SCLEROTHERAPY of VARICOSE VEINS* GUIDELINE of THE GERMAN SOCIETY of PHLEBOLOGY

SCLÉROTHÉRAPIE des VEINES VARIQUEUSES : RECOMMANDATIONS de la SOCIÉTÉ ALLEMANDE de PHLÉBOLOGIE

E. RABE[1], F. PANNIER, H. GERLACH, F.X. BREU, S. GUGGENBICHLER, J.C. WOLLMANN

PREAMBLE

Guidelines are systematically elaborated recommendations designed to support the clinician and practitioner in his or her decisions about the appropriate care of patients in specific clinical situations.

Guidelines apply to "standard situations" and take into account the currently available scientific knowledge relating to the subject under consideration. Guidelines require ongoing review and possibly modification, in order to adapt to the most recent scientific findings and to practicability in daily routine. Guidelines are not intended to restrict the doctor's freedom to choose the most appropriate method of treatment. Compliance with the recommendations does not always guarantee diagnostic and therapeutic success. Guidelines make no claim to completeness. The decision about the appropriateness of any action to be taken is still the responsibility of the doctor in the light of the individual situation.

DEFINITION

Sclerotherapy involves the injection of a sclerosant for the targeted elimination of intracutaneous, subcutaneous, and/or transfascial varicose veins (perforating veins) as well as the sclerosation of subfascial varicose vessels in the case of venous malformation. The various sclerosants induce marked damage of the vascular endothelium and possibly of the entire vascular wall. After successful sclerotherapy and in the long term, the veins are transformed into a fibrous cord, a process known as sclerosis [21, 39, 73]. The purpose of sclerotherapy is not merely to achieve thrombosis of the vessel, which *per se* may be amenable to recanalisation, but definitive transformation into a fibrous cord. This cannot recanalise and the functional result is equivalent to the surgical removal of a varicose vein.

INDICATIONS

The objectives of sclerotherapy are:

- treatment of varicosis and prevention of possible complications;
- reduction or elimination of existing symptoms;
- improvement of pathologically altered haemodynamics;
- achievement of a good result that satisfies aesthetic and functional criteria [2].

In principle all types of varicose veins are amenable to sclerotherapy, in particular:

- truncal veins (long saphenous vein (LSV) and short saphenous vein (SSV));
- collateral veins;
- varicose veins associated with perforator incompetence;
- reticular varicose veins;
- spider veins;

* This guideline was drafted on behalf of the German Society of Phlebology (Deutsche Gesellschaft für Phlebologie, DGP), adopted by the Committee and Scientific Advisory Board of the DGP on 15.06.2001, and amended on 26.09.2007: it replaces the previous version of 12.05.2003 (75). This guideline considers the present state of knowledge as reflected in the literature but not the licensing requirements for the various medicinal products, which are different in each case.

1. University of Bonn Sigmund Freud Str. 25. 53105 BONN Allemagne.

© Éditions Phlébologiques Françaises, vol.61, n° 1/2008, p.43-51

• residual and recurrent varicose veins after interventions to eliminate varicosities;

• genital and perigenital varicose veins;

• peri-ulcerous veins [19, 48, 89];

• venous malformations [103].

Sclerotherapy is considered to be the method of choice for the treatment of small-calibre varicose veins (reticular varicose veins, spider veins) [2].

For the obliteration of varicose collateral veins and incompetent perforating veins, sclerotherapy competes with percutaneous phlebextraction and with ligation of perforating veins or endoscopic dissection of perforating veins [24, 59].

In the treatment of varicose truncal veins involving elimination of the proximal leakage point and of the incompetent venous portion, surgery is considered to be the method of choice. Nevertheless, treatment of truncal veins by sclerotherapy is also possible [13, 84, 94]. This applies in particular to foam sclerotherapy, as has been demonstrated by studies conducted in recent years [16, 44, 45, 74, 102].

CONTRAINDICATIONS

Absolute contraindications are [2, 73, 94]:

• known allergy to the sclerosant;

• severe systemic disease;

• acute deep vein thrombosis;

• local infection in the area of sclerotherapy or severe generalised infection;

• lasting immobility and confinement to bed;

• advanced peripheral arterial occlusive disease (Stage III or IV);

• hyperthyroidism (in the case of sclerosants containing iodine);

• pregnancy (unless a compelling medical reason exists).

For foam sclerotherapy:

• known symptomatic patent foramen ovale.

Relative contraindications are [2, 73, 93]:

• leg oedema, uncompensated;

• late complications of diabetes (e.g. polyneuropathy);

• arterial occlusive disease, Stage II;

• poor general health;

• bronchial asthma;

• marked allergic diathesis;

• known thrombophilia or hypercoagulable state with or without a history of deep vein thrombosis [9, 26, 46].

For foam sclerotherapy:

• known asymptomatic patent foramen ovale [9];

• high risk of thromboembolic events;

• visual disturbances or neurological disturbances following previous foam sclerotherapy.

In addition, it is urgently recommended that due account be taken of the current prescribing information for the sclerosants used [57].

COMPLICATIONS AND RISKS

If performed properly, sclerotherapy is an efficient treatment method with a low incidence of complications. In the context of therapy a number of adverse events may be encountered in principle [39, 43, 49, 67, 97]. In particular, these are:

• allergic reaction [27, 28, 72];

• skin necroses [6, 23, 30, 40];

• excessive sclerosing reaction (and thrombophlebitis);

• pigmentation [18, 40, 96];

• matting [40];

• nerve damage [85, 92, 104];

• scintillating scotomas [43];

• migraine-like symptoms [5, 58, 77];

• orthostatic collapse;

• thromboembolism [11, 32, 49].

