

Foam sclerotherapy

How to improve results and reduce side effects?

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Keywords

Foam sclerotherapy, transthoracic echocardiography, transcranial Doppler

Summary

Methods to improve the efficacy of foam sclerotherapy might include: more vigorous agitation methods to produce more stable foam with smaller bubble size, increasing the volume and/or concentration of the sclerosing agent, use of an intravenous catheter, and leg elevation to evacuate as much blood as possible. Methods to improve the safety of foam sclerotherapy might include: use of an intravenous indwelling catheter; saphenofemoral junction occlusion; low foam volume; use of low silicon syringes; use of non air-based foam; avoidance of high concentration sclerosing agents in patients with duplicated femoral vein segments; leg elevation before or after injection of foam; and maintaining patient immobility after injection.

A series of studies and exercises are described which call into question many methods proposed to limit the dispersal of injected foam. The use of non air-based foam may reduce the incidence of side effects.

Schlüsselwörter

Schaumsklerotherapie, transthorakale Echokardiographie, transkranialer Doppler

Zusammenfassung

Verfahren zur Verbesserung der Wirksamkeit der Schaumsklerotherapie sind: turbulente Mischverfahren, um stabilen Schaum mit kleinen Blasen zu erzeugen, Erhöhung des Volumens und/oder der Konzentration des Sklerosierungsmittels, Einsatz eines Venenkatheters, Hochlagern der Beine, um Blutleere zu erzeugen. Verfahren zur Verbesserung der Sicherheit der Schaumsklerotherapie sind: Einsatz von Venenverweilkathetern, saphenofemorale Ligatur, geringes Schaumvolumen, Einsatz von Spritzen mit niedrigem Silikonanteil, Verwendung von Schaum, der als Gaskomponente keine Luft enthält, Vermeidung hoher Sklerosierungsmittel-Konzentrationen bei Patienten mit doppelt angelegten Segmenten der Oberschenkelvene, Hochlagern der Beine vor und nach Schauminjektion und Einhaltung der Liegezeit nach Injektion.

Mehrere Studien und Tests werden beschrieben, die viele Verfahren in Frage stellen, die zur Begrenzung der Ausbreitung des injizierten Schaums empfohlen wurden. Mit Schaum ohne Luft als Gaskomponente kann die Inzidenz von Nebenwirkungen verringert werden.

Mots clés

Sclérothérapie à la mousse, échocardiographie trans-thoracique, doppler trans-crânien

Résumé

Les méthodes pour améliorer l'efficacité de la sclérothérapie à la mousse sont nombreuses : il faut mélanger avec vigueur le liquide pour obtenir les bulles les plus petites possibles, augmenter le volume et/ou la concentration de l'agent sclérosant, utiliser un cathéter intraveineux et surélever la jambe pour en vider le maximum de sang possible. Pour augmenter la sécurité du traitement il faut : placer correctement le cathéter intraveineux, obtenir l'occlusion de la jonction saphéno-fémorale, utiliser un faible volume de mousse, avoir des seringues faiblement siliconées. La mousse ne doit pas être mélangée à de l'air; il faut éviter les fortes concentrations d'agent sclérosant chez des patients avec des segments veineux fémoraux dupliqués; la surélévation de la jambe doit être faite avant ou après l'injection de mousse; le patient doit rester immobile après l'injection. Il existe une série d'études et de méthodes dont le but est de limiter la dispersion de la mousse injectée. L'usage d'une mousse produite sans air doit réduire le nombre des effets secondaires.

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Schaumsklerotherapie

Wie können Therapieergebnisse verbessert und Nebenwirkungen reduziert werden?

Sclérothérapie à la mousse

Peut-on améliorer les résultats et diminuer les effets secondaires ?

Reports of sclerosis of abnormal lower extremity veins using foam sclerotherapy (UGFS) have appeared in the world literature since 1950 (1). Beginning with personal reports by Antonio Luis Cabrera, and then with literature reports in 1997 (2), discussion has continued to gain momentum (3–6). The detergents used to create foam for sclerosis are:

- sodium morrhuate,
- ethanolamine oleate,
- sodium tetradecyl sulfate (STS), and
- polidocanol.

In most reports either polidocanol or STS has been utilized.

Successful ablation rates have been reported to range from 68% (7) to 96% (8), although interpretation of these results is made more difficult because of the differences in definitions of success, the use of surrogate markers (occlusion of treated vein, resolution of reflux), differing primary outcome markers (resolution of symptoms, improved quality of life scores, recurrent varices, ulcer healing), and the number of UGFS sessions needed to achieve success, among others. Moreover, reports of follow up periods range from one month to ten years, although the studies reporting results of over 3 years demonstrated success rates of 81%–92% (9–12).

To demonstrate the difficulty in obtaining accurate information from duplex scans following treatment, we have shown that efforts to identify and report a surrogate marker such as incomplete ablation of the treated vein by duplex scan are plagued by inconsistencies in the sensitivity of duplex equipment (13). These inconsistencies directly affect the ability to detect residual flow in the treated vein, and potentially lead to overestimation of success rates. Furthermore, the accuracy of the follow up duplex examination is dependent on the expertise and independence of the examiner, and the vigour with which the examination is conducted.

