The Balance Between Success and Treatment-Related Side Effects in Endovenous Ablation of Saphenous Veins

Understanding the significance of energy dosing and the risks of favoring low side effect profiles over reliably successful ablation.

BY THOMAS M. PROEBSTLE, MD, PHD

The spectrum of endovenous ablation techniques for saphenous veins in daily clinical practice includes the injection of sclerosants and the application of endothermal techniques. Among the latter options, radiofrequency (RF)-powered segmental ablation and various laser systems share the market, while pressurized steam ablation is still in clinical trials. In terms of efficacy and side effect profile, chemical endovenous ablation using liquids or foam injection—with or without the help of catheters and duplex ultrasound—still does not meet the benchmarks set by endothermal ablation techniques.

Since the publication of the relationship between energy dosing and treatment success in 2004, an ablation rate exceeding 99% is generally possible for all endothermal techniques. The current standards set by RF-powered segmental thermal ablation, namely an initial success rate of more than 99% in combination with a very smooth side effect profile, obviously stimulated many laser companies to develop new fiber tips to further improve the side effect profile. In some cases, the recommended energy dose was reduced to further ameliorate observed side effects and increase periprocedural quality of life. However, with all the efforts to reduce side effects as much as possible, a high initial success rate of more than 99% must still be preserved.

CHEMICAL ABLATION: SCLEROSANTS

Endovascular ablation of saphenous veins in general can be achieved by injection of chemically active substances such as polidocanol or sodium tetradecyl sulfate, which are used as liquid or—outside the United States—preferably as foam. They act as detergents to remove the endothelial layer and furthermore to provide substantial damage to the vein wall's media layer. Apart from a transient spasm, they do not cause substantial acute vein wall shrinkage. A clot or *sclerus*—a term used preferably by some opinion-leading sclerotherapists—has to occlude the vein before a subsequent inflammatory tissue response finally leads to a fibrotic cord several weeks or months later.

It is generally accepted and supported by good study data that foam is much more effective in achieving chemoablation than liquid sclerotherapy.[1] For example, a single injection with 3% polidocanol foam achieved the intended ablation of truncal reflux in 85% of greater saphenous veins (GSVs) with diameters between 4 and 8 mm, whereas the same amount of liquid polidocanol 3% achieved occlusion in only 35% of cases. Two years later, the observed success rates were only 53% and 12%, respectively.[1] Another study showed reflux ablation 3 months

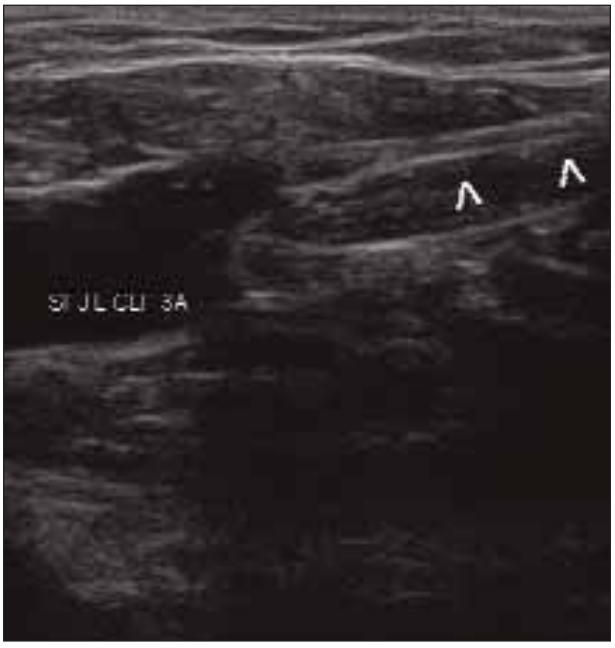

Figure 1. Three-year follow-up ultrasound B-scan of the saphenofemoral junction of the first human case ever treated with segmental thermal ablation. The supine GSV diameter at 3 cm distal to the saphenofemoral junction was 6.7 mm before treatment. The diameter of the remaining fibrotic cord at the same location was 3.9 mm at 3 months and 1.1 mm at 3 years after treatment with ClosureFast (arrows).

after foam injection in 69% of GSVs, but only 27% after injection of liquid polidocanol 3%.[2] In addition to the rather low occlusion rates after one treatment, the side effect profile is not negligible with sclerotherapy. Common side effects, such as phlebitis or hyperpigmentation, were observed in up to 50% of cases after foam injection.[3] Furthermore, sclerotherapy-specific side effects, such as visual disturbance and central nervous system symptoms of short duration, happen infrequently. Even brain ischemia has been reported after the use of sclerosant foam.[4] In patients with a patent foramen ovale in particular, intracarotid foam bubbles can be detected only a few seconds after injection of the sclerosant foam at any site in the leg. Catheter-based techniques with or without balloon occlusion of the treated venous segments have been tested to obtain control over the foam motility but have not been successful in preventing foam from entering the general circulation via the deep-vein system (eg, through perforator veins).