In addition, it is urgently recommended that due account be taken of the current prescribing information for the sclerosants used [57].

Allergic skin reactions occur occasionally in the form of allergic dermatitis, contact urticaria or erythema. Anaphylactic shock as well as inadvertent intra-arterial injection are extremely rare complications constituting an emergency situation [27, 28, 70, 72].

Transient migraine-like symptoms occur more commonly after foam sclerotherapy than after liquid sclerotherapy [43]. In this context it has been speculated whether a patent foramen ovale (PFO), which is present in 15-25% of the population, might be a factor here, allowing foam bubbles to pass into the arterial circulation [29, 66, 71, 95].

Thromboembolic events (deep vein thrombosis, pulmonary embolism or stroke) occur in rare exceptional circumstances after sclerotherapy. A higher risk is present when larger volumes of sclerosant are used, particularly in the form of foam [10, 32, 101], and in patients with a previous history of thromboembolism or known thrombophilia [46]. In patients with these risk factors the indication for sclerotherapy must be established absolutely and additional precautionary measures must be observed [9].

Skin necroses have been described both after paravascular injection of sclerosants in higher concentrations and – rarely – after properly performed intravascular injection with sclerosants in various concentrations, for example, 0.5% polidocanol in the treatment of spider veins [30, 40]. In the latter case, a mechanism involving passage of the sclerosant into the arterial circulation via arteriovenous anastomoses has been suggested [6].

In individual cases, this has been described as embolia cutis medicamentosa [37, 56, 79].

Extensive necroses occur after inadvertent intra-arterial injection [30, 40, 70].

Instances of hyperpigmentation have been reported with frequencies ranging from 0.3% to 10% [36, 96]. In general, this phenomenon regresses slowly. The incidence of pigmentation is likely to be higher after foam sclerotherapy [43].

Matting, fine telangiectasias in the area of a sclerosed vein, is an unpredictable individual reaction of the patient and can also occur after surgical removal of a varicose vein [40].

Nerve damage has been reported experimentally after paravascular injection [85, 92, 104]. Local paraesthesia after sclerotherapy is very rare.

Other transitory phenomena after sclerotherapy include intravascular clots, phlebitis, haematomas, disturbed sense of taste, feeling of tightness in the chest, pain at the injection site, swelling, induration, mild cardiovascular reactions, and nausea. Additionally, complications may arise due to the compressive bandage, such as blister formation (e.g. blisters in the vicinity of an adhesive plaster) [39, 73]. Intravascular clots can be squeezed out after a stab incision to reduce the development of hyperpigmentation.

Sclerotherapy is an intervention that requires patients to be appropriately informed.

Diagnosis before sclerotherapy

Successful sclerotherapy requires thorough planning. Sclerotherapy is generally performed in the order of leakage points, proceeding from the larger to the smaller varicose veins. Therefore, a proper diagnostic evaluation should be performed prior to treatment [2, 39, 73, 93].

Diagnostic evaluation includes history-taking, clinical examination and Doppler ultrasound investigation.

Additionally, functional examinations (e.g., photoplethysmography, phlebo-dynamometry, venous occlusion plethysmography) and imaging modalities (e.g., duplex ultrasound, phlebography) may be considered.

Functional examinations make it possible to assess the improvement in venous function, which is to be expected for the elimination of varicosis.

Diagnostic imaging is especially suitable for identifying incompetent junctions with the deep venous system and for locating pathological reflux, as well as for clarifying post-thrombotic changes [34, 86] and for selecting the most appropriate treatment option.

Implementation of sclerotherapy of varicose veins

Aethoxysklerol®, which contains the active ingredient polidocanol in concentrations of 0.25/0.5/1/2/3 and 4%, is licensed in Germany for sclerotherapy of varicose veins:

The maximum daily dose of polidocanol is 2 mg/kg body weight [57].

Sclerotherapy with sclerosant solutions (liquid sclerotherapy)

Table 1 provides guide values for concentration and volume per injection for liquid sclerotherapy [57].

Sclerosants containing polidocanol		
Indications	**Volume/injection**	**Concentration**
Spider veins	0.1-0.2 ml	0.25-0.5%
Central veins of spider veins	0.1-0.2 ml	0.25-1%
Reticular varicose veins	0.1-0.3 ml	1%
Small varicose veins	0.1-0.3 ml	1%
Medium-size varicose veins	0.5-2.0 ml	2-3%
Large varicose veins	1.0-2.0 ml	3-4%

Table I. – Guide values for concentration and volume per injection for sclerosants containing polidocanol used for liquid sclerotherapy

A smoothly functioning disposable or glass syringe is required for sclerotherapy as well as a cannula with a small diameter. Cotton-wool rolls or pads and adhesive paper tapes are used for local compression. The different techniques vary considerably [3]. The following principles apply to liquid sclerotherapy proper:

- Puncture of the veins to be sclerosed can be performed with the patient standing or lying down.
- The injection is usually given with the patient lying down. After the vein has been punctured with the free cannula or with the syringe attached, the intravascular position is checked.
- Intravascular injection of the sclerosant is performed slowly, possibly in fractions and checking that the cannula is positioned inside the vein. Severe pain during injection may be indicative of paravascular injection.
- Immediately after injection of the sclerosant and removal of the cannula, local compression is performed along the course of the sclerosed vein [21, 73, 88, 90].
- After sclerotherapy, compression is applied to the treated extremity. When sclerosing spider veins, compression is achieved in a variety of ways. Compression can be performed using both a compression stocking and a compression bandage [21, 25, 38].
- Local compression can be removed the same evening or on the next day. Depending on the diameter and location of the varicose veins, compression is performed for hours up to several days and weeks after completion of sclerotherapy [2, 78, 93].
- After a sclerotherapy session using the traditional technique, the patient should walk around for a while (physical thromboprophylaxis) A careful watch must be kept for any signs of allergic reactions.
- Intensive sports activity, hot baths, saunas, and strong UV irradiation (solarium use) should be avoided in the initial days after sclerotherapy.