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Many methods have been proposed to improve efficacy and safety have appeared in the literature and have been presented in scientific congresses around the world. These methods will be the subject of this article.

Improvements

Efficacy

Suggestions to improve efficacy (Tab. 1) have included agitation methods which enhance the durability and uniformity of foam (4, 14), increasing the concentration of the liquid sclerosant (15–16), and increasing the volume of foam utilized during and injection session (15, 17–18).

However, in a review of the published and unpublished data available in the world literature, Jia et al (19) concluded that there exists „insufficient data to determine the optimal volume of foam, optimal concentration and optimal foam-producing method.”

Foam sclerotherapy of the saphenous vein via an indwelling catheter may be able to better deliver sclerosant foam to the endothelium of the targeted vein (20). However, according to the 2nd European Consensus Conference on Foam Sclerotherapy, there is no clear consensus on the use of catheters for foam sclerotherapy (21).

Foam production methods that create microbubbles of smaller size may add to the efficacy by increasing the direct contact of the sclerosing agent with the endothelium first by displacing blood as much as possible from the targeted vein; and second by greatly increasing the total surface area of the smaller bubbles to which the active sclerosant is attached, thereby increasing endothelial contact (22–23).

For similar reasons, leg elevation prior to the injection will also help clear blood from the vein, thus allowing greater sclerosant contact with the endothelium and less sclerosant mixing with and deactivation by blood (24).

And finally, it is clear that simply creating thrombosis of a target vein will likely not result in permanent occlusion of the vein. Damage to or destruction of the vein wall is necessary to assure sclerosis (24–25) (Tab. 1).

Tab. 1 Increased efficacy

- agitation methods
- increased sclerosant concentration
- increased sclerosant volume
- indwelling catheter
- smaller bubble size
- leg elevation (for empty vein)

Safety

Just as with liquid sclerotherapy, all of the methods proposed to improve efficacy carry the risk of side effects and complications (19). Many reports in the literature mention the safety of foam sclerotherapy anecdotally (15, 26–35), and there are numerous reports describing infrequent or rare neurologic or visual disturbances (15, 22, 27, 30, 33–38). A few reports examine specific complications of foam (39–42), but studies that critically examine the overall safety of foam for sclerosis of abnormal leg veins remain scant (22, 36, 43).

Several methods have been proposed to improve the safety of foam sclerotherapy, some of which are listed in Table 2. One method to improve safety of ultrasound guided foam sclerotherapy is to insert an indwelling catheter for the delivery of foam rather than direct injection (20, 44). By aspiration of blood and a small test dose of foam injected through the catheter into the target vein, this method will give the phlebologist more assurance that the catheter is intravenous and thus foam is being delivered to the targeted vein. It will also allow for the formation of foam to immediately precede injection, thus producing a more robust foam as there will be little time for foam

Tab. 2 Safety

- indwelling catheter (balloon-tipped or open-ended)
- SFJ occlusion
- limitations on sclerosant volume
- low silicon syringe
- non air-based foam
- avoidance of duplicated femoral vein thrombosis
- leg elevation pre-injection
- leg elevation post-injection
- patient immobility

SFJ: sapheno-femoral junction

degradation that produces bubble coalescence, larger bubble size, and thereby less active sclerosant made available for endothelial contact. Large bubbles migrating into the central circulation potentially carry an increased risk of lodging in the arterial microcirculation in the presence of a right-to-left shunt (39). When foam is prepared and then injected through the syringe and needle directly into a vein, there will be necessarily some time between foam production and injection, depending on how long it takes to image the target vein and advance the needle into the vein. Factors influencing this lag time are the technical skill of the person acquiring the target vein image and the skill of the phlebologist in needle puncture of the target vein.

A balloon-tipped catheter will allow for occlusion of the saphenous junction, theoretically preventing foam from entering the deep venous system. However, during a study using just such a catheter in the author's center, foam bubbles could be seen by duplex examination entering the deep venous system during balloon inflation through small thigh perforators resulting in a significantly higher incidence of deep venous thrombosis (4/27 patients, 15% – unpublished data) (45).

And in fact many European phlebologists think it is better to have foam gradually migrating into the deep venous system than to have a large bolus enter the central circulation when the occlusive balloon is deflated.

Limiting the volume of foamed sclerosant injected at any one time has been proposed as a method to improve safety (21–22). In a study from the author's center, examination of the side effects and complications of large volume air-based foam is described below (46).

Four studies, three exercises

Study 1

Objective: A prospective clinical trial of 49 consecutive patients with truncal or nontruncal superficial venous insuffi-

ciency, treated with UGFS using 1% polidocanol air-based foam, to analyze rates of perioperative toxicity and complications, and to establish an adverse effect profile.

