A Review of Sclerosing Foam Stability in the Treatment of Varicose Veins

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BACKGROUND Varicose veins are common clinical entities. Foam sclerotherapy is a minimally invasive and simple procedure; however, the side effects, efficacy, and stability of sclerosing foam are not ideal.

OBJECTIVE To summarize the current studies on sclerosing foam stability and promote foam sclerotherapy development.

MATERIALS AND METHODS We reviewed the literature before June 2018 and included only representatives studies on sclerosing foam stability. We summarized the foam half-life time (FHT) of polidocanol (POL) under 17 preparation conditions and the FHT of sodium tetradecyl sulfate under 21 preparation conditions. The preparation conditions included various combinations of temperature, liquid–gas ratio, preparation method, etc.

RESULTS The FHT of POL varied between 40 and 4,000 seconds under different conditions. The FHT of sodium tetradecyl sulfate varied from 25.7 to 390 seconds. The higher the drug concentration, the lower the temperature required to increase foam stability. The addition of surfactant greatly increased foam stability. For different gas compositions, the FHT sequence was as follows: $CO_2 < CO_2 + O_2 < O_2 <$ air.

CONCLUSION Foam stability can be improved by changing the preparation conditions; therefore, the role of surfactants and predictive methods for FHT are worth investigating further.

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Varicose veins and venous malformations are common venous diseases.[1] Until the 1990s, traditional surgery and sclerotherapy have been the most important treatments for varicose veins.[2,3]

Many other minimally invasive techniques such as laser ablation, radiofrequency ablation, and foam sclerotherapy are gradually being used to treat varicose veins of the lower extremities.[4–9] Among these treatment options, foam sclerotherapy is simple to perform, creates only small wounds, does not require hospitalization, and is low-cost.[10–12]

Foam sclerotherapy uses a liquid sclerosing drug such as polidocanol (POL), sodium tetradecyl sulfate (STS), and sodium morrhuate in certain volume ratios with a gas (e.g., air, CO_2, CO_2/O_2, etc.). These are mixed to form a foam that can be injected into varicose veins. Blood is displaced by the foam, and continuous pressure after the procedure forces the veins to collapse. The sclerosing drug comes in contact with the vein wall and causes a sterile inflammatory reaction. Granulation tissue and fibrosis develop in the collapsed vein lumen and eventually form a fibrous cord, which achieves the overall purpose of treating varicose vein

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venous malformations.[13–15] The European Consensus Meetings on Foam Sclerotherapy in 2003[16] and 2006[17] made clear that this method is an optimal choice for the treatment of varicose veins. Foam sclerotherapy has become one of the most important developments in the field of phlebology over the past decade.[18]

Despite these benefits, the safety of foam sclerotherapy has long been a concern. Because of irregularities in drug selection and inconsistencies in the drug concentration proportions, many complications still occur after foam sclerotherapy, including pulmonary embolism and deep vein thrombosis (0.6%–3.2%), phlebitis (4.7%), visual impairment (1.5%), migraine (4.2%), pigmentation changes (17.8%), and skin necrosis (1%).[19–21] Cerebral ischemic shock may also occur in patients with patent stroke.[22] The complications are caused by foaming or liquefied sclerosing drug and gases embolizing to other parts of the body.[19] The purpose of this review was to summarize the current studies on sclerosing foam stability and promote foam sclerotherapy development.

Methods

A systematic literature search of original studies in humans was performed using the PubMed database (last accessed on June 2018) without restrictions on the year of publication. The search terms were "foam half life time" or "FHT" or "foam stability" or "foam sclerotherapy" or "varicose veins." We excluded relatively weak papers and selected 31 articles on sclerosing foam stability from more than 100 papers. Among them, the FHT of 16 articles is summarized in Tables 1 and 2; 9 of them were on the FHT of polidocanol (POL) and 10 on STS (3 papers focused on POL and STS). We summarized the FHT of POL under 17 preparation conditions and the FHT of STS under 21 preparation conditions. These preparation conditions included various combinations of temperature, liquid–gas ratio, sclerotherapy drug concentration, preparation method, surfactants, gas composition, foam drainage time (FDT), and preparation speed. Because of the high heterogeneity of the studies, a meta-analysis was not performed.