Sclerotherapy guided by duplex ultrasound

Duplex ultrasound-guided sclerotherapy has proved to be a useful addition to the range of methods for sclerosing saphenous junctions, truncal veins close to saphenous junctions, and perforating veins [30, 33, 41, 42, 80, 81, 82]. In this procedure, the vein to be sclerosed is visualised by duplex ultrasound with the patient lying down and puncture is performed under visual control. The needle is visible on the ultrasound image, and intravascular injection can be monitored. Some authors recommend intermittent compression using the ultrasound transducer after injection [81, 82]. This enables the contraction of the injected venous segment and the length of the sclerosed portion to be assessed. The purpose of this method is to achieve a more controlled procedure with fewer complications and increased efficacy.

Sclerotherapy with foam sclerosants (foam sclerotherapy)

The literature has long contained reports of sclerotherapy with foamed sclerosants [14, 31, 34, 61, 86, 99]. In recent years, as the technology has improved, foam sclerotherapy has become established particularly for the treatment of larger varicose veins [47, 65, 80]. Detergent-type sclerosants such as polidocanol can be transformed into a fine-bubbled foam by special techniques.

In the Monfreux technique [65] negative pressure is generated by drawing back the plunger of a glass syringe, the tip of which is tightly closed. The resulting influx of air produces a large-bubbled, fairly fluid foam [99]. In the Tessari technique the foam generated is fine-bubbled and fluid at low concentrations and rather viscous at high concentrations and it is produced by the turbulent mixture of liquid and air in two syringes connected via a three-way stopcock. The mixing ratio for sclerosant + air is 1 + 3 to 1 + 4 [91]. The DSS (double syringe system) technique involves the turbulent mixing of polidocanol with air in a sclerosant + air ratio of 1 + 4 in two syringes linked via a connector. The resulting product is a fine-bubbled, viscous foam [8, 99].

The standardised transformation of a licensed liquid sclerosant into a foam sclerosant and treatment with it is permissible provided that the patient has been adequately informed about the procedure and about the benefits and risks of the method and consents to its use. Even if foam is used off-lable, the published evidence and data documents the use as a standard procedure.

The Second European Consensus Conference on Foam Sclerotherapy took place at Tegernsee in April 2006. On the basis of the expert's own experience and the available literature, the following recommendations on foam sclerotherapy were given [9], partially modified for this guideline.

Puncture and injection:

• When treating the long saphenous vein (LSV) by direct puncture, it is recommended that venous puncture be performed in the proximal thigh area. If long catheters are used it is recommended to make the access to the LSV below the knee.

• When treating the short saphenous vein (SSV) by direct puncture, it is recommended that venous puncture be performed in the proximal or middle part of the lower leg.

• When treating the perforating veins it is recommended that the injection should not be made directly into the affected vein.

Foam generation, concentrations and volumes:

• The Tessari and Tessari/DSS methods are recommended for the generation of foam sclerosant for all indications.

• Air is accepted and/or proposed as the gas component for the generation of foam sclerosant for all indications. A mixture of carbon dioxide and oxygen may also be used.

• The preferred ratio of liquid sclerosant and gas for the generation of a foam sclerosant is 1 + 4 (1 part liquid + 4 parts gas). Ratios between 1 + 1 and 1 + 5 are used for reticular varicose veins and spider veins, but the 1 + 4 ratio is also used by the majority.

• The preferred foam volumes per venous puncture are shown in Table 2 and the preferred concentrations are outlined in Table 3.

	Mean foam volume per puncture	Maximum foam volume per puncture
LSV	2 to 4 ml	Up to 6 ml
SSV	2 to 4 ml	Up to 4 ml
Collateral veins	Up to 4 ml	Up to 6 ml
Recurrent varicose veins	Up to 4 ml	Up to 8 ml
Perforating veins	Up to 2 ml	Up to 4 ml
Reticular varicose veins	< 0.5 ml	< 1 ml
Spider veins	< 0.5 ml	< 0.5 ml
Venous malformations	2 to 6 ml	< 8 ml

Table II. – Foam volume per venous puncture

• The recommended maximum foam volume per leg and session (given in a single injection or in several injections) is 10 ml.

• When treating large-calibre varicose veins, the foam sclerosant should be as viscous as possible.

Safety measures:

• Safety during foam sclerotherapy of the GSV and SSV can be improved by:

– avoiding immediate compression of the injected areas;

– using ultrasound to monitor foam distribution;

– injecting a highly viscous foam;

– ensuring there is no patient or leg movement for 2 to 5 minutes, no Valsalva manoeuvre or other muscle movement;

– encouraging active muscle movement, e.g. repeated foot flexion, if a larger volume of foam is detected in the deep venous system.