Patients, material and methods:

Forty-nine patients with truncal or non-truncal venous insufficiency, all with previous ablation of the proximal great saphenous vein, were treated with 1% polidocanol foam, injected under ultrasound guidance into the distal great or small saphenous veins and/or tributaries. Polidocanol foam was produced by the Tessari method, using room air and 1% Sclerovein[®], mixed in a 4:1 ratio. Injected volumes ranged from 8–52 ml (mean, 27 ml). Patient interviews and monitoring of BP, pulse rate, respiratory rate, EKG, and pulse oximetry were conducted preoperatively, at 15-minute intervals during treatment, immediately postoperatively, 30 and 60 minutes after completion of treatment (longer if symptoms occurred). Patients were then interviewed 2, 6, and 24 hours post treatment. Adverse effects were monitored for 24 hours or until resolution, and included: chest discomfort, dry cough, changes in BP, pulse rate, EKG, or pO₂, dizziness, visual disturbances, and nausea.

Results: Statistically significant decreases in heart rate occurred ($p < 0.001$), less than 5 bpm, which were not physiologically significant. Blood pressure, respiratory rate, electrocardiogram, and partial oxygen pressure (pO₂) did not change significantly during UGFS or for 60 minutes afterwards ($p > 0.05$). The most commonly occurring adverse effects were dry cough, chest discomfort, and visual disturbances (none of which occurred in patients receiving less than 16 ml of foam), although only with dry cough was there a positive correlation between symptoms and increasing volume of injectate over 16 ml. Chest discomfort was seen in 18% (4/49). Visual disturbances were experienced by 8.2% (4/49). Other adverse effects included dizziness reported in 12% and nausea in 4%. Side effects rarely lasted more than 1–4 hours. No deep vein thromboses

(DVTs) were detected by follow-up duplex scan performed in response to symptoms.

Conclusions: Ultrasound-guided injection of polidocanol foam, in large volumes, appears to be associated with few significant complications, although some short-lived adverse effects do occur in patients injected with more than 16 ml of foam. Concerning these adverse effects, only dry cough appeared to have a direct correlation with the volume of foam injected (>16 ml).

Use of low-silicone syringes enhances foam stability, it is presumed because silicone helps speed foam degradation. Thus foam microbubbles will remain stable for a longer time with silicone-free or low-silicone syringes, allowing for more time to complete a successful injection (23, 47).

Foam degradation will also be influenced by the type of gas used to create the foam. While the use of CO₂-based foam may be desirable to lower the side effect profile (46), the same high solubility coefficient and high diffusibility in body fluids results in rapid degradation and thus significantly shortens the time period between foam production and injection (16). As interest grew in replacing the air used to produce foam with a more soluble and diffusible gas (27, 39), a second clinical trial was conducted to test the theory that because of its presumably more rapid dissolution CO₂-based foam would produce fewer adverse effects than air-based foam.

Study 2

Objective: To report a prospective clinical trial, enrolling 128 patients with truncal or nontruncal superficial venous insufficiency, treated with ultrasound-guided injection of 1% polidocanol CO₂-based foam, analyzing rates of toxicity and complications in the perioperative period, and to establish an adverse effect profile.

Patients, materials and methods:

This study was a follow up to the study using air-based foam, and was performed

in precisely the same manner, utilizing different patients who also had previously undergone saphenous vein ablation procedures. In this study, pure CO₂ was used to produce the foamed sclerosant instead of air with a range of injected foam volume of 6–45 ml (mean 26 ml).

Results: As in Study 1, no physiologically significant changes were seen while monitoring blood pressure, electrocardiogram, heart rate, respiratory rate, or pO₂. Chest tightness, dry cough, and dizziness occurred in 3.1% (4/128), 1.6% (4/128), and 3.1% (4/128) respectively, statistically significantly less often with CO₂-based foam than with air-based foam ($p < 0.001$, $p < 0.001$, $p < 0.02$, respectively) (Tab. 3).

Visual disturbances and nausea were seen to trend lower for an incidence of 3.1% (4/128) and 2% (3/128) respectively, compared to the air-based foam group (8.2% and 4% respectively, $p = 0.15$).

Conclusions: Comparing CO₂-based foam with air-based foam, adverse effects decreased statistically significantly (or trended downward) if CO₂ was employed to produce the sclerosing foam.

Tessari has shown that a gas combination of 70% CO₂ and 30% O₂ to produce foam will result in a more stable, longer-lasting foam than pure CO₂-based foam (48). Of practical significance is if, as in most of Europe, the phlebologist must also function as the sonographer, use of the more stable CO₂/O₂-based foam will be more advanced

Tab. 3 Comparison of side effects of patients treated with CO₂-based foam and air-based foam

symptom	air		CO ₂		chi-square p
	n	%	n	%	
chest tightness	9	18	4	3.1	<0.001
dry cough	8	16	2	1.6	
dizziness	6	12	4	3.1	0.019
metallic, medicinal taste	0	0	2	1.6	0.39
nausea	2	4	3	2	0.53
circumoral paraesthesia	0	0	1	0.8	