Research Status of Sclerosing Foam Stability

Sclerosing foam stability, which is closely related to its efficacy and the potential for adverse reactions, involves complex physicochemical properties of the sclerosing drugs and gases. It is affected by the preparation process, type of drug used, drug concentration and viscosity, environmental factors (air pressure, temperature, etc.), and foam volume. Stable foam provides a more effective barrier to blood and allows the sclerosing drugs remain in prolonged contact with the vein wall. Foam half-life time is the time when the foam drainage rate is 50%. Foam drainage time is the time in which the liquid is visible, and foam coalescence time (FCT) is the time at which the bubble is visible. In recent years, many scholars have conducted various types of experimental studies on the stability of foam sclerotherapy.[23,24] We have summarized some of these scholars' research studies on FHT (Tables 1 and 2), and their reports indicating that FHT has a wide range of variation. The researchers controlled a variety of factors to achieve longer FHTs. For POL, the FHT value increased from 30 to 200 seconds. For STS, the FHT value increased from 25 to 390 seconds. The foam adhesiveness and compactness allows the foam to be easily controlled after injection to drain the blood and reduce dilution. The same dose of the drug can be used to treat long-segment veins after foaming. Whenever the foam has a longer half-life, its therapeutic effect is guaranteed. Stable foam reduces the dosage and concentration required and reduces complications. The main causes of foam decay are drainage and gas diffusion. The rate of drainage is determined by the nature of the solution. The rate of gas diffusion is primarily determined by uniformity of the mean bubble diameter in the foam. There are many factors that affect foam stability; however, current research on sclerosing foam stability is not sufficiently clear. The nature of the foam itself and the factors that affect its stability have not been clarified. To this end, we have reviewed the following studies on foam stability in terms of temperature, liquid–gas ratio, foam sclerosing concentration, preparation method, additives, gas composition, injection time, and other factors.

TABLE 1. FHT of POL

Drug Concentration	Temperature (°C)	Surfactant	Gas Composition	FHT (s) 1:3	FHT (s) 1:4	FHT (s) 1:5
0.25%	20–25	—	Air	—	84[40]	—
0.5%	20–25	—	Air	45[45]	50,[45] 104–107[40]	52[45]
1.0%	20–25	—	Air	65,[45] 135–157[28]	95,[45] 126–135,[28] 110,[40] 115–145,[28] 120–150[37]	105[45]
3.0%	10–20	—	Air	—	120–200[25]	—
	20–25	—	Air	110,[45] 167–191[28]	125,[45] 129,[47] 157–183,[28] 143–192[28]	145[45]
		Tween80	Air	—	220[45]	—
		Xanthan gum	Air	—	4,000[45]	—
		SUL	Air	—	90–107[48]	—
		Glycerin	Air	—	190,[45] 189–260[47]	—
	20–40	—	Air	245–383[46]	50–120[25]	—

CO_2, carbon dioxide; FHT, foam half-life time; O_2, oxygen; POL, polidocanol; SUL, sulodexide.

Temperature Effects

In 2013, Valenzuela and colleagues[25] initially explored the effects of temperature on sclerosing foam stability. The stability of the 4 sclerosing drugs composed from STS and POL at temperatures between 10 and 40°C was studied. They also evaluated the 2 preparation processes without regard to temperature differences and found that the lower the temperature, the better the foam stability. Yue and colleagues[26] looked at temperature change and found it to be negatively correlated with sclerosing foam stability.

Although the previously described studies accounted for different temperature conditions, their temperature differences are not consistent with clinical temperature changes. To that end, Bai and colleagues[27] developed a new process for studying foam preparation at 6 different temperatures 10, 16, 20, 23, 25, and 27°C, which were immediately transferred to a 37°C water bath. They simulated the temperature change in the sclerosing foam as it went from room temperature to body temperature and identified the significant effects of sudden changes in ambient temperature on the inner edge foam stability. They found that when the preparation temperature was increased, the foam became unstable and its FHT was shortened. It is believed that the increased fluidity of the liquid in the foam and the weakening of the viscosity caused by the temperature increase are the main reasons why the foam was more susceptible to decay. In particular, sudden changes in temperature caused the foam at the wall of the tube to become more susceptible to decay.