	Liquid	0.25%	0.5%	1%	2%	3%	4%
LSV				+	++	++	
SSV				+	++	+	
Collateral veins				++			
Recurrent varicose veins			(+)	++	++	+	
Perforating veins			(+)	++	+	(+)	
Reticular varicose veins	(+)	(+)	++	+			
Spider veins*	++	(+)	(+)				
Venous malformations			+	++	+		

The stated concentrations refer to the liquid polidocanol solution from which foam is generated.

* Foam sclerotherapy is not the treatment of choice for vessels less than 1 mm in diameter. For sclerotherapy of spider veins the recommendation is first to use polidocanol in liquid form. Where foam is used, small volumes of a 0.25% foam (possibly even of a 0.5% foam) should be given.

Table III. – Guide values for concentration and volume per injection for sclerosants containing polidocanol used for liquid sclerotherapy

• The known presence of a patent foramen ovale (PFO) is a relative contraindication for foam sclerotherapy. In such patients the following is recommended:

– the patient should remain lying down for longer (8 to 30 minutes);

– use only small volumes of foam (2 ml) or liquid sclerotherapy;

– avoid Valsalva manoeuvres;

– elevate the patient's leg by ca. 30 cm.

• Prior to foam sclerotherapy it is not necessary to perform specific investigations for PFO.

• A high risk of thromboembolism in the patient's history and known thrombophilia (especially in combination with a high risk of thromboembolism) is a relative contraindication for foam sclerotherapy. In such patients the following is recommended:

– institute adequate LMW heparin prophylaxis (in line with relevant guidelines/recommendations);

– implement physical prophylaxis;

– use low sclerosant concentrations for foam generation;

– use small volumes of foam;

– decide on a case-by-case basis (perform a benefit-risk assessment based on the particular indication).

• Prior to foam sclerotherapy it is not necessary to perform specific investigations for thrombophilia.

Patient information:

• Before foam sclerotherapy patients should be informed about risks and possible adverse effects in the same way as before liquid sclerotherapy. In addition, they should be told that:

– there is a slightly higher risk of hyperpigmentation and inflammation;

– there is a risk of developing (transient) neurological symptoms;

– there is a risk of developing (transient) visual disturbances;

– there is a risk of triggering migraine.

• As before liquid sclerotherapy, patients should be informed about the expected treatment outcome. In addition, they should be told that:

– short-term outcomes are highly satisfactory;

– further therapy is possible and may be necessary in some cases, especially in treatment for large varicose veins;

– foam sclerotherapy is more effective than liquid sclerotherapy.

Duplex ultrasound in foam sclerotherapy:

• The therapeutic effect of foam sclerotherapy on the patient and on the patient's leg should be assessed clinically and on the basis of symptoms.

• The therapeutic effect of foam sclerotherapy on the LSV, SSV, collateral branches, recurrent varicose veins, perforating veins and on venous malformations can be assessed additionally using duplex ultrasound.

• In terms of puncturing non-visible varicose veins, duplex-guided ultrasound is an important instrument that enables puncture errors to be avoided. Ultrasound visualisation (preferably duplex-guided) is necessary for the direct puncture of non-visible LSV, SSV and perforating veins as well as of non-visible varicose veins in the groin and popliteal fossa.

• Duplex guidance is recommended for other non-visible varicose veins.

Criteria for assessing the therapeutic effect of foam sclerotherapy are presented in Table 4.

Grade/Name	Duplex criteria		Clinical criteria	Symptoms
2 Successful	No REFLUX	a) – Complete disappearance of treated vein or – "Fibrous cord" (non-compressible, echogenic cord at the site of the treated vein) b) Complete occlusion (non-compressibility) of the treated venous segment c) Patency of the treated venous segment with reduced diameter and antegrade blood flow	Normalised (i.e. no visible varicose veins)	Absent or improved
1 Partially successful	REFLUX < 1 sec	– Partial non-compressibility and – Partial occlusion of the treated venous segment and – Diameter reduction	Normalised or improved (i.e. varicose veins less visible)	Absent or improved
0 Unsuccessful	REFLUX > 1 sec or unchanged	– Complete (or incomplete) patency and/or – Diameter unchanged	No change or worse (i.e. larger varicose veins or deterioration in terms of CEAP)	No change or worse

Further information:
- Duplex ultrasound is performed with the patient standing.
- The length of the occluded venous segment must be compared with the length of the incompetent venous segment that was to be occluded by sclerotherapy injection. (The segment to be treated must therefore be defined before injection.) This is important for establishing after sclerotherapy whether the "whole vein" is occluded.
- Reflux is assessed during a Valsalva manoeuvre or during distal compression/decompression.
- In terms of symptom assessment – where appropriate – more sophisticated and standardised symptom scores such as the VCSS may be used; otherwise visual analogue scales (VAS) from 1-10 are helpful and simple to use.
- In terms of clinical assessment – where appropriate – more sophisticated and standardised classifications such as in the CEAP classification may be used.
- When treatment is being given simultaneously for medical and aesthetic reasons, two separate assessment forms should be used.
- This classification is applicable for all endovenous treatment methods (laser, radiofrequency and sclerotherapy techniques) and should facilitate comparability.
- Details of the number of treatments (injections and sessions) and the type of treatment should be recorded.

Table IV. – Assessment of treatment outcome following foam sclerotherapy

EFFICACY

A wealth of published clinical series [e.g. 4, 7, 10, 12, 15, 17, 18, 20, 50, 53, 64, 68, 83, 89, 98] and controlled clinical trials [1, 16, 44, 45, 52, 74, 76, 102] provide undoubted evidence to corroborate the elimination of intracutaneous and subcutaneous varicose veins by sclerotherapy. The success rates of sclerotherapy vary depending on technique, sclerosant (liquid or foam) and venous calibre.