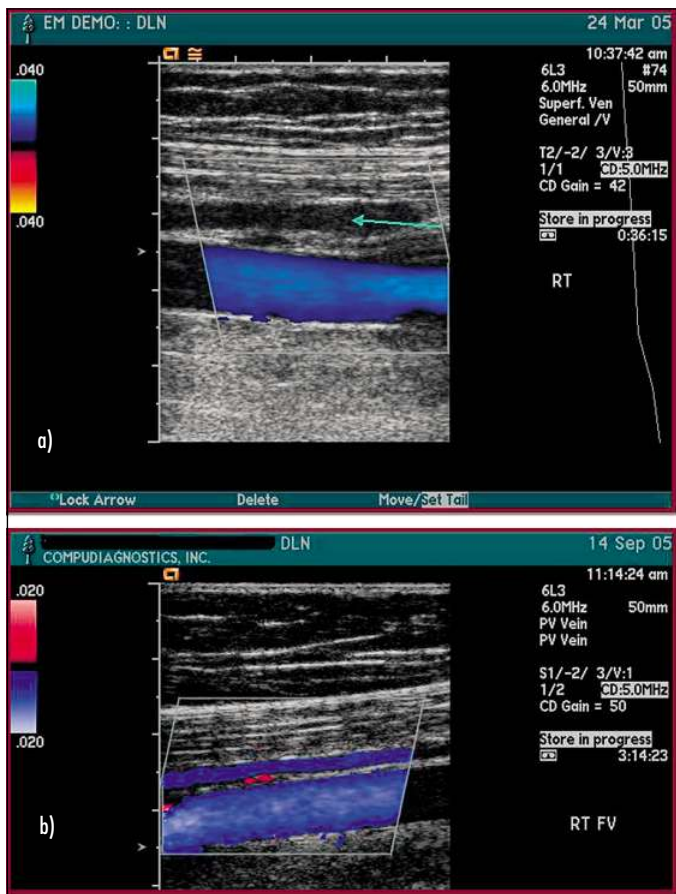


Fig. 1
Colour Doppler
(Courtesy Compu-
dianostics, D Neuhardt)
a) antegrade flow in
duplicated femoral vein
segment
b) post foam sclero-
therapy showing
thrombosed duplicated
femoral vein segment

tageous allowing for more time to acquire the target vein image, direct the needle into the vein, and inject foam. The side effect profile advantage of a more soluble gas such as the CO₂/O₂ combination as compared to air is also maintained.

In a follow up study to the previous two studies, reported in November, 2007, another cohort of patients were injected with CO₂/O₂-based foam and the side effect profile was compared to that of the air-based foam and the pure CO₂-based foam (49). Patients in the CO₂/O₂-based foam group were 40 times less likely to experience the side effects of dry cough, metallic taste, and chest tightness than patients in the air-based foam group. And patients in the CO₂/O₂-based foam group were 7 times less likely to experience nausea, visual disturbances, and dizziness than patients in the air-based foam group.

Another specific safety concern regarding complications of foam sclerotherapy is the incidence of deep vein thrombosis (15,

27, 32, 36, 50, 51). An apparently high incidence of thrombosis in duplicated femoral vein segments following UGFS has been seen in our center. The following study was conducted to see if the presence of a duplicated femoral vein represents a risk factor for thrombosis.

Study 3

Objective: Because it has been reported that approximately 30% of the normal population has a duplicated femoral vein segment (26, 52), and the incidence of deep vein thrombosis (DVT) following ultrasound guided foam sclerotherapy is generally reported to be <1% (32, 36, 50, 51), the aim is to determine if the presence of a duplicated femoral vein segment is a risk factor for development of deep vein thrombosis following ultrasound guided foam sclerotherapy.

Patients, materials and methods:

Forty-three patients with duplex ultrasound-documented true duplicated segments of femoral veins were treated with ultrasound guided foam sclerotherapy for superficial venous insufficiency, using a foam volume range of 1.5–9 ml. One to three percent polidocanol and sodium tetradecylsulfate foamed with air or CO₂ gas was injected into truncal and non truncal superficial veins of the lower extremity. Injections were delivered by needle or a balloon-tipped catheter. Standard post sclerotherapy treatment included immediate and continued compression and ambulation, with 30–40 mmHg compression hose for three weeks. Detailed duplex examination of the treated leg was conducted within 48 hours, including evaluation of the common femoral vein, femoral vein, profunda femoral vein, popliteal vein, posterior tibial veins, anterior tibial veins, peroneal veins, and gastrocnemius veins. If thrombosis of any vein was identified, follow up duplex examination was continued until resolution or stabilization of the thrombosis was confirmed. If no thrombosis was identified, the patient was re-examined at one week and six weeks.

Results: Five of 43 patients (8.6%) were found to have complete thrombosis of the duplicated femoral vein segment (Fig. 1). In four of the five patients with thrombosis 3% STS air-based foam was used, and in the remaining patient 3% polidocanol CO₂-based foam was used. No other deep venous thromboses were identified.

Conclusion: The presence of a duplicated femoral vein segment in patients undergoing ultrasound guided foam sclerotherapy appears to be a risk factor for deep vein thrombosis in the duplicated segment especially with the use of 3% detergent sclerosants.