Although foam sclerotherapy still seems to be an excellent alternative to surgery for the treatment of recurrent varicose veins,[5] today's published data do not support the use of this technique for the primary treatment of the incompetent GSV.

THERMAL ABLATION: ENERGY DOSING

Thermal techniques rely on the delivery of a sufficient heat dosage to provide substantial and irreversible damage to the vein wall. RF-driven catheters and laser energy deployed through special laser fibers are currently the two major players in the field. Hyperpressurized steam may play a role in the future as well, but this option is currently being evaluated in clinical trials.

All systems are usually placed using Seldinger's technique under ultrasound control. Most frequently, the delivery of energy is performed solely under tumescent local anesthesia.

LINEAR ENDOVENOUS ENERGY DENSITY AND ENDOVENOUS FLUENCE EQUIVALENT

Before 2004, endothermal procedures had already been quite successful; however, neither RF nor laser ablation were able to provide a 100% guarantee for a successful endovenous ablation of GSVs, and it was not clear why. Most of the reported immediate occlusion rates were in the range of 90%, but they only rarely exceeded a success rate of 95%. In our clinic in 2002, with the switch from stepwise to continuous laser fiber pullback and without changing the laser power of 15 W, we noticed an unexplained increase in immediate failures and early recanalizations with unacceptably low occlusion rates of approximately 90% at 3 months after treatment. Although we were uncertain as to the real reason for these failures and recanalizations, a multiple regression analysis of various clinical and procedural parameters revealed the energy dose as the crucial parameter.

In an initial statistical run, a parameter with the dimension of joules per centimeter of vein length (which we later called *linear endovenous energy density* [LEED]), was selected by the mathematical regression model. However, to take into account also the diameter of the vein (a bigger vein should need more joules per centimeter than a smaller one), we created another parameter that we called *endovenous fluence equivalent* (EFE). This parameter describes the amount of joules delivered per cm^2 of inner vein wall surface, and it proved to be the parameter that is statistically linked to a sustained GSV occlusion or an early recanalization at 3 months after laser ablation.[6] The inner surface of the GSV was calculated by cylindrical approximation using the biggest diameter of the GSV measured while the patient was in the supine position. We finally tested this concept in a subsequent prospective series of GSV diode laser ablations and found that a 100% occlusion rate and a recanalization rate of not more than 1% was possible during a 1-year follow-up period if an EFE of more than 20 J/cm^2 is delivered.[7]

RADIOFREQUENCY CLOSURE

RF Closure (Vnus Medical Technologies, Inc., San Jose, CA) of the GSV is performed via a bipolar endovenous

catheter system with a feedback mechanism using a 460-kHz AC current to heat up the vein wall to a target temperature of 85 to 90°C. The system has a feedback loop regulating the delivered RF power, typically ranging between 2 and 4 W to maintain the preset target temperature. If we look at energy dosing instead of temperatures (eg, to achieve a LEED of 120 J/cm with an average power of 2 W), the pullback speed of the RF catheter needs to be as slow as 1 cm/min. This slow system has the potential to lose some of the delivered heat energy via steal effects, such as a partially remaining intravascular blood flow. Therefore, the vein must be emptied as much as possible using the Trendelenburg position and external compression. RF closure proved its clinical value in randomized trials comparing it to ligation and stripping,[8] as well as studies with up to 5-year follow-up showing long-term occlusion rates of the GSV between 85% to 90% without the presence of neovascularization.[9]