Sclerotherapy is considered to be the standard treatment for intracutaneous varicose veins (spider veins and reticular veins), allowing improvement of up to 90% to be achieved [6, 22, 51, 54, 62, 69].

Compression treatment with medical compression stockings may improve the result of sclerotherapy for spider veins [55, 60, 63, 96]. The incidence of pigmentation decreases significantly [38, 96].

Local eccentric compression significantly increases local pressure in the sclerosed area and improves the efficacy of sclerotherapy [88].

In older studies with liquid sclerotherapy, surgery was significantly more effective in the treatment of truncal varices [24]. In the sclerosis of truncal varicose veins foam sclerotherapy is significantly more effective than liquid sclerotherapy [44, 74, 102].

RÉFÉRENCES

1. Alos J., Carreno P., Lopez J.A., Estadella B., Serra-Prat M., Marinel-Lo J. Efficacy and safety of sclerotherapy using Polidocanol foam: a controlled clinical trial. *Eur J Vasc Endovasc Surg* 2006; 31: 101-7.

2. Baccaglini U., Spreafico G., Castoro C., Sorrentino P. Consensus Conference on Sclerotherapy or Varicose Veins of the Lower Limbs. *Phlebology* 1997; 12: 2-16.

3. Baccaglini U., Stemmer R., Partsch U. Internationale Fragebogenaktion zur Praxis der Verödungsbehandlung. *Phlebologie* 1997; 26: 129-42.

4. Barrett J.M., Allen B., Ockelford A., Goldman M.P. Microfoam ultrasound-guided sclerotherapy of varicose veins in 100 legs. *Dermatol Surg* 2004; 20: 6-12.

5. Benigni J.P. Sclérothérapie à la mousse et migraines à aura. *Phlébologie* 2005; 58: 323-4.

6. Bergan J.J., Weiss R.A., Goldman M.P. Extensive tissue necrosis following high concentration sclerotherapy for varicose veins. *Dermatol Surg* 2000; 26: 535-42.

7. Bergan J.J., Pascarella L., Mekenas L. Venous disorders: treatment with sclerosant foam. *J Cardiovasc Surg* 2006; 47: 9-18.

8. Breu F.X., Guggenbichler S. European consensus meeting on foam sclerotherapy. April, 4-6, 2003, Tegernsee, Germany. *Dermatol Surg* 2004; 30: 709-17.

9. Breu F.X., Guggenbichler, Wollmann J.C. 2nd European Consensus Meeting on Foam Sclerotherapy, 28-30 April 2006, Tegernsee, Germany. *Vasa* 2008; 37: 1-32.

10. Breu F.X., Marshall M. Sklerotherapie mit Polidocanol in einer angiologisch-phlebologischen Spezialpraxis. Prospektive und retrospektive Erhebung über Ergebnisse und Komplikationen. *Phlebologie* 2003; 32: 76-80.

11. Breu F.X., Partsch B. Reversible neurologische Komplikationen bei der Schaum-Sklerotherapie. *Phlebologie* 2006; 3: 115-6.

12. Brodersen J.P. Catheter-assisted vein sclerotherapy: a new approach for sclerotherapy of the greater saphenous vein with a double-lumen balloon catheter. *Dermatol Surg* 2007; 33: 469-75.

13. Bullens-Goessens Y.I.J.M., Mentink L.F., Nelemans P.J., Van Geest A.J., Veraart J.C.J.M. Ultrasound-guided sclerotherapy of the insufficient short saphenous vein. *Phlebologie Germany* 2004; 33: 89-91.

14. Cabrera J., Redondo P., Becerra A., Garrido C., Cabrera J. Jr, Garcia-Olmedo M.A., Sierra A., Lloret P., et al. Ultrasound-guided injection of Polidocanol microfoam in the management of venous leg ulcers. *Arch Dermatol* 2004; 140: 667-73.

15. Cavezzi A., Frullini A., Ricci S., Tessari L. Treatment of varicose veins by foam sclerotherapy: two clinical series. *Phlebology* 2002; 17: 13-8.

16. Ceulen R.P.M., Bullens-Goessens Y.I.J.M., Pi-Van De Venne S.J.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: 276-81.

17. Coleridge Smith P.D. Chronic venous disease treated by ultrasound guided foam sclerotherapy. *Eur J Vasc Endovasc Surg* 2006; 32: 577-83.

18. Conrad P., Malouf G.M., Stacey M.C. The Australian Polidocanol (Aethoxysklerol) study. Results at 2 years. *Dermatol Surg* 1995; 21: 334-6.

19. De Waard M.M., Der Kinderen D.J. Duplex ultrasonography-guided foam sclerotherapy of incompetent perforator veins in a patient with bilateral venous leg ulcers. *Dermatol Surg* 2005; 31: 580-3.

20. Darke S.G., Baker S.J. Ultrasound-guided foam sclerotherapy for the treatment of varicose veins. *Br J Surg* 2006; 8: 969-74.

21. Drake L.A., Dinehart S.M., Goltz R.W., Graham G.F., Hordinsky M.K., Lewis C.W., Pariser D.M., Skouge J.W., Webster S.B., Whitaker D.C., Butler B., Lowery B.J. Guidelines of care for sclerotherapy treatment of varicose and telangiectatic leg veins. *J Am Acad Dermatol* 1996; 34: 523-8.

22. Dover J., Sadick N., Goldman M.P. The role of lasers and light sources in the treatment of leg veins. *Derm Surg* 1999; 25: 328-36.