Next, because of uncertainty regarding the extent to which foam travels from the target vein and the belief expressed in scientific assemblies and the literature that the dispersal of foam, once injected, could be controlled and specifically prevented from entering the deep venous system, a series of exercises were designed and

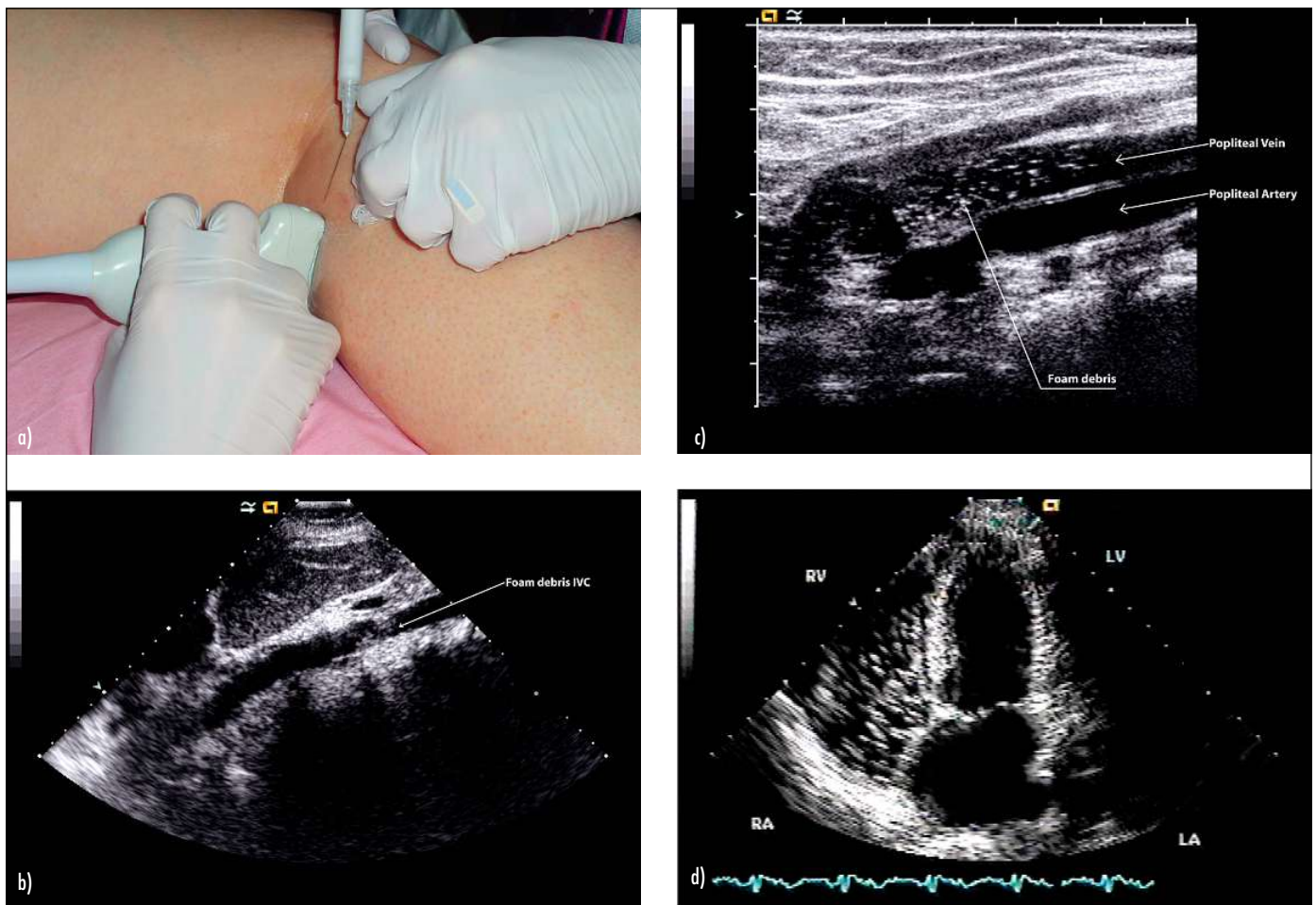


Fig. 2 Under ultrasound guidance, a 1 mm peripheral leg vein is injected with foam (a), bubbles are seen in a perforator vein (b, ←), at the entrance of the inferior vena cava to the right heart (c, ←), and in the right heart (d); Courtesy Compudiagnostics, D Neuhardt
R(L)V: right (left) ventricle; R(L)A: right (left) atrium

conducted to follow the course of foam injected into peripheral superficial leg veins.

Exercise 1

Objective: Follow course of foam from peripheral vein injection site to deep venous system and heart.

Patients, materials and methods:

Twenty-one patients undergoing ultrasound guided foam sclerotherapy using 1% foamed sclerosant, were injected with 1–2 ml of foamed sclerosant into 1–2 mm peripheral superficial leg veins. The foam was produced in the standard Tessari method (33) – 4:1 ratio of room air to 1% liquid polidocanol. All patients had a pre-

operative transthoracic echocardiogram negative for right-to-left shunt. All patients had transthoracic echocardiography simultaneous with ultrasound guided injection of foam (Fig. 2).