Segmental Thermal Ablation: ClosureFast

To overcome the problems of procedural lengths and potential energy dosing issues, a new type of RF-powered catheter for endovenous ablation was introduced in 2006. The functional unit of the 7-F diameter ClosureFast (CLF) catheter consists of a 7-cm-long heating coil and a thermal sensor. The heat energy inside the vein is no longer produced by RF currents flowing through a patient's vein wall tissue; instead, the coil at the catheter tip is heated to 120°C for intervals of 20 seconds before the catheter is pulled back 65 mm to heat the next segment. The CLF technology eliminates the problem of maintaining a constant pullback speed; thermal ablation has essentially become segmental ablation. If necessary due to a large GSV diameter, the segmental ablation can be repeated one or two times at the same site before the pullback of the catheter. Interestingly, energy dosing was shown to surpass energy doses delivered in a typical cohort of endovenous laser patients[10] with average LEED values of 68 J/cm in single-treated segments and 116 J/cm in double-treated segments. These high-energy doses are certainly the reason for immediate GSV occlusion at the saphenofemoral junction in more than 99% of cases. As with other endothermal procedures, neovascularization at the saphenofemoral junction can only rarely be observed during follow-up. Additionally, a remarkable shrinkage of the GSV and the remaining fibrotic cord could be observed (Figure 1). Despite this high efficacy, CLF has kept the extremely favorable side effect profile of its preceding Closure technology—only about 20% of patients needed moderate pain medication after the CLF procedure.

ENDOVENOUS LASER ABLATION

Endovenous laser ablation of GSV evolved during the last years of the 20th century, but at that time, not much was known about the mechanisms of action and the most important confounders of successful ablation. In the beginning, mostly diode lasers ranging from 810- to 980-nm wavelengths were used, always causing a more pronounced side effect profile than RF Closure with comparable success rates. However, from 2004 on, after the energy dosing issue had been addressed, successful ablation of the GSV was possible in almost 100% of cases with essentially any kind of available laser. This advantage of the laser systems over the old-style Closure technique and the cheaper single-use materials caused a rapid increase in the use of laser systems.

It was not before the introduction of the ClosureFast system to the market in early 2007 when the situation changed again. With both laser and RF segmental ablation reaching immediate ablation rates close to 100%, the new primary focus became side effects and periprocedural quality of life. A recently published randomized trial brought the results everybody expected: ClosureFast showed a significantly favorable side effect profile compared to the 980-nm diode laser.[11]

RECENT AND FUTURE DEVELOPMENTS

With the focus back on side effects and quality of life, more expensive laser systems like the 1,320-nm Nd:YAG improved their sales chances. Using 1,320-nm lasers—in contrast to diode lasers—energy is preferably absorbed by water instead by of hemoglobin, and perforations of the vein wall are much less frequent. If comparing the side effect profile of a diode laser to a 1,320-nm laser, the side effects of a 1,320-nm laser are occurring less frequently and are observed for shorter durations. In general, the 1,320-nm laser behaves more like RF closure than like a typical diode laser. An additional diode laser system with another water-absorbed wavelength of 1,470 nm has entered the market in the meantime. On top of that, laser companies offer laser fibers with covered tips that should generally be able to ameliorate the rough cutting and perforation properties of the formerly used bare fibers (AngioDynamics, Inc., Queensbury, NY; Vascular Solutions, Inc., Minneapolis, MN). Another company offers a new fiber type delivering the laser beam in a radial fashion to the vein wall with high efficacy in GSV ablation (biolitec, Inc., East Longmeadow, MA). However, particularly with the attempt to reduce the volume of tumescent local anesthesia, the reported rate of thigh paresthesia has been unexpectedly high in the latter case.

CONCLUSION

All of these new ideas aimed at making lasers behave like RF segmental ablation are interesting; however, their theoretical potential must be verified in clinical trials. Certainly, the current focus in the field is on venous ablation systems that do not impair the patient, treating the medical condition 100% successfully in combination with a moderate

side effect profile allowing the patient to return to normal life on the day of treatment. Newer laser systems and fiber types must be studied carefully in state-of-the-art clinical trials. The introduction of more frequent (or totally new) side effects is unacceptable, just as it is unacceptable to achieve successful GSV ablation in only 90% of patients at 3-month follow-up. ■

Thomas M. Proebstle, MD, PhD, is the Professor of Dermatology at the University of Pecs in Hungary; Associate Professor in the Department of Dermatology at the University of Mainz in Germany; and Director at Private Clinic Proebstle in Mannheim, Germany. He has disclosed that he is a paid consultant and speaker for Vnus Medical Technologies, Inc. Dr. Proebstle may be reached at info@privatklinik-proebstle.de.

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