Review Article

Phlebology

Phlebology
2014, Vol. 29(1S) 55–60

DOI: 10.1177/0268355514526681
phl.sagepub.com

Are Non-Tumescent Ablation Procedures Ready to Take Over?

Mikel Sadek and Lowell S Kabnick

Abstract

Tumescent anesthesia refers to the percutaneous administration of large volume anesthetic to cause the target tissue to become swollen or firm. The use of tumescent anesthesia is essential for the treatment of refluxing truncal veins using endothermal technologies. In order to obviate the use of tumescent anesthesia as an adjunct to treatment, one has to evaluate the technologies that do not employ thermal energy as the modality for treatment. These technologies include foam sclerotherapy, mechanicochemical ablation (MOCA), and the use of glue (Sapheon™ closure system). The following review juxtaposes the literature supporting the use of tumescent-based techniques to the literature supporting the use of tumescent-less techniques

Keywords

Tumescent, endothermal ablation, mechanicochemical ablation, Sapheon™

Introduction

The short answer is that we do not yet know the answer to the question at hand. Prior to discussing non-tumescent ablation procedures and the associated data in the literature, it bears reviewing the principles behind tumescent anesthesia, and its use in venous ablation procedures for the treatment of truncal reflux.

Tumescent anesthesia refers to the use of large volume administration of dilute local anesthetic to cause the target tissue to tumescence or to become swollen and firm. The regional anesthesia and heat sink properties of this technique allow for the use of endothermal techniques. The typical solution used consists of a combination of dilute lidocaine, epinephrine, and bicarbonate in a normal saline solution.[1,2] Jeffrey Klein developed the technique of using tumescent anesthesia, as delineated in his report from 1986.[3] Initially, the technique was employed for liposuction, but it has since been generalized to a variety of cosmetic and dermatologic procedures.[4,5] With the rise of endothermal technologies in the late 1990s, the technique of administering tumescent anesthesia was translated to the endothermal ablation procedure. The two most commonly used technologies are endovenous laser ablation (EVLA) and radiofrequency ablation (RFA).

Tumescent anesthesia refers to the large volume administration of fluid that causes the tissue to tumescence thereby allowing the vein to collapse onto the catheter. This has the secondary effect of permitting more efficient ablation of the vein due to improved vein wall apposition, and a decreased incidence of surrounding thermal injury because it acts as a heat sink. Consequently, the use of tumescent anesthesia in the office setting is characterized by several advantages including a proven safety profile, diminished blood loss, avoidance of general anesthesia, reduced thermal injury resulting in pain, bruising, paresthesias, pigmentation, skin retraction and cost-effectiveness. For the aforementioned reasons, the use of tumescent anesthetic is essential for the treatment of refluxing truncal veins that use endothermal technologies. The primary disadvantage of tumescent anesthesia is the associated risk of lidocaine toxicity, which usually manifest as neurologic followed by cardiac cardiac sequelae. With regards to the dosage of lidocaine used in the setting of tumescent anesthesia, it should be kept to less than 35–45 mg/kg.[6,7] In addition, tumescent anesthetic needs to be administered percutaneously resulting in multiple needles sticks and associated procedural pain.

New York University Langone Medical Center, Department of Surgery, New York, NY, USA

Corresponding author:
Lowell S Kabnick, New York University Langone Medical Center, Department of Surgery, Division of Vascular Surgery, 530 First Avenue, Suite 6F, New York, NY 10016, USA.
Email: Lowell.Kabnick@nyumc.org

In order to obviate the use of tumescent anesthesia as an adjunct to treatment, one has to evaluate the technologies that do not employ thermal energy as the modality for treatment. These technologies include foam sclerotherapy, mechanicochemical ablation (MOCA), and the use of glue (Sapheon closure system). The following review will juxtapose the literature supporting the use of endothermal ablation techniques that utilize tumescent anesthesia to the literature supporting the use of non-tumescent based techniques for the treatment of truncal reflux resulting in chronic venous insufficiency.

