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REVIEW

The VenaSeal Procedure: Review of an Advanced Treatment Modality for Varicose Veins

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Abstract

Varicose veins are caused by the insufficient function of the venous system of the legs. They manifest as dilated, elongated, or coiled superficial veins, which can be seen in the legs. Their incidence is higher in women (51.9 cases per 1000) than in men (39.4 cases per 1000). Minimally invasive endovenous modalities for varicose vein treatment, such as VenaSeal, are becoming more popular among clinicians. VenaSeal is a comparatively new procedure and belongs to the third generation of varicose vein treatment. The procedure has reduced side effects, almost negligible pain score, no hypesthesia, no phlebitis, a sporadic occurrence of skin pigmentation, improved patient quality of life, significantly lower rates of secondary procedures, and less post-procedure ecchymosis. This procedure requires no use of tumescent anesthesia or compression stockings as well. Some complications include complex hypersensitivity and irritation reaction, endovenous glue-induced thrombosis, numbness, tightness, pigmentation, and distal thrombosis. Despite these advantages, there are limitations to this procedure. Several studies have been conducted recently, but no review has been done to compile all that information. Here we provide an overview of cyanoacrylate adhesive and the preclinical and clinical studies conducted to date to prove the efficacy, detailed procedure, advantages, complications, and limitations of the VenaSeal procedure.

Introduction

Varicose veins are caused by the insufficient function of the venous system of the legs, manifesting as dilated, elongated, or coiled superficial veins. Due to the inefficiency of superficial, deep, or perforating veins, venous pressure in the lower limb rises, causing hyperpigmentation of the skin and ulceration.[1] This condition is mostly associated with the great saphenous vein (GSV).[2] Development of varicose veins depends upon several factors, such as advanced age, gender, history of pregnancy, body weight, stature, ethnicity, dietary habits, work engagement, past occurrences of deep vein thrombosis (DVT), hereditary traits, and gastrointestinal irregularities.[3]

The Clinical, Etiological, Anatomical, and Pathophysiological (CEAP) classification framework classifies varicose veins as C2. This classification system includes different classes from C0 to C6, where C0 denotes the least severe stage and C6 the most severe stage of the condition. The comprehensive understanding of the pathogenesis of varicose veins is complex, involving many factors, but the specific genetic and environmental influences contributing to their development have yet to be extensively studied.[3-5] More than half of the female population and over one-fifth of the male population affected by varicose veins experience chronic venous insufficiency (CVI), characterized by leg pain and swelling.6 Progressive venous insufficiency can lead to venous ulceration, affecting millions of people yearly. Chronic venous disorders encompass a range of clinical features thought to be linked to CVI in the legs. Clinical features include symptoms directly related to CVI, such as itching, swelling, tension, heaviness, muscle spasms, skin irritation, congestion, tenderness, and pain, and it may manifest as varicose veins of any type; vein-related skin changes and pitting edema.[6,7]

According to a 2019 study by Elamrawy et al, the global incidence rate of varicose veins is higher in women (51.9 cases per 1000) than in men (39.4 cases per 1000).[8] There are several methods for treating varicose veins, such as conservative treatments (compression stockings, elevating legs, oral anti-inflammatory medication, weight loss, exercise), injection sclerotherapy, surgical treatment (saphenous vein inversion and removal, high saphenous ligation), ambulatory phlebectomy, transilluminated powered

phlebectomy, and endovascular management.[3,9-12] Over the years, there has been a shift among doctors from traditional surgical stripping (SS) toward minimally invasive endovenous methods for varicose vein treatment. These modalities include endovenous laser treatment (ELT), radiofrequency ablation, ClariVein (Merit), and VenaSeal (Medtronic).[13-16] Approximately 90% of individuals undergo surgery involving the GSV, with approximately 20% of these procedures performed to address recurrent varicose veins (RVV).[17] The standard treatment has been surgery only, with high ligation and stripping to knee level, combined with phlebectomy.[2] An alternative to surgery is endovenous thermal ablation. This method has proven long-term success in closing the veins. However, one limitation is the possibility of thermal injury to surrounding healthy tissues.[12] A minimally invasive endovenous method such as VenaSeal is another alternative; even though it is not a current standard treatment, it does not cause thermal damage and demonstrates satisfactory outcomes with rapid recovery.[18]

VenaSeal is a comparatively new minimally invasive endovenous modality. There have been few recent reviews on the VenaSeal procedure, and the available review studies do not explicitly discuss the limitations of the VenaSeal procedure. Our objective is to extract substantial information about the VenaSeal procedure based on the findings of recent studies and highlight the advantages and limitations of this procedure.

