phlébologie; 2004. Réunion du 4 décembre 2004 − Abstract.
9 Yamaki T, Nozaki M, Iwasaka S. Comparative study of duplex-guided foam sclerotherapy and duplex-guided liquid sclerotherapy for the treatment of superficial venous insufficiency. *Dermatol Surg* 2004;**30**(5):718−722.
10 Breu FX, Guggenbichler S. European consensus meeting on foam sclerotherapy, April 4−6, 2003, Tegernsee, Germany. *Dermatol Surg* 2004 May;**30**(5):709−717.
11 Wollmann JC. Schaum − zwischen Vergangenheit und Zukunft. 8. Bonner Venentage 15−16. Feb. *Vasomed* 2002;**16**(1):34−35.
12 Hamel-Desnos C, Allaert FA, Benigni JP, Boitelle G, Chleir F, Ouvry P *et al*. Pour la Société Française de Phlébologie. ≪Etude 3/1. Mousse de Polidocanol 3% versus 1% dans la grande veine saphène. Premiers résultats≫. *Phlébologie* 2005;**58**(2):165−173.
13 Hamel-Desnos C, Desnos P. L'écho-sclérothérapie à la mousse en 2004. Technique de la ponction-injection directe. *Phlébologie* 2004; **57**(3):289−300.
14 Coleridge Smith P. Chronic venous disease treated by ultrasound guided foam sclerotherapy. *Eur J Vasc Endovasc Surg* 2006;**32**:577−583.
15 Cavezzi A, Frullini A, Ricci S, Tessari L. Treatment of varicose veins by foam sclerotherapy: two clinical series. *Phlebology* 2002;**17**:13−18.
16 Cabrera J, Cabrera Jr J, Garcia-Olmedo MA. Treatment of varicose great saphenous veins with sclerosant in micro-foam form: long term outcomes. *Phlebology* 2000;**15**:19−23.
17 Frullini A, Cavezzi A. Echosclérose par mousse de tétradécylsulfate de sodium et de polidocanol: deux années d'expérience. *Phlébologie* 2000;**53**(4):431−435.
18 Wright D, Gobin JP, Bradbury AW, Coleridge-Smith P, Spoelstra H, Berridge D, *et al*., The Varisolve® European Phase III Investigators Group. Varisolve® polidocanol microfoam compared with surgery or sclerotherapy in the management of varicose veins in the presence of trunk vein incompetence: European randomized controlled trial. *Phlebology* 2006;**21**(4):180−190.
19 Barett JM, Allen B, Ockelford A, Goldman M. Microfoam ultrasound-guided sclerotherapy of varicose veins in 100 legs. *Dermatol Surg* January 2004;**30**(1):6−12.
20 Hamel-Desnos C, Ramelet AA, Guias B. Efficacité des mousses de sclérosants: synthèse des principaux essais cliniques publiés. *Angéiologie* 2004;**56**(2):39−44.
21 Bergan J, Pascarella L, Mekenas L. Venous disorders: treatment with sclerosant foam. *J Cardiovasc Surg* 2006 Feb;**47**(1):9−18.
22 Bountouroglou DG, Azzam M, Kakkos SK, Pathmarajah M, Young P, Geroulakos G. Ultrasound-guided foam sclerotherapy combined with sapheno-femoral ligation compared to surgical treatment of varicose veins: early results of a randomised controlled trial. *Eur J Vasc Endovasc Surg* 2006;**31**:93−100.
23 Guex JJ, Allaert FA, Gillet JL, Chleir F. Immediate and midterm complications of sclerotherapy: report of a prospective multicenter. Registry of 12,173 sclerotherapy sessions. *Dermatol Surg* 2005;**31**:123−128.
24 Hobbs JT. Surgery or sclerotherapy for varicose veins: 10-year results of a random trial. In: Tesi M, Dormandy JA, eds. *Superficial and deep venous diseases of the lower limbs*. Turin: Panminerva Medica; Sept 1984, pp. 243−248.
25 Tessari L. Nouvelle technique d'obtention de la scléro-mousse. *Phlébologie* 2000;**53**(1):129.
26 Rao J, Goldman M. Stability of foam in sclerotherapy: differences between sodium tetradecyl sulfate and polidocanol and the type of connector used in the double-syringe system technique. *Dermatol Surg* 2005;**31**(1):19−22.
27 Ceulen RP, Bullens-Goessens YI, Pi-Van De Venne SJ, Nelemans PJ, Veraart JJ, Sommer A. Outcomes and side effects of duplex-guided sclerotherapy in the treatment of great saphenous veins with 1% versus 3% polidocanol foam: results of a randomized controlled trial with 1-year follow-up. *Dermatol Surg* 2007;**33**:276−281.
28 Myers K, Jolley D, Clough A, Kirwan J. Outcome of ultrasound-guided sclerotherapy for varicose veins: medium-term results assessed by ultrasound surveillance. *Eur J Vasc Endovasc Surg* 2007;**33**:116−121.
29 Frullini A. Foam sclerotherapy: a review. *Phlebolymphology* 2003; **40**:125−129.

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