Tumescent-based techniques

EVLA

There are multiple iterations and variables that characterize the laser ablation modality. The initial endothermal technologies utilized laser wavelengths that are on the lower end of the spectrum. These lower wavelengths target hemoglobin as the chromophore, and are labeled hemoglobin-specific laser wavelengths (HSLW): 810, 940, 980, and 1064 nm.[8] By targeting hemoglobin as the chromophore, this generates damaging thermal energy to the intima and results in ablation of the treated vein.[9] By utilizing longer treatment wavelengths, lasers exhibit an increasing affinity for water as the chromophore. By targeting water within the vein wall or red blood cell, thermal energy is absorbed more efficiently. These lasers are referred to as water-specific laser wavelengths (WSLW), and some examples are: 1320, 1470 and 1510 nm.[9] Additional variations exist with regards to fiber tip, power setting, and the linear endovenous energy density (LEED) utilized.

The safety and efficacy of EVLA has been well established. Kabnick conducted a randomized trial comparing the 810 nm laser to the 980 nm laser.[10] There were 30 patients in each group, and the treatment groups were standardized to the same LEED (49.2 J/cm vs. 45.9 J/cm, P = NS). Only 2 treatment failures occurred per group on one-year follow-up. The bruising score was higher in the 810 nm group as compared to the 980 nm group (810 nm: 2.4 vs. 980 nm: 1.6, P = 0.005), presumably secondary to a slightly increased specificity to water as the chromophore, but the overall rates of complications were low in both groups. Numerous studies were performed subsequently to compare the HSLW to WSWL lasers. Proebstle et al. compared the 940 nm HSLW laser (at 15 W and 30 W) to the 1320 nm WSLW laser (at 8 W).[11] With regards to efficacy, the occlusion rates were similar in both groups at 3 months follow-up (90.3% vs. 100% vs. 97%) in the three groups. With regards to post-procedural symptoms the 1320 nm group as compared to the 940 nm (30 W) group exhibited significantly less pain (50% vs. 81%, P < 0.005) and bruising. Mackay et al. chose to compare the same laser wavelengths of 940 nm and 1320 nm within the same patient, in those patients that required bilateral lower extremity venous ablation procedures.[8] The overall settings were similar between the two groups, specifically ensuring an equivalent LEED. The previously reported results were reproduced, whereby the efficacy rates were the same, but post-procedural pain and bruising scores were lower in the limbs treated using the 1320 nm laser. The efficacy and durability of laser ablation have also been corroborated by a multicenter registry created by the International Endovenous Laser Working Group (IEWG).[12] The dataset was derived from 11 participating centers in the United States and Europe and comprised 1020 limbs treated using a 980 nm bare-tip laser. Life-table analyses revealed failure rates of 7.7% at 1 year, 5.4% at 2 years, and no additional reported cases of treatment failures at 3 years.

RFA

The RFA procedure, now referred to as the Venefit™ procedure (Covidien, Mansfield, MA), is another tumescent-based treatment that is well-validated, safe and efficacious.[13] The VNUS ClosureFast catheter represents the most recent iteration of the technology that utilizes segmental ablation at 7 cm intervals as compared to a continuous pull-back technique. The different iterations of the RFA technology have demonstrated safety and efficacy profiles comparable to that for EVLA. With regards to the segmental ablation technique, the most recent prospective evaluation by Proebstle et al. demonstrated the mid-term efficacy of the treatment. Specifically, 256 patients were treated using the ClosureFast device, and the reported vein occlusion rate at three years was 95.7%.[14,15] The data has been replicated on numerous occasions in other retrospective series.[16]

Tumescent-less techniques

These techniques comprise well-validated treatment modalities as well as newer technologies that share the common characteristic of not utilizing thermal energy to effect venous ablation. The criticisms of these newer techniques or modalities reside in the lack of level I evidence that demonstrates their safety and efficacy.