Results: Bubbles could be identified by ultrasound in the injected peripheral vein, perforator vein, deep venous system, inferior vena cava, and the right heart 10–30 seconds after every injection. Furthermore, bubbles could still be seen in the right heart more than two minutes after each injection.

Conclusion: Small volumes of foamed sclerosants injected into peripheral venous leg tributaries are quickly and persistently identified within the perforators, deep venous system, inferior vena

cava, and heart, even several minutes following the initial injection. Dispersal of foam microbubbles is rapid and extensive.

Because bubbles passed so quickly to the right heart, the next exercise was designed to determine if a right-to-left shunt could be identified by means of the appearance of bubbles in the left heart.

Exercise 2

Objective: To test whether it is possible to reliably identify right-to-left shunting during ultrasound guided foam sclerotherapy using simultaneous transthoracic echocardiography.

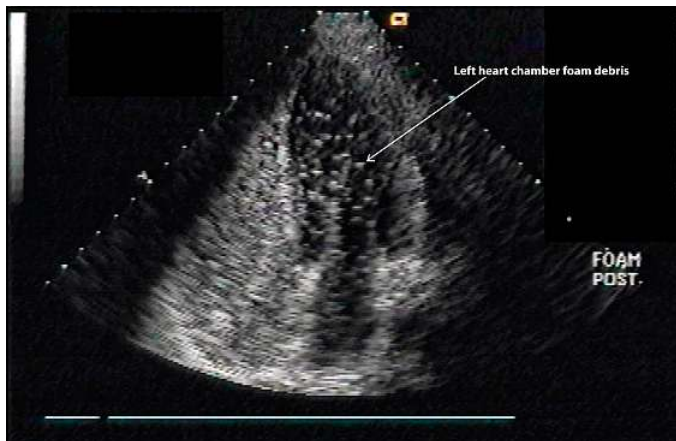


Fig. 3
Four chamber trans-thoracic echo showing left heart with bubbles from right heart within 10 seconds of initial injection of foam into peripheral leg vein (Courtesy Compu-diagnostics, D Neuhardt).

Patients, materials and methods:

With symptoms of visual disturbances, headache, or altered mentation following UGFS 21 patients were studied using additional UGFS simultaneous with transthoracic echocardiography. Patients in reversed Trendelenberg and modified left lateral decubitus positions, during and after injection of 1–3 ml of foam into a peripheral leg vein, were studied with transthoracic echocardiography. Pressure gradients were then established by asking patients to perform Valsalva's maneuver or cough.

Results: No right-to-left shunts could be demonstrated on preoperative transthoracic echocardiography and none were seen immediately following ultrasound guided foam injection into a peripheral leg vein, even though bubbles were readily identified in the right heart. However, following the establishment of pressure gradients with Valsalva's maneuver or cough there was demonstrated right-to-left shunting in 7 of 21 patients (30%). This ratio approximates that in the normal population expected to have patent foramen ovale (Fig. 3) (53).

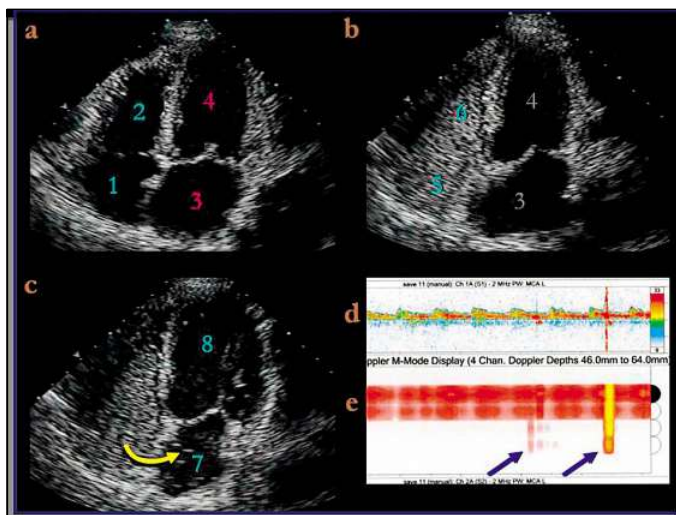


Fig. 4
Transthoracic echocardiography (a–c) and transcranial Doppler (d, e); Courtesy Compu-diagnostics, D Neuhardt
a) four chamber view of heart
b) bubbles filling right atrium and ventricle following injection of foam sclerosant into peripheral leg vein
c) bubbles (yellow arrow) progressing from right atrium through patent foramen ovale into left atrium
d, e) images depicting HITS (blue arrows) in middle cerebral artery following foam injection into peripheral leg vein

Conclusion: It is possible to reliably identify right-to-left shunts in patients undergoing peripheral leg vein ultrasound guided foam sclerotherapy with the use of transthoracic echocardiography and the establishment of a pressure gradient.

Because bubbles could readily be identified in the left heart in patients with right-to-left shunts, the question arose as to whether bubble emboli could be identified by transcranial Doppler (TCD) monitoring of the middle cerebral arteries in patients with proven right-to-left shunts. Exercise 3 examines this question.

Exercise 3

Objective: Examine the middle cerebral artery for emboli during and following UGFS by means of transcranial Doppler via the temporal window in patients with known right-to-left shunts undergoing UGFS.

Patients, materials and methods: Seven patients found to have right-to-left shunts during simultaneous ultrasound guided foam sclerotherapy of peripheral superficial veins of the lower extremity and transthoracic echocardiography were re-examined adding bilateral transcranial Doppler monitoring of the middle cerebral arteries. One to three ml of foam were injected into a peripheral leg vein 1–2 mm in diameter under ultrasound guidance, with the patient in a modified left lateral supine position (in order to permit simultaneous UGFS, transthoracic echocardiography, and transcranial Doppler monitoring), followed by multiple active calf pumps to mobilize the foam into the central circulation.

Results: Four of seven patients (57%) were found to have middle cerebral artery HITS (high-intensity transient signals) during the transcranial Doppler examination, confirmed with 97% likelihood to be emboli.

Conclusions: Emboli can be detected and followed through the heart into the

cerebral circulation by use of transcranial Doppler in patients undergoing UGFS who have right-to-left shunts (Fig. 4).

Because the exercise described above is cumbersome for patients, technologists, and physicians, we are attempting to simplify our investigations by designing a protocol wherein only bilateral transcranial Doppler monitoring is performed during ultrasound guided foam sclerotherapy on a series of patients in which the status of any right-to-left shunting was unknown. We have observed that patients frequently will not develop neurologic or visual symptoms until they move upon completion of the foam sclerotherapy session. We are examining the timing of the symptoms to test for a temporal correlation to emboli in the middle cerebral arteries. This study is ongoing and will be presented with a detailed analysis of the data at the 22nd Annual American College of Phlebology Congress, November, 2008.

A major question that remains unanswered is whether neurologic or visual symptoms can be correlated with bubble emboli in the cerebral circulation. One could postulate that these emboli could lodge in the cerebral microcirculation, causing ischemia which produces the transient symptoms described by patients. An elegant study was conducted by David Eckmann, MD, et al³⁹, sponsored in part by the manufacturer of a commercial foam preparation, to compare flow characteristics of commercial foam to so-called "homemade" foam (such as is prepared in all vein treatment centers currently using foam sclerotherapy).

Study 4: Microvascular embolization following polidocanol microfoam sclerosant administration*

Objective: To determine the relationship between polidocanol microfoam formulation and arteriolar embolization bubble lodging and clearance in vivo.

Materials and methods: Polidocanol microfoam formulations using different

* David M. Eckmann, Shunji Kobayashi, Min Li

Fig. 5 Four chamber trans-thoracic echocardiogram three seconds following injection with patient in Trendelenberg (Courtesy Compudiagnostics, D Neuhardt): Bubbles are seen to fill the right atrium (RA) and ventricle (RV).



physiologic gas mixtures composed primarily of oxygen and carbon dioxide were mixed with venous blood and injected into the rat cremaster arterial microcirculation. Bubble dimensions and dynamics were recorded using intravital microscopy. This was, in essence, a comparison of so-called homemade foam (air-based polidocanol foam as produced by the majority of phlebologists using the Tessari method) and commercially-prepared foam (Varisolve – Provensis, BTG).

Results: Bubble entry frequency, size, and dynamics depended on microfoam formulation. Air-based bubbles lodged in arterioles, obliterating blood flow. Varisolve bubbles entered but either did not lodge or cleared within seconds. Bubble size and number were different among these microfoams. The commercially-prepared foam bubbles were smaller than homemade foam bubbles, and did not ap-

pear to obstruct micro-arterial flow as did the bubbles from homemade foam.

Conclusions: The Varisolve formulations produced smaller embolism bubbles than occurred with air-based microfoam. Rapid clearance of Varisolve bubbles suggests that they are so small that they do not have adequate surface area available for significant binding interactions with arteriolar endothelium. Larger air-based bubbles obstruct arteriolar vessels and block blood flow.

While Dr. Eckmann did not speculate as to whether neurologic or visual symptoms might be caused by obstruction in the cerebral arterial microcirculation by bubble emboli, it has been postulated that certain maneuvers might have a protective effect on the cerebral circulation by limiting or preventing bubbles from arriving in the brain. We conducted a series of experiments designed to test the efficacy of these ma-

Fig. 6 Four chamber trans-thoracic echocardiogram following ultrasound guided injection (Courtesy Compudiagnostics, D Neuhardt): Bubbles can still be detected in the right heart more than ten minutes following initiation of injection. (Note timer at 10:42)

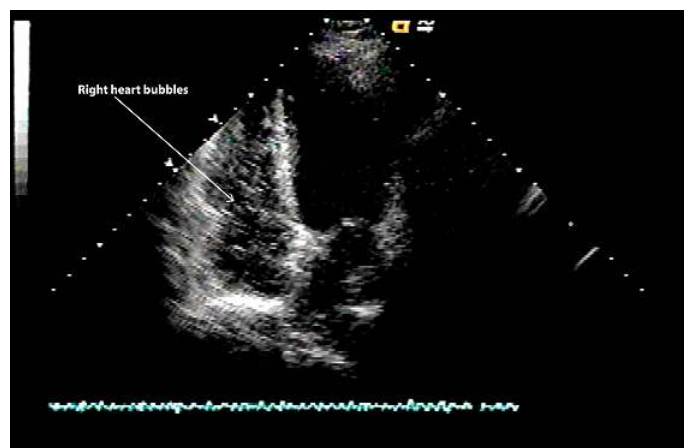




Fig. 7 Four chamber trans-thoracic view showing right heart filled with bubbles, and also in the left heart (7) (yellow arrow) into the left atrium; Courtesy CompuDiagnostics, D Neuhardt

nevers in limiting or preventing the dispersal of microbubbles.

Five testing theories

Theory 1

If the patient is kept in a moderate Trendelenberg position, foam injected into truncular veins of the leg under ultrasound guidance will “rise” to the distal leg rather than progress into the central circulation.

Method: 3 ml of 1% Polidocanol air-based foam injected into the great saphenous vein in the distal thigh under ultrasound guidance in five patients (Fig. 5).

Conclusion: Trendelenberg position does not prevent foam from entering the central circulation

Theory 2

Keeping patients immobile following ultrasound guided foam sclerotherapy will prevent bubbles from dispersing into the central circulation (21).

Method: 2 ml of 1% Polidocanol air-based foam injected into a 1.7 mm peripheral leg vein under ultrasound guidance, with the patient immobile for over 10 minutes, while continuously monitoring the heart for bubbles using transthoracic echocardiography (Fig. 6).

Conclusion: Maintaining patient immobility for a period of time following and ultrasound guided foam injection into a peripheral leg vein will not prevent bubbles from entering the central circulation

Theory 3

If the patient remains immobile during ultrasound guided foam sclerotherapy, bubbles will not pass into the left heart through a right-to-left shunt (Fig. 7)

Conclusion: In patients with existent right-to-left, maintaining patient immobility following UGFS does not prevent bubbles from circulating to the left heart.

Theory 4

If the patient remains immobile for several minutes after ultrasound guided foam sclerotherapy, foam will then not embolize to the cerebral circulation. (Fig. 8)

Conclusion: Following injection of a small peripheral leg vein, using small volumes of foamed sclerosant, just as foam is detected in the left heart in patients with right-to-left shunts following UGFS, emboli can also be detected in the middle cerebral artery when the patient sits up after maintaining immobility for as long as 15 minutes.



Fig. 8 Transcranial Doppler tracing of middle cerebral artery in a patient 15 minutes after being injected with 3 ml of 1% foamed sclerosant into a 2 mm peripheral leg vein under ultrasound guidance (Courtesy CompuDiagnostics, D Neuhardt): The patient remained immobile following the injection, and then carefully (to avoid disruption of the TCD monitoring device) sat up. Several emboli can be identified in the middle cerebral artery (lower row 2A–2D).

Theory 5

Using low volumes of foam during ultrasound guided foam sclerotherapy will prevent cerebral embolization (see Fig. 8 above) (54).

Conclusion: Cerebral emboli can readily be detected by TCD following injection of as little as 3 ml of foam during UGFS. Limiting the volume of foam injected in any one sclerotherapy session will not prevent cerebral emboli in patients with right-to-left shunts.

Questions

- While some information may be gleaned from these studies, other questions have arisen or remain unanswered.

- Do the bubbles seen in the heart on trans-thoracic echocardiography during UGFS contain active sclerosing agent?
- Are the cerebral emboli seen on transcranial Doppler following UGFS gas bubbles, cellular debris, or other particles with or without active sclerosant agent?
- Is there a positive correlation between the number of emboli and the development of symptoms?
- Is there a positive correlation between the number of emboli and the volume of foam injected, or with the development of symptoms?
- And lastly, since all of the adverse effects in Table 4 have been reported following the use of liquid sclerosants (15), are these symptoms now reported following UGFS related to the chemical sclerosant itself, cellular debris from vein wall destruction, the foam transmission agent and resultant gas bubbles, or something else entirely?

The answers to some of these questions may come as a result of carefully-conducted clinical trials currently ongoing in the U.S., specifically looking for adverse effects of cerebral, cardiac, and renal origin.

Tab. 4 Adverse effects

- dry cough
- migraine
- chest tightness
- circumoral paraesthesia
- metallic taste
- nausea
- dizziness
- hyperpigmentation
- ocular migraine
- visual disturbance
- panic attack
- respiratory difficulty
- cutaneous necrosis
- deep vein thrombosis
- STP

Conclusions

In spite of the fact that it is not possible to control the course and dispersal of foam injected into peripheral or truncal superficial veins, and in light of the thousands of UGFS sessions performed throughout the world on a daily basis with minimal or rare adverse effects reported, UGFS appears to be a reasonably safe method of superficial venous ablation. However, it may be prudent that caution should guide the phlebologist as more information on the physiologic effects of foam is forthcoming.

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