23. Duffy D.M. Cutaneous necrosis following sclerotherapy. *J Anesthetic Dermatol Cosmetic Surg* 1999; 1, 2: 157-68.

24. Einarsson E., Eklöf B., Neglén P. Sclerotherapy or surgery as treatment for varicose veins: A prospective randomized study. *Phlebology* 1993; 8: 22-6.

25. Fegan W.G. Continuous compression technique of infecting varicose veins. *Lancet* 1963; 2: 109-12.

26. Feied C.F. Deep vein thrombosis: the risks of sclerotherapy in hypercoagulable states. *Sem Dermatol* 1993; 12: 135-49.

27. Feied C.F., Jackson J.J., Bren T.S., Bond O.B., Fernando C.E., Young V.C., Hashemiyoon R.B. Allergic reactions to Polidocanol for vein sclerosis. *J Dermatol Surg Oncol* 1994; 20: 466-8.

28. Feuerstein W. Schwere anaphylaktische Reaktion auf Hydroxypolyaethoxydodecan. *VASA* 1973; 3: 292-4.

29. Fisher D.C., Fisher E.A., Budd J.H., et al. The incidence of patent foramen ovale in 1 000 consecutive patients. *Chest* 1995; 107: 1504-9.

30. Fisher D.A. Regarding extensive tissue necrosis following high concentration sclerotherapy for varicose veins. *Dermatol Surg* 2000; 26: 1081.

31. Flückiger P. Nicht-operative retrograde Varicenverödung mit Varisylschaum. *Schweiz Med Wochenschr* 1956; 48: 1368-70.

32. Forlee M.V., Grouden M., Moore D.J., et al. Stroke after varicose vein foam injection sclerotherapy. *J Vasc Surg* 2006; 43: 162-4.

33. Frullini A., Cavezzi A. Ultrasound guided sclerotherapy in the treatment of long saphenous vein insufficiency. *Vasomed* 1999; 11: 8.

34. Frullini A., Cavezzi A. Sclerosing foam in the treatment of varicose veins and telangiectases: history and analysis of safety and complications. *Derm Surg* 2002; 28: 11-5.

35. Geerts W.H., Pineo G.F., Heit J.A., Bergqvist D., et al. Prevention of Venous thromboembolism. The Seventh ACCP Conference on Antithrombotic and Thrombolytic Therapy. *Chest* 2004; 126: 338S-400S.

36. Georgiev M. Postsclerotherapy hyperpigmentations. *J Dermatol Surg Oncol* 1993; 19: 649-52.

37. Geukens J., Rabe E., Bieber T. Embolia cutis medicamentosa of the foot after sclerotherapy. *Eur J Dermatol* 1999; 9: 132-3.

38. Goldman P.M., Beaudoing D., Marley W., Lopez L., Butie A. Compression in the treatment of leg teleangiectasia: a preliminary report. *J Dermatol Surg Oncol* 1990: 16: 322-5.

39. Goldmann P.M., Bergan J.J., Guex J.J. Sclerotherapy – Treatment of varicose veins and telangiectatic leg veins, fourth Edition. Mosby Elsevier, *Philadelphia* 2007.

40. Goldman M.P., Sadick N.S., Weiss R.A. Cutaneous necrosis, telangiectatic matting and hyperpigmentation following Sclerotherapy. *Dermatol Surg* 1995; 21: 19-29.

41. Grondin L., Young R., Wouters L. Sclérothérapie écho-guidée et sécurité : comparaison des techniques. *Phlébologie* 1997; 50: 241-5.

42. Guex J.J. Ultrasound Guided Sclerotherapy (USGS) for perforating veins. *Hawaii Med J* 2000; 59: 261-2.

43. Guex J.J., Allaert F.A., Gillet J.L. Immediate and midterm complications of sclerotherapy: report of a prospective multicenter registry of 12,173 sclerotherapy sessions. *Dermatol Surg* 2005; 31: 123-8.

44. Hamel-Desnos C., Desnos P., Wollmann J.C., et al. Evaluation of the efficacy of Polidocanol in the form of foam compared with liquid form in sclerotherapy of the long saphenous vein: initial results. *Dermatol Surg* 2003; 29: 1170-5.

45. Hamel-Desnos C., Ouvry P., Benigni J.P., Boitelle G., Schadeck M., Desnos P., Allaert F.A. 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". *Eur J Vasc Endovasc Surg* 2007; 34: 723-9.

46. Hamel-Desnos C., Ouvry P., Desnos P., Escalard J.M., Allaert F.A. Sclérothérapie et thrombophilie : démarche pour un consensus dans la sclérothérapie chez les thrombophiles *Phlébologie* 2003; 56: 165-9.

47. Henriet J.P. One year experience with sclerotherapy of reticular veins and telangiectases using Polidocanol foam in daily Routine: feasibility results, complications. *Phlébologie* 1997; 50: 355-60.

48. Hertzman P.A., Owens R. Rapid healing of chronic venous ulcers following ultrasound-guided foam sclerotherapy. *Phlebology* 2007; 22: 34-9.

49. Hohlbaum G. Über iatrogene Schäden bei der Varizensklerosierung. in: Staubesand J., Schöpf E. (Hrsg.): *Neuere Aspekte der Sklerosierungstherapie*. Springer Verlag, Berlin, Heidelberg, New York, 1990 : 70-81.

50. Hübner K. Ambulante Therapie der Stammvarikose mittels Krossektomie und Sklerotherapie-ein Beitrag aus der Praxis des niedergelassenen Phlebologen. *Phlebologie* 1991; 20: 104-8.