Liquid–Gas Ratio

Foam decay is affected by its inflow and gas diffusion; gas diffusion is determined by the diameter of the foam. The liquid–gas ratio determines the dryness and wetness of the foam and determines the inflow and diffusion rate.

Van Deurzen and colleagues[28] found that different liquid–gas ratios had little effect on foam stability or the size of the foam produced; however, Cameron and colleagues[29] arrived at different conclusions. They studied foam stability when it was injected into a blood-filled vein simulation model in 1:2, 1:3, 1:4, and 1:8 liquid–gas ratios. Foam filled the model lumen at all liquid–gas ratios except the 1:2 ratio. As the liquid–gas ratio increased, the diameter of the foam increased. In their study, the initial mean bubble diameter in the foam was less than 30 μm, which increased in diameter to form microfoam (<250 μm); after 3 minutes, a microfoam (250–500 μm) was formed and finally a large foam (>500 μm) was formed at 7.5 minutes. They found that the closer the foam was to the surface, the larger its size, and conversely, as the depth increased, the foam size was smaller.

TABLE 2. FHT of STS

Drug Concentration	*Temperature (°C)*	*Surfactant*	*Gas Composition*	*FHT (s)*
0.25%	20–25	—	Air	85.7,[43] 95[40]
			CO_2	25.3[43]
			O_2	85.7[43]
			$CO_2 + O_2$	54.3[43]
0.50%	20–25	SUL	Air	82–109[6]
		Glycerin	Air	89–117.7[30]
		—	Air	70–183,[45] 89,[43] 97–99,[41] 59–106[41]
		—	CO_2	25.7[43]
		—	O_2	79[43]
		—	$CO_2 + O_2$	58[43]
1%	20–25	—	Air	90.7,[8] 92[40]
		—	CO_2	28.3[43]
		—	O_2	73[43]
		—	$CO_2 + O_2$	49.7[43]
		—	Air	142.8[34]
		Hyaluronic acid	Air	310–390[34]
3%	3	—	$CO_2 + O_2$	75–100[49]
			Air	105–195[49]
	10–20	—	Air	10–120[25]
	20–40	—	Air	78–128,[49] 50–100[25]
			$CO_2 + O_2$	46–72[49]

CO_2, carbon dioxide; FHT, foam half-life time; O_2, oxygen; STS, sodium tetradecyl sulfate; SUL, sulodexide.

As research has progressed, study results have gradually become more controversial. Li and colleagues[23] used FHT, FDT, and FCT as indicators of stability and evaluated different liquid–gas ratios from 1:1 to 1:9. They showed that the FDT and FCT of the 1:2 group were the highest and the FHT was also higher. However, Bai and colleagues[27] conducted more detailed studies. They divided the liquid–gas ratio into 1:2, 1:4, and 1:6 groups and found that the foam stability increased first and then decreased with the increasing gas ratio. It is worth mentioning that they fit the foam decay process onto an exponential curve, which provided a more theoretically worthwhile process with respect to foam decay.

Foam Sclerosing Concentration

High foam sclerosing concentration can make vascular fibrosis occur faster and produce foam with better stability. This is beneficial to the treatment effect. However, there are safety hazards in excessive drug residues.

Valenzuela and colleagues[25] reported similar conclusions using Wollmann's test of POL concentration and stability; however, they also found that the effects of STS concentration changes on FHT were not significant. Peterson and Goldman[30] found that at lower concentrations of STS (0.25%, 0.5%, and 1%), small increases in STS foam concentration increased the FHT.

Wollmann[31] tested POL concentrations of 0.25%, 1%, and 3%. The results showed FHTs of 30, 130, and 180 seconds, respectively, indicating that the lower the POL concentration, the faster the foam decay and the greater its instability. Van Deurzen and colleagues[28] reached similar conclusions and found that there were no significant differences in average foam size at different concentrations.