Sclerotherapy

Sclerotherapy in the setting of the treatment of chronic venous insufficiency refers to the direct injection of a vein using a chemical sclerosant, either in the liquid or

foam form. For the purposes of this discussion, sclerotherapy refers to the direct treatment of refluxing truncal veins in the setting of chronic venous insufficiency. The administered sclerosant functions by causing an inflammatory reaction in the vein wall thereby resulting in vein wall contraction, scarring and ablation. In the setting of truncal ablation, foam sclerotherapy is used more commonly due its inherent ability to treat a larger surface area. Commonly used sclerosant solutions include 1–3% polidocanol (in the United States 1% polidocanol is the maximum concentration allowed) and 1.5%–3% sodium tetradecyl sulphate (STS).[17–19] Even though tumescent anesthesia is not required due to the lack of potential damage secondary to thermal effects, foam sclerotherapy treatments may require local anesthesia at the time of administration. Bradbury et al. evaluated 1252 treated limbs treated with foam sclerotherapy for truncal reflux.[20] With regards to efficacy, re-treatment was required in 12.9 % of patients at a mean of 17 months following the initial procedure. Three patients developed a deep venous thrombosis (DVT) and one developed a pulmonary embolus, for a 0.4% thromboembolic complication rate. Unique to foam sclerotherapy, five patients developed peri-procedural transient visual disturbance but no other neurological sequelae.

For truncal veins, the data suggest that foam sclerotherapy is less effective than RFA or EVLA. A meta-analysis evaluated 64 studies (N = 12,320) comparing RFA, EVLA, foam sclerotherapy and traditional surgery. Estimated pooled success rates at 3 years were 84% for RFA, 94% for EVLA, 78% for surgery, and 77% for foam sclerotherapy.[21] Another study evaluated foam sclerotherapy (N = 53) as compared to EVLA (N = 45) for the treatment of refluxing truncal veins, and at one year 93.4% of EVLA-treated veins remained occluded as compared to 77.4% in the foam sclerotherapy group.[22]

Given the decreased effectiveness of foam sclerotherapy as compared to the endothermal ablation technologies, the cost-effectiveness of the said procedure has also been evaluated. Gohel et al. evaluated the published data comparing surgery, EVLA, RFA and foam sclerotherapy.[23] EVLA and RFA were found to be equally cost-effective to traditional surgery. Foam sclerotherapy was least expensive initially. Nevertheless, the increased rate of reintervention required for foam sclerotherapy made it the least cost-effective in the long-term as compared to the other modalities.

MOCA

The use of a combination of mechanical and chemical ablation (MOCA^{TM}) has been touted as a methodology to treat superficial venous reflux without the use of tumescent anesthesia. The ClariVein® device is comprised of an infusion catheter that has tips which rotate at 3500 rpm at 2–3 second intervals.[24] As the catheter is withdrawn, the device effects vein ablation by scoring the vein wall while simultaneously infusing a sclerosant solution. Elias et al. evaluated 30 patients who underwent GSV ablation using the ClariVein® device.[24] A 96.7% closure rate was observed on follow-up with intervals ranging from 6.0 to 8.5 months. No adverse events, including DVTs, were noted. In another study 30 limbs in 25 patients treated using the ClariVein® device with polidocanol as the slcerosant were evaluated.[25] The occlusion rate at 6 weeks was noted to be 87%. The complications were minor such that 9 patients developed ecchymosis, and 4 patients developed thrombophlebitis that was self-limiting. There were no DVTs. With regards to quality of life, there was also a significant improvement in the average venous clinical severity score (VCSS) at 6 weeks. The largest study to date evaluated 268 limbs using the ClariVein® system. The treated veins included 210 great saphenous veins, 44 small saphenous veins and 14 anterolateral side branches. At 6 months follow-up, there was a 94% occlusion rate. In this study a higher percentage of patients than reported previously exhibited minor complication. Twenty one percent of patients experienced superficial thrombophlebitis, and 26% of patients developed a hematoma at the puncture site.[26] Most recently, a prospective evaluation was performed on 50 consecutive patient who underwent treatment of the small saphenous vein (SSA) using MOCA.[27] At 1 year follow-up anatomic success identified by duplex ultrasound was achieved in 94% of patients. VCSS improved from 3.0 to 1.0 at 1 year follow-up ($P < 0.001$). Lastly, there were no major complications including DVTs or nerve injury. To date, one prospective evaluation has been performed to compare RFA to MOCA.[28] A total of 68 patients exhibiting unilateral GSV reflux were compared. The pain visual analog scale was used to compare the two cohorts at 2 weeks and the results were improved significantly in the MOCA cohort (MOCA: 4.8 ± 9.7 mm vs. RFA: 18.6 ± 17.0 mm; $P < .001$). Both general and disease specific quality of life questionnaires that were evaluated at 6 weeks revealed improved quality of life scores in the MOCA group as compared to the RFA group.

Sapheon

The VenaSeal^{TM} Sapheon closure system uses catheter delivered glue (a proprietary formulation of n-butyl cyanoacrylate) to treat refluxing truncal veins.[29] The glue functions by polymerization on contact with an anion containing solution, typically blood when used in the vascular system. It has been used commonly in

Table 1. Risk-benefit profile for tumescent-based as compared to tumescent-less ablation techniques.

	Benefits	Risks
Tumescent-based (EVLA, RFA)	– Safe – Efficacious – Durable	– Multiple needle-sticks – Thermal injury (nerve, skin, etc.) – Thrombophlebitis – Endothermal heat-induced thrombosis
Tumescent-less (Foam, MOCA™, Sapheon™)	– Safe (likely)	– Efficacy is less for foam, and still being established for others – Limited amount of sclerotherapy solution for MOCA™ – Thrombophlebitis with Sapheon™ (? Acute and chronic foreign body reaction) – Thrombus extension – Limited and conflicting efficacy data – No durability data

the arterial and venous systems in order to treat various pathologies requiring adhesive-based or occlusion-based treatments, and at the doses typically used in endovenous or endovascular procedures it does not exhibit any toxic effects. Once again, the VenaSeal™ system provides for a tumescentless procedure, since no thermal energy is required. When initially reported, successful treatment of the great saphenous vein was achieved in 8 people.[30] More recently, the first-in-man dataset was expanded to 38 patients, and technical success was achieved in 100% of patients, and no DVTs were reported. Sixteen percent of patients developed self-limiting thrombophlebitis, which has been described as an erysipeloidphlebitic skin reaction.[31] The one-year occlusion rate was 92.1%. In addition, a prospective multi-center European study was conducted on 69 patients.[32] The total occlusion rate at 3 months was 94.2%. There was one patient that developed a thrombus extension into the common femoral vein, and this was self-limiting without the use of anticoagulation. The thrombophlebitis rate was 8.7%. The VCSS did improve from an average of 4.4 to 1.8 on one month follow-up.

Discussion

Now that a general overview of the data has been presented, one needs to address the original question of, ''are non-tumescent ablation procedures ready to take over?'' In order to answer yes to the aforementioned question, the data should demonstrate non-inferiority of the tumescent-less procedures as compared to the tumescent-based procedures. Subsequently, the data must show a statistically significant improvement in the tumescentless procedures as compared to the tumescent-based procedures. In addition, one has to evaluate the risk-benefit profile of the various procedures (Table 1).

To date, foam sclerotherapy is the only modality that has been compared directly to the endothermal ablation technologies in a reproducible way. The data is delineated above, and it demonstrates that from a safety, efficacy, durability, quality-of-life and cost-effectiveness perspective, the endothermal ablation procedures are superior to foam sclerotherapy, and in fact superior to traditional surgery. With regards to the MOCA™ and VenaSeal™ procedures, the majority of the data reported is based on single-cohort series. The data comparing the said technologies to endothermal ablation need to be reproduced and are still forthcoming. In addition, the safety and more significantly, the efficacy data, have been conflicting. Lastly, there is no durability or long-term safety data, which may be pertinent in the setting of leaving a foreign-body (i.e. glue) in the vasculature. Although one can speculate that the aforementioned risks are negligible, they need to be borne out by rigorous analysis. This is especially true given that there is already a proven alternative. Currently used endothermal techniques are safe, efficacious, expeditious, cost-effective and have stood the test of time.