51. Kahle B. Effizienz der Sklerosierungstherapie von Besenreisern. Eine prospektive, randomisierte, doppelblinde, placebokontroliierte Studie. *Vasomed* 2006; 18: 148.

52. Kahle B., Leng K. Efficacy of sclerotherapy in varicose veins – a prospective, blinded placebocontrolled study. *Dermatol Surg* 2004; 30: 723-8.

53. Kakkos S.K., Bountouroglou D.G., Azzam M., et al. Effectiveness and safety of ultrasound-guided foam sclerotherapy for recurrent varicose veins: Immediate results. *J Endovasc Ther* 2006; 13: 357-64.

54. Kern P., Ramelet A.A., Wütschert R., et al. Single-blind, randomized study comparing Chromated Glycerin, Polidocanol solution and Polidocanol foam for treatment of telangiectatic leg veins. *Dermatol Surg* 2004; 3: 367-72.

55. Kern P., Ramelet A.A., Wütschert R., Hayoz D. Compression after sclerotherapy for telangiectasias and reticular leg veins. A randomized controlled study. *J Vas Surg* 2007; 45: 1212-6.

56. Kersting E., Hornschuh B., Bröcker E.B. Embolia cutis medicamentosa nach Varizensklerosierung mit Polidocanol. *Phlebologie* 1998; 27: 55-7.

57. Kreussler. Fachinformationen Aethoxysklerol 0,25%/0,5%/1%/2% Stand 06/2005, Aethoxysklerol 3%/4%, Stand 09/2005, Chemische Fabrik Kreussler & Co GmbH.

58. Künzelberger B., Pieck C., Altmeyer P., Stücker M. Migraine ophtalmique with reversible scotomas after sclerotherapy with liquid 1% Polidocanol. *Derm Surg* 2006; 32: 1410.

59. Malouf G.M. Ambulatory venous surgery versus sclerotherapy. *Hawaii Med J* 2000; 59: 248-9.

60. Massay R.A. Regarding the use of compression stockings after sclerotherapy. *Dermatol Surg* 1999; 25: 517.

61. Mayer H., Brücke H. Zur Ätiologie und Behandlung der Varizen der unteren Extremität. *Chir Praxis* 1957; 4: 521-8.

62. McCoy S., Evans A., Spurrier N. Sclerotherapy for leg telangiectasia – a blinded comparative trial of polidocanol and hypertonic saline. *Dermatol Surg* 1999; 25: 381-6.

63. McDonagh B. Comments on the use of post-sclerotherapy compression. *Dermatol Surg* 1999; 25: 519-21.

64. Milleret R, Garandeau C. Sclérose des grandes veines saphènes à la mousse délivrée par cathéter écho-guidé sur veine vide : Alpha-technique – Bilan des 1 000 treatments. *Phlébologie* 2006; 59: 53-8.

65. Monfreux A. Traitement sclérosant des troncs saphéniens et leurs collatérales de gros calibre par la méthode Mus. *Phlébologie* 1997; 50: 351-3.

66. Morrison N., Cavezzi A., Bergan J., Partsch H. Regarding "stroke after varicose vein foam injection sclerotherapy". *J Vasc Surg* 2006; 44: 224-5.

67. Munavalli G.S., Weiss R.A. Complications of sclerotherapy. *Semin Cutan Med Surg* 2007; 26: 22-8.

68. Myers K.A., Jolley D., Clough A., et al. Outcome of ultrasound-guided sclerotherapy for varicose veins: medium-term results assessed by ultrasound surveillance. *Eur J Vasc Endovasc Surg* 2007; 33: 116-21.

69. Norris M.J., Carlin M.C., Ratz J.L. Treatment of essential telangiectasia: effects of increasing concentrations of polidocanol. *J Am Acad of Dermatol* 1989; 20: 643-9.

70. Oesch A., Stirnemann P., Mahler F. The acute ischemic syndrome of the foot after sclerotherapy of varicose veins. *Schweiz Med Wochenschr* 1984; 114: 1155-8.

71. Passariello F. Sclerosing foam and patent foramen ovale. The final report. In: Word Congress of the International Union of Phlebology; 2007 Jun 18-20; Kyoto, Japan. *Int Angiol* 2007; 26: 87.

72. Pradalier A., Vincent D., Hentschel V., Cohen-Jonathan A.M., Daniel E. Allergie aux sclérosants des varices. *Rev Fr Allergol* 1995; 35: 440-3.

73. Rabe E. (Hrsg.): Grundlagen der Phlebologie. 3. erweiterte und vollständig überarbeitete Neuauflage, Viavital, Köln 2003.

74. Rabe E., Otto J., Schliephake D., Pannier F. Efficacy and safety of great saphenous vein sclerotherapy using standardised Polidocanol foam (ESAF): A randomised controlled multicentre clinical trial. *Eur J Endovasc Vasc Surg*, accepted for publication.

75. Rabe E., Pannier-Fischer F., Gerlach H., Breu F.X., et al. Guidelines for sclerotherapy of varicose veins (ICD 10: I83.0, I83.1, I83.2, and I83.9). *Dermatol Surg* 2004; 30: 687-93.

76. Rao J., Wildemore J.K., Goldmann M.P. Double-blind prospective comparative trial between foamed and liquid Polidocanol and Natrium Tetradecyl Sulfate in the treatment of varicose and telangiectatic leg veins. *Dermatol Surg* 2005; 31: 631-5.