Pigmentation is a clinical symptom of varicose veins and has a significant impact on aesthetics. However, high drug concentrations cause pigmentation changes, which reflect negative results of treatment. Studies have shown that a 1% solution is far less effective

than a 3% solution in the treatment of variceal venous occlusion and aesthetics after rehabilitation. However, 3% concentration may produce more side effects such as superficial phlebitis and pigmentation changes.[32–35]

All in all, the results of the aforementioned studies are limited to experimental phenomena, and the possible mechanisms have not been explored. The effect of concentration on FHT is closely related to ionic charge and the effect on surface tension. It should be pointed out that the current research is far from sufficient, and the results remain controversial.

Preparation Methods

The most common clinically available foam preparation methods in current use include double-injection systems (DSS) and Tessari technology. The foam stability produced by these 2 technologies requires improvement. Therefore, many scholars have changed the original technology or explored new foam preparation methods to produce more stable foams that are suitable for use under different clinical conditions.

In 2014, Whiteley and Patel[36] improved the traditional Tessari technique (Figure 1), which solved the problem of foam adhesion and embolism during the foam injection process. His three-syringe technology allows the foam to be delivered to a third syringe. Subsequently, Xu and colleagues[37] also improved the traditional Tessari technology. They solved the problem of small volumes of foam prepared in a single injection. They added a syringe that could draw up twice the volume of sclerosing liquid and air. This solution not only produced more foam but also improved foam stability. However, the mechanism for improving its stability has not been studied.

In 2015, Carugo and colleagues[38] studied the DSS, the Tessari technology, and the commercially available standard automated POL injection foam polidocanol endovenous microfoam (PEM) to produce sclerosing foam in a biomimetic vein model. They found that the order of FDT in the vein model was PEM > DSS > Tessari. The PEM had a smaller mean bubble diameter in the foam than a physician-compounded foam having a similar CO_2 and O_2 composition. The Tessari method provides foam that is larger in size and dispersion than DSS at the same CO_2 and O_2 composition. PEM provides a smaller and more uniform foam and always exhibits strong stability. In their research in 2017,[39] Critello and colleagues innovatively used low-frequency ultrasound to prepare their sclerosing foam. Theirs was compared with a mechanically stirred foam prepared using the manual Tessari method. They showed that the average size of ultrasonically produced foam was 2 times smaller than that produced by mechanical agitation and 1.6 times smaller than that produced by the manual Tessari method. The maximum foam size was 3 times smaller than that achieved from the clinically used Tessari method. Therefore, ultrasound may be a method to be used for future improvements in foam preparation.

Some scholars have conducted experimental research on whether filters can enhance foam stability. In 2007, Jaggi Rao and Goldman[40] and Shirazi and Mitchel Goldman[41] produced foam stability with a 5-mm filter and a conventional two-way connector. The FHT of the filter element group was significantly higher, which confirmed that the use of a filter can improve foam stability. They considered that the foam became more even and tight as it passed through the filter. In 2011, McMaster[42] performed a similar study using 1.5% STS, which confirmed the results of Shirazi and Mitchel Goldman. However, there was no significant increase in foam stability. The filter had a positive effect on foam stability, the method was simple and convenient, and the cost was low. However, current research on filters needs to be verified through additional studies.

Different foam preparation methods affect the average diameter and uniformity of the foam and foam stability. In general, the smaller the mean bubble diameter in the foam, the more uniform the foam and the better the foam stability. The sclerosing foams prepared by those methods have greater clinical application value due to their higher stability and controllability. They also provide a new direction for research into producing more stable sclerosing foam in the future.