The VenaSeal Technique

VenaSeal is a simple but effective method for sealing veins without the use of radio waves and lasers. VenaSeal was developed 20 years ago, and its use began in Europe after getting approval from Conformité Européene in 2011.[19-21] It received FDA approval in 2015.[22] As millions of people are affected yearly by varicose veins, new techniques such as VenaSeal can treat them quickly and painlessly.[6,23] Regarding efficacy and safety, the VenaSeal procedure, in which the lumen is closed with the help of cyanoacrylate adhesive, has also shown better results than other procedures.[11] In particular, it can be helpful for the older population with severe pain and swelling, considering that the severity of CVI increases as age increases. Also, an older person cannot put on compression stockings, required in almost every other treatment modality of varicose veins, by themselves. They would need a caregiver for the same, which makes this a disadvantage of other treatment modalities.[7,19,24] Compression stockings or bandages are not required in the VenaSeal procedure.[25,26] The use of VenaSeal for cyanoacrylate closure (CAC) is becoming increasingly popular due to its nonthermal technique and the fact that it does not use tumescent anesthesia.[2,13] The risk of injury is reduced to the adjacent tissues when using this technique in place of endovenous thermal ablation. Therefore, there is no requirement to use tumescent anesthesia.[12,27] With this evolved technique, complications can be reduced and better results can be obtained.[28] The VenaSeal procedure can be described as the third generation of varicose vein treatment.[18]

Cyanoacrylate Adhesive

Cyanoacrylate is a liquid adhesive that undergoes rapid polymerization when it comes into contact with anions containing solutions such as blood.[29] The strong adhesive properties of VenaSeal cause endothelial stripping and disruption. This induces an acute inflammatory response that leads to granulomatous inflammation. Simultaneously, the patent vein transforms into an occluded fibrotic cord due to the gradual resorption of the polymer cyanoacrylate.[30] It is used operating departments such as orthodontics, surgery, orthopedics, ophthalmology, and dermatology. Interventional radiologists have used this adhesive to treat vascular malformations since 1981.[19] Use of endovenous cyanoacrylate to treat GSV reflux is safe.[20] Further research has also demonstrated its significant efficacy in varicose vein treatment, showing full blockage for more than 90% of subjects at 1-year evaluation, indicating that its clinical efficacy is at least on par with endothermal ablation.[29] Although the endothermal ablation procedure provides efficacy rates above 97%, the use of tumescent anesthesia can be uncomfortable for patients.[28,31] CAC represents a relatively recent intravascular technique used in varicose vein treatment. Contemporary findings suggest a comparable effectiveness of CAC compared with alternative endovenous modalities while demonstrating a heightened emphasis on safety and tolerance.[29,32] The adhesive's high viscosity and polymerization characteristics facilitate accurate positioning in the vascular lumen with minimal movement.[33]

Preclinical Studies

In 2011, Almeida et al carried out a study aimed at assessing cyanoacrylate adhesive's efficacy and effect on the vein wall in an animal model while assessing its feasibility for vein closure. Two pigs were used for the study. In each pig, a catheter was inserted approximately 2.0 cm below the point where the superficial epigastric and abdominus rectus veins meet. Cyanoacrylate adhesive was injected in a volume of 0.16 mL under ultrasound guidance. Surgical harvesting and histological examination were done for the veins 60 days after implantation. The observed histological changes suggested a chronic inflammatory response similar to that typically associated with foreign bodies. The study concluded that injecting cyanoacrylate adhesive is feasible for the closure of superficial veins in animal models. Vein closure is achieved via an inflammatory process that ultimately leads to fibrosis.[34]

In 2012, Min et al performed an animal experiment illustrating a new method of using a proprietary cyanoacrylate adhesive to close superficial veins. They chose the superficial epigastric veins on the right and left sides of the 2 pig models because they closely resemble the human GSV. Using ultrasound guidance, they gained access to the target area and advanced a 5F introducer catheter to the junction of the superficial epigastric and abdominus rectus veins. Thirty days after implantation, the treated veins were blocked entirely and there was no sign of reopening or movement. The results of this initial study demonstrate the feasibility of using intravascular injections of a specific agent (cyanoacrylate adhesive) to occlude superficial veins in animal models.[35]

Clinical Studies

In 2022, Shah et al conducted a research investigation to assess results of the VenaSeal procedure regarding vein occlusion rate and improvement in Venous Clinical Severity Score (VCSS). This prospective study was conducted at a solitary medical center and included a cohort of 50 patients for 1 year and 4 months, with follow-up assessments at 3 and 6 months. The study findings revealed that around 90% of participants suffered from early-stage (C2/C3) varicose vein disease. Regional anesthesia, such as sciatic and femoral block or general anesthesia, was used on all patients before they underwent the intervention in the supine position. For varicose vein treatment, advanced procedures were performed as required. The occlusion rate for the target vein reached 100% at 3 months but decreased to 97.75% at 6 months. These findings confirm that the VenaSeal procedure is a promising, viable, and successful treatment modality for varicose veins. It can be conveniently performed in the outpatient department due to its favorable properties.[11]

In 2020, Zierau et al conducted a research investigation focusing on the long-term results of treating trunk varicose veins with cyanoacrylate adhesive. The study included a 100-month follow-up period and 1509 cases involving 2912 trunk varicose veins. It was concluded from the results that the VenaSeal procedure is the first choice in the range of catheter-supported therapeutic procedures for