77. Ratanahirana H., Benigni J.P., Bousser M.G. Injection of Polidocanol foam (PF) in varicose veins as a trigger for attacks of migraine with visual aura. *Cephalalgia* 2003; 23: 850-1.

78. Reddy P., Wickers J., Terry T., Lamont P., Moller J., Dormandy J.A. What is the correct period of bandaging following sclerotherapy? *Phlebology* 1986; 1: 217-20.

79. Remy W., Vogt H.J., Borelli S. Embolia cutis medicamentosa – artige Hautnekrosen nach Sklerosierungsbehandlung. *Phlebol Proktol* 1978; 7: 67-72.

80. Sadoun S., Benigni J.P., Sica M. Étude prospective de l'efficacité de la mousse de sclérosant dans le traitement des varices tronculaires des membres inférieurs. *Phlébologie* 2002; 55: 259-62.

81. Schadeck M. Duplex-kontrollierte Sklerosierungsbehandlung der Vena saphena magna. *Phlebologie* 1996; 25: 78-82.

82. Schadeck M., Allaert F.A. Résultats à long terme de la sclérothérapie des saphènes internes. *Phlébologie* 1997; 50: 257-62.

83. Schadeck M. Sclérose de la petite veine saphène : éviter les mauvais résultats ? *Phlébologie* 2004 ; 2 : 165-9.

84. Schultz-Ehrenburg U., Tourbier H. Doppler-kontrollierte Verödungsbehandlung der Vena saphena magna. *Phlebol u Proktol* 1984; 13: 117-22.

85. Seydewitz V., Staubesand J. Das ultrastrukturelle Substrat der Wirkung paravasal und intraarteriell applizierter Sklerosierungsmittel: Ein experimenteller Beitrag zum Problem iatrogener Schäden nach Sklerotherapie. In: Staubesand J., Schöpf E. (Hrsg.): Neuere Aspekte der Sklerosierungstherapie. Springer, Heidelberg, 1990: 40-65.

86. Sigg K. Neuere Gesichtspunkte zur Technik der Varizenbehandlung. Ther Umschau 1949; 6: 127-34.

87. Snow V., Qaseem A., Barry P., Hornbake E.R., et al. Management of venous thromboembolism: a clinical practice guideline from the American College of Physicians and the American Academy of Family Physicians. *Ann Intern Med* 2007; 146: 204-10.

88. Stanley P.R.W., Bickerton D.R., Campbell W.B. Injection sclerotherapy for varicose veins – a comparison of materials for applying local compression. *Phlebology* 1991; 6: 37-9.

89. Stücker M., Reich S., Hermes N., et al. Safety and efficiency of perilesional sclerotherapy in leg ulcer patients with postthrombotic syndrome and/or oral anticoagulation with Phenprocoumon. *JDDG* 2006; 4: 734-8.

90. Tazelaar D.J., Neumann H.A.M., de Roos K.P. Long cotton wool rolls as compression enhancers in macrosclerotherapy for varicose veins. *Dermatol Surg* 1999; 25: 38-40.

91. Tessari L., Cavezzi A., Frullini A. Preliminary experience with a new sclerosing foam in the treatment of varicose veins. *Dermatol Surg* 2001; 27: 58-60.

92. Van der Plas J.P.L., Lambers J.C., van Wersch J.W., Koehler P.J. Reversible ischaemic neurological deficit after sclerotherapy of varicose veins. *Lancet* 1994; 343: 428.

93. Villavicencio J., Pfeifer J., Lohr J., Goldman M., Cranley R., Spence R. Sclerotherapy for varicose veins: practice guidelines and sclerotherapy procedures. In: Glovicki P., Yao J. eds. *Handbook of venous disorders*. Chapmann & Hall Medical, London 1996 : 337-54.

94. Vin F. Principes de la sclérothéraphie des troncs saphènes internes. *Phlébologie* 1997; 50: 229-34.

95. Wagdi P. Migräne und offenes Foramen Ovale: nur ein vorübergehender Hoffnungsschimmer? *Kardiovasc Med* 2006; 9: 32-6.

96. Weiss R.A., Sadick N.S., Goldman M.P., Weiss M.A. Post-sclerotherapy compression: controlled comparative study of duration of compression and its effects on clinical outcome. *Dermatol Surg* 1999; 25: 105-8.

97. Weiss R.A., Weiss M.A. Incidence of side effects in the treatment of telangiectasias by compression sclerotherapy: Hypertonics Saline vs. Polidocanol. *J Dermatol Surg Oncol* 1990; 16: 800-4.

98. Wildenhues B. Endovenöse kathetergestützte Schaumsklerosierung. *Phlebologie Germany* 2005; 34: 165-70.

99. Wollmann J.C. Schaum-zwischen Vergangenheit und Zukunft. *Vasomed* 2002; 16: 34-8.

100. Wollmann J.C. The history of sclerosing foams. *Dermatol Surg* 2004; 30: 694-703.

101. Wright D., Gobin J.P., Bradbury A.W., Coleridge-Smith P., Spoelstra H., Berridge D., Wittens C.H.A., Sommer A., Nelzen O., Chanter D., 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: 180-90.

102. 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: 718-22.

103. Yamaki T., Nozaki M., Sasaki K. Color duplex-guided sclerotherapy for the treatment of venous malformations. *Dermatol Surg* 2000; 26: 323-8.

104. Zipper S.G. Nervus peronäus-Schaden nach Varizensklerosierung mit Aethoxysklerol. *Versicherungsmedizin* 2000; 4: 185-7.