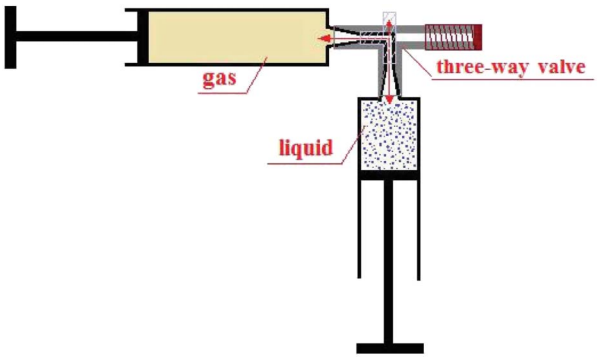

Figure 1. The Tessari method.

Surfactants

Surfactants have been widely used in the industry to enhance foam stability by altering its viscosity and surface tension. Therefore, some scholars have studied the addition of surfactants to sclerosing foams.

In 2011, Peterson and Golman[30] added different volumes of glycerol to STS foam produced by DSS. They found that the addition of a small amount of glycerol increased the FHT of the STS foam, but further addition of glycerol resulted in a decrease in foam stability. This may be because glycerin itself does not have foaming properties. In 2014, Rial and colleagues[24] used the Tessari method to add different concentrations of glycerin to a 3% POL sclerosant to prepare foam. They added a small amount of glycerin (1.66%) to sclerosing foam with good results in stability and quality. Subsequently, Chen and colleagues[34] found that when 0.1 mL 1% hyaluronic acid was added to 1% POL, the FHT of POL foam was extended by 173.38%, significantly enhancing its stability. In 2018, Bai and colleagues[32] studied the effects of 5 surfactants such as poloxamer 188 on foam stability. They found that the stability enhancement effect was obvious, and surfactant enhanced the overall effect of the foam.

The side effects from slower rates of foam degradation caused by additives are still controversial. Peterson and Goldman[30] believed that the combination of glycerol and STS may have caused an increase in the incidence of distal side effects. Rial and colleagues[24] and Chen and colleagues[34] believed that the foam was more stable, and the degradation rate was slower, which may have reduced the occurrence of distal air emboli. Rial and colleagues reported that their group regularly used POL foam containing a small amount of glycerol for 2 years, and no significant complications were observed.

The benefit of using an additive in sclerosing foam is that it enhances the simplicity of the procedure and improves the stability. It is necessary to find more safe and harmless additives and determine the optimum concentrations to be added.

Gas Composition

The gas used in initial foam sclerotherapy processes was room air. N_2 at 80% is minimally soluble in blood, making it more likely to cause an increased risk of gas embolism, which manifests initially as chest tightness and neurological symptoms.[33] Pure CO_2 and CO_2–O_2 gas mixtures can be dissolved and consumed, thus reducing the risk of embolism. Therefore, some scholars have studied preparation methods using O_2, CO_2, or gas mixtures of O_2 and CO_2 instead of room air.

In 2011, McMaster[42] compared the stability of room air and CO_2 foam. They found that CO_2 foam degraded faster. Those authors suggested changing the injection technique to shorten the time between foam preparation and injection to take advantage of the decreased risks associated with the CO_2 foam. In 2011, Frullini[43] studied the stability of air, CO_2, O_2, and mixed gas (CO_2 and O_2) foams under the conditions of foaming by DSS. The order of FHT was found to be room air > CO_2 + O_2 > CO_2. The use of CO_2 + O_2 greatly improved foam stability.

In general, the gas composition of the sclerosing foam is very important. Carbon dioxide is more soluble in the blood,[37] and the rate of degradation is faster. The addition of O_2 facilitates foam formation. Gas type and ratio have a greater impact on the treatment effect.

Other Factors

Pump speed is one of the important factors affecting foam stability and can result in vortex changes during

foam preparation. In 2016, Bai and colleagues[35] developed a self-made foam automatic preparation device. It allowed precise control with preparation speeds ranging from 100 to 350 mm/s. Their results showed that the speed of the injection had a significant impact on foam stability. The FHT peaked at a bolus speed of 275 mm/s and began to decrease thereafter. Those authors believed that the phenomenon may have been related to the formation of foam during foam preparation, including changes in vortex and CO_2 solubility. The following year, Yue and colleagues[26] used polylactic alcohol foam to study the correlation between preparation speed and stability. They reported that the faster the foam was prepared, the higher the foam stability. Clinically, the most suitable pump speed should be chosen to increase foam stability. The lack of uniform manufacturing equipment is a huge problem currently, and the relationship between foam stability and pump speed needs further exploration.