Conclusion

To conclude, the tumescentless procedures have demonstrated some promising, although conflicting, initial safety and efficacy data. They should continue to be evaluated and used in a trial setting. Once enough trial data is accrued to provide for a substantive life-table analysis, and once the treatment is compared in a randomized fashion to the presently established endothermal-based techniques and non-inferiority is established, then non-tumescent ablation procedures may be ready to take over. For now, the Klein pumps should remain primed.

Funding

This research received no specific grant from any funding agency in the public, commercial, or not-for- profit sectors.

Conflict of interest

Dr. Sadek does not have any conflicts of interest to declare. Dr. Kabnick is a consultant for the following companies: Angiodynamics, BTG, and Vascular Insights.

References

1. Janne d'Othée B, Faintuch S, Schirmang T and Lang EV. Endovenous laser ablation of the saphenous veins: bilateral versus unilateral single-session procedures. *J Vasc Interv Radiol* 2008; 19: 211–215.
2. Keel D and Goldman MP. Tumescent anesthesia in ambulatory phlebectomy: addition of epinephrine. *Dermatol Surg* 1999; 25: 371–372.
3. Welch JD. History of tumescent anesthesia, part I: from American surgical textbooks of the 1920s and 1930s. *Aesthet Surg J* 1998; 18: 353–357.
4. Habbema L. Safety of liposuction using exclusively tumescent local anesthesia in 3,240 consecutive cases. *Dermatol Surg* 2009; 35: 1728–1735.
5. Boeni R. Safety of tumescent liposuction under local anesthesia in a series of 4,380 patients. *Dermatology* 2011; 222: 278–281.
6. Mysore V; IADVL Dermatosurgery Task Force. Tumescent liposuction: standard guidelines of care. *Indian J Dermatol Venereol Leprol* 2008; 74(Suppl): S54–60.
7. Janne d'Othée B, Faintuch S, Schirmang T and Lang EV. Endovenous laser ablation of the aphenous veins: bilateral versus unilateral single-session procedures. *J Vasc Interv Radiol* 2008; 19: 211–215.
8. Mackay EG, Almeida JI and Raines JK. Do different laser wavelengths translate into different patient experiences? *Endovascular Today* 2006; 45–48.
9. Munavalli GS and Weiss RA. Advances in Techniques for Endovenous Ablation of Truncal Veins. *Skin Therapy Lett* 2006; 11: 4–7.
10. Kabnick LS. Outcome of different endovenous laser wavelengths for great saphenous vein ablation. *J Vasc Surg* 2006; 43: 88–93.
11. Proebstle TM, Moehler T, Gül D and Herdemann S. Endovenous treatment of the great saphenous vein using a 1,320 nm Nd:YAG laser causes fewer side effects than using a 940 nm diode laser. *Dermatol Surg* 2005; 31: 1678–83; discussion 1683–1684.
12. Spreafico G, Kabnick L, Berland TL, Cayne NS, Maldonado TS, Jacobowitz GS, Rockman CR, Lamparello PJ, Baccaglini U, Rudarakanchana N and Adelman MA. Laser saphenous ablations in more than 1,000 limbs with long-term duplex examination follow-up. *Ann Vasc Surg* 2011; 25: 71–8.
13. Gómez-Palacio Villazón M and Águila-Márquez R. Minimally invasive venous surgery. *Cir Cir* 2010; 78: 497–504.
14. Proebstle TM, Vago B, Alm J, Göckeritz O, Lebard C and Pichot O. Treatment of the incompetent great saphenous vein by endovenous radiofrequency powered segmental thermal ablation: first clinical experience. *J Vasc Surg* 2008; 47: 151–156.
15. Proebstle TM, Alm J, Göckeritz O, Wenzel C, Noppeney T, Lebard C, Pichot O, Sessa C and Creton D European Closure Fast Clinical Study Group. Three-year European follow-up of endovenous radiofrequency-powered segmental thermal ablation of the great saphenous vein with or without treatment of calf varicosities. *J Vasc Surg* 2011; 54: 146–152.
16. Creton D, Pichot O, Sessa C and Proebstle TM ClosureFast Europe Group. Radiofrequency-powered segmental thermal obliteration carried out with the ClosureFast procedure: results at 1 year. *Ann Vasc Surg* 2010; 24: 360–366.
17. Coleridge Smith P. Sclerotherapy and foam sclerotherapy for varicose veins. *Phlebology* 2009; 24: 260–269.
18. Kakkos SK, Bountouroglou DG, Azzam M, Kalodiki E, Daskalopoulos M and Geroulakos G. Effectiveness and safety of ultrasound-guided foam sclerotherapy for recurrent varicoseveins: immediate results. *J Endovasc Ther* 2006; 13: 357–364.
19. Ikponmwosa A, Abbott C, Graham A, Homer-Vanniasinkam S and Gough MJ. The impact of different concentrations of sodium tetradecyl sulphate and initial balloon denudation on endothelial cell loss and tunica media injury in a model of foam sclerotherapy. *Eur J Vasc Endovasc Surg* 2010; 39: 366–371.
20. Bradbury AW, Bate G, Pang K, Darvall KA and Adam DJ. Ultrasound-guided foam sclerotherapy is a safe and clinically effective treatment for superficial venous reflux. *J Vasc Surg* 2010; 52: 939–945.
21. van den Bos R, Arends L, Kockaert M, Neumann M and Nijsten T. Endovenous therapies of lower extremity varicosities: a meta-analysis. *J Vasc Surg* 2009; 49: 230–239.
22. Gonzalez-Zeh R, Armisen R and Barahona S. Endovenous laser and echo-guided foam ablation in great saphenous vein reflux: one-year follow-up results. *J Vasc Surg* 2008; 48: 940–946.
23. Gohel MS, Epstein DM and Davies AH. Cost-effectiveness of traditional and endovenous treatments for varicose veins. *Br J Surg* 2010; 97: 1815–23.
24. Elias S and Raines JK. Mechanochemical tumescentless endovenous ablation: final results of the initial clinical trial. *Phlebology* 2012; 27: 67–72.
25. van Eekeren RR, Boersma D, Elias S, Holewijn S, Werson DA, de Vries JP and Reijnen MM. Endovenous mechanochemical ablation of great saphenous vein incompetence using the ClariVein device: a safety study. *J Endovasc Ther* 2011; 18: 328–334.
26. Boersma D, van Eekeren RR, Werson DA, et al. Mechano-chemical endovenous ablation in great and small saphenous vein incompetence using ClariVein®; Initial results of an innovative tumescentless technique. *Phlebologie* 2011.
27. Boersma D, van Eekeren RR, Werson DA, van der Waal RI, Reijnen MM and de Vries JP. Mechanochemical endovenous ablation of small saphenous vein

insufficiency using the ClariVein® device: one-year results of a prospective series. *Eur J Vasc Endovasc Surg* 2013; 45: 299–303.
28. van Eekeren RR, Boersma D, Konijn V, de Vries JP and Reijnen MM. Postoperative pain and early quality of life after radiofrequency ablation and mechanochemical endovenous ablation of incompetent great saphenous veins. *J Vasc Surg* 2013; 57: 445–50.
29. Lawson J, Gauw S, van Vlijmen C, Pronk P, Gaastra M, Mooij M and Wittens CH. Sapheon: the solution? *Phlebology* 2013; 28(Suppl 1): 2–9.
30. Almeida JI. Nonthermal ablation for the treatment of varicose veins. Endovascular Today 2011; bmctoday.net/evtoday/2011/04/article.asp?f=nonthermal-ablation-for-the-treatment-of-varicose-veins (accessed October 2011).
31. Almeida JI, Javier JJ, Mackay EG, Bautista C and Proebstle T. Cyanoacrylate glue great saphenous vein ablation: preliminary 180-day follow-up of a first-in-man feasibility study of a no-compression-no-local-anesthesia technique. *J Vasc Surg* 2012; 55: 297.
32. Proebstle TM, Almeida J, Rasmussen L, Dimitri S, Lawson JA, Whiteley M, Franklin IJ and Davies AH. The European Multicenter Study on Cyanoacrylate Embolization of Refluxing Great Saphenous Veins without Tumescent Anesthesia and without Compression Therapy. *Journal of Vascular Surgery: Venous and Lymphatic Disorders* 2013; 1: 101.