In 2011, McMaster[42] used 1% POL foam to explore the relationship between 5- and 3-mL syringes and foam stability. Their results showed that the relationship between syringe size and FHT was not significant. However, because of the small range of syringe sizes, their data may not be sufficient to explain the problem. Bai and colleagues[44] used 2-, 5-, 10-, 20-, and 30-mL syringes in their 2018 study. The foam was prepared using a self-made device, and they found that smaller syringes produced more uniform foam. However, this conclusion requires further verification. In 2005, Jaggi Rao and Goldman[40] used a 0.5% concentration of STS and a 0.5% concentration of POL. He explored the correlation between the 6 connector types and foam stability. The results showed that the type of connector had no significant effect.

In 2011, Van Deurzen and colleagues[28] compared the foam stability of 1% POL under needle-free, 21-G needle, 23-G needle, and 18-G needle conditions. Foam stability was evaluated by photographing the foam size under a microscope. The results showed that needles of different sizes had little effect on mean bubble diameter in the foam. When the foam was injected directly without a needle, the mean bubble diameter in the foam was slightly smaller. However, the timing of the syringe and pillow connection process was not considered. In the same year, McMaster[42] reacted T1 (75% foam residue) and T2 (50% foam residue required time) to reflect foam stability and found that smaller needles were more likely to produce less stable foam, but the difference was not significant. They also explored the effect of needle size on foam stability in terms of FHT and mean bubble diameter in the foam. However, this requires further exploration and research; the behavior of the patient's intravenous foam has yet to be verified. The effect of atmospheric pressure (and hence altitude) might explain different results from different clinics at vastly different altitudes and different time of year (hence why Patel and colleagues looked at atmospheric pressure as well as temperature). The effect of silicone and nonsilicone syringes can influence the choice of syringe that practitioners use.

Conclusion

Many factors affect the foam stability of sclerosing drugs that are used in the treatment of varicose veins, and the mechanisms are complicated. The conclusions of one particular study cannot definitively be applied to all situations. To address this requires researchers to conduct a large number of studies to evaluate and create a comprehensive system of standard methods of improving foam stability. More importantly, in clinical foam applications, foam performance cannot be evaluated in advance, which hampers the current safety and operational development of foam sclerotherapy. Therefore, the current library of basic experimental studies on the foam stability is insufficient.

To better study the factors affecting foam sclerosing stability, the mechanism of foam decay requires a deeper understanding. New studies to guide experimental research and clinical practice must be designed. The development of foam sclerotherapy requires a more comprehensive approach to foam stability assessments and applications. It is recommended that the Intravenous Association develops a set of requirements for uniform foam preparation in clinical or scientific research, as well as a system that can evaluate foam performance in advance.

References

1. Hamdan A. Management of varicose veins and venous insufficiency. JAMA 2012;308:2612–21.
2. Evans CJ, Fowkes FGR, Ruckley CV, Lee AJ. Prevalence of varicose veins and chronic venous insufficiency in men and women in the general population: Edinburgh vein study. J Epidemiol Community Health 1999;53:149–53.
3. Beebe-Dimmer JL, Pfeifer JR, Engle JS, Schottenfeld D. The epidemiology of chronic venous insufficiency and varicose veins. Ann Epidemiol 2005;15:175–84.
4. Spitz GA, Braxton JM, Bergan JJ. Outpatient varicose vein surgery with transilluminated powered phlebectomy. Vasc Surg 2000;34:547–55.
5. Min RJ, Zimmet SE, Isaacs MN, Forrestal MD. Endovenous laser treatment of the incompetent greater saphenous vein. J Vasc Interv Radiol 2001;12:1167–71.
6. Espinola C. Endovenous treatment of the greater saphenous vein with a 940-nm diode laser: thrombotic occlusion after endoluminal thermal damage by laser-generated steam foams. J Vasc Surg 2002;35:729–36.
7. Goldman MP, Mauricio M, Rao J. Intravascular 1320-nm laser closure of the great saphenous vein: a 6- to 12-month follow-up study. Dermatol Surg 2010;30:1380–5.
8. Kistner RL. Endovascular obliteration of the great er saphenous vein: the closure procedure. Jpn J Phlebol 2002;13:325–33.
9. Pavlović MD, Schuller-Petrović S. Endovascular techniques for the treatment of chronic insufficiency of the lower limb's superficial venous system. Rev Vasc Med 2014;2:107–17.
10. Bergan J, Pascarella L, Mekenas L. Venous disorders: treatment with sclerosant foam. J Cardiovasc Surg (Torino) 2006;47:9–18.
11. O'Hare JL, Earnshaw JJ. The use of foam sclerotherapy for varicose veins: a survey of the members of the Vascular Society of Great Britain and Ireland. Eur J Vasc Endovascular Surg 2007;34:232–5.
12. Gibson KD, Ferris BL, Pepper D. Foam sclerotherapy for the treatment of superficial venous insufficiency. Surg Clin North Am 2007;87:1285–xiii.
13. Committee G, Force T. Guidelines of care for sclerotherapy treatment of varicose and telangiectatic leg veins. J Am Acad Dermatol 1996;34:523–8.
14. Michiels C, Bouaziz N, Remacle J. Role of the endothelium and blood stasis in the appearance of varicose veins. Int Angiol 2002;21:1–8.
15. Wollmann JC. Re: the history of sclerosing foam. Dermatol Surg 2005;31:249.
16. Breu FX, Guggenbichler S. European Consensus Meeting on Foam Sclerotherapy. 2003, Tegernsee, Germany. Dermatol Surg 2003;30:709–17.
17. Breu FX, Guggenbichler S, Wollmann JC. 2nd European consensus meeting on foam sclerotherapy 2006, Tegernsee, Germany. VASA 2008;37:1–29.
18. Jia X, Mowatt G, Burr JM, Cassar K, et al. Systematic review of foam sclerotherapy for varicose veins. Br J Surg 2007;94:925–36.
19. 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 2010;30:718–22.
20. Gillet JL, Guedes JM, Guex JJ, Hamel-Desnos C, et al. Side-effects and complications of foam sclerotherapy of the great and small saphenous veins: a controlled multicentre prospective study including 1,025 patients. Phlebology 2009;24:131–8.
21. Siribumrungwong B, Noorit P, Wilasrusmee C, Thakkinstian A. A systematic review and meta-analysis of randomised controlled trials comparing endovenous ablation and surgical intervention in patients with varicose vein. Eur J Vasc Endovasc Surg 2012;56:576–7.
22. Morrison NA, Bergan J, Partsch H. Regarding "Stroke after varicose vein foam injection sclerotherapy". J Vasc Surg 2006;44:224–5.
23. Li L, Feng J, Zeng XQ, Li YH. Fluoroscopy-guided foam sclerotherapy with sodium morrhuate for peripheral venous malformations: preliminary experience. J Vasc Surg 2009;49:961–7.
24. Rial R, Hervas LS, Monux G, Galindo A, et al. Polidocanol foam stability in terms of its association with glycerin. Phlebology 2014;29:304–9.
25. Valenzuela GC, Wong K, Connor DE, Behnia M, et al. Foam sclerosants are more stable at lower temperatures. Eur J Vasc Endovasc Surg 2013;46:593–9.
26. Yue L, Wang Y, Dong J, Chen A, et al. Influence of temperature on the stability of lauromacrogol foam for sclerotherapy. China J Oral Maxillofacial Surg 2017;15:198–201.
27. Bai T, Chen Y, Jiang W, Yan F, et al. Studies on foam decay trend and influence of temperature jump on foam stability in sclerotherapy. Vasc Endovascular Surg 2017;52:98–106.
28. Van Deurzen B, Ceulen RP, Tellings SS, Van DGC, et al. Polidocanol concentration and time affect the properties of foam used for sclerotherapy. Dermatol Surg 2011;37:1448–55.
29. Cameron E, Chen T, Connor DE, Behnia M, et al. Sclerosant foam structure and stability is strongly influenced by liquid air fraction. Eur J Vasc Endovasc Surg 2013;46:488–94.
30. Peterson JD, Goldman MP. An investigation on the influence of glycerin on sclerosant foam stability. Phlebology 2011;26:232–4.
31. Wollmann JC. The history of sclerosing foams. Dermatol Surg 2010;30:694–703.
32. Bai T, Liu Y, Liu J, Yu C, et al. A comparison of different surfactants on foam stability in foam sclerotherapy in vitro. J Vasc Surg 2019;69:581–e1.
33. Coleridge SP. Sclerotherapy and foam sclerotherapy for varicose veins. Phlebology 2009;24:260–9.
34. Chen AW, Liu YR, Li K, Liu SH. An investigation on the influence of hyaluronic acid on polidocanol foam stability. Dermatol Surg 2015;42:56–8.
35. Bai T, Jiang W, Zhao W, Wan H, et al. Experimental study on influence of driving speed on foam stability in sclerotherapy for the treatment of varicose veins. J Biomed Eng 2016;35:891–5.
36. Whiteley MS, Patel SB. Modified Tessari Tourbillon technique for making foam sclerotherapy with silicone-free syringes. Phlebology 2015;30:614–7.
37. Xu J, Wang YF, Chen AW, Wang T, et al. A modified Tessari method for producing more foam. Springerplus 2016;5:129–3.
38. Carugo CD, Ankrett DN, O'Byrne V, Wright DD, et al. The role of clinically-relevant parameters on the cohesiveness of sclerosing foam in a biomimetic vein model. J Mater Sci Mater Med 2015;26:258.
39. Critello CD, Fiorillo AS, Matula TJ. Size of sclerosing foam prepared by ultrasound, mechanical agitation, and the handmade Tessari method for treatment of varicose veins. J Ultrasound Med 2017;36:649–58.
40. Jaggi Rao MD, Goldman MP. A 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 2010;31:19–22.

41. Shirazi R, Mitchel Goldman MD. The use of a 5-μm filter hub increases foam stability when using the double-syringe technique. Dermatol Surg 2010;34:91–2.

42. McMaster S. Sodium tetradecyl sulphate foam stability prior to injection: factors affecting liquid reformation. Phlebology 2011;26:222–6.

43. Frullini A. Commentary: an investigation into the influence of various gases and concentrations of sclerosants on foam stability. Dermatol Surg 2011;37:12–7.

44. Bai T, Jiang W, Fan Y. Influence of syringe volume on foam stability in sclerotherapy for varicose vein treatment. Dermatol Surg 2018;44:689–96.

45. Nastasa V, Samaras K, Ampatzidis Ch, Karapantsios TD, et al. Properties of polidocanol foam in view of its use in sclerotherapy. Int J Pharm 2015;478:588–96.

46. Mcaree B, Ikponmwosa A, Brockbank K, Abbott C, et al. Comparative stability of sodium tetradecyl sulphate (STD) and polidocanol foam: impact on vein damage in an in-vitro model. Eur J Vasc Endovascular Surg 2012;43:721–5.

47. Morrisona N, Rogers CR, Mceown J, McEown J, et al. Incidence of side effects using carbon dioxide–oxygen foam for chemical ablation of superficial veins of the lower extremity. Eur J Vasc Endovascular Surg 2010;40:407–13.

48. Davide CC , Fiorillo AS , Chiara CM , Stefano DF, et al. Effects of sulodexide on stability of sclerosing foams. Phlebology: J Venous Dis 2018;34:191–200.

49. Patel SB, Ostler AE, Dos Santos SJ, Piriea TM, et al. The effects of environmental and compositional manipulations on the longevity of Tessari-made foam for sclerotherapy. J Vasc Surg Venous Lymphat Disord 2014;3:312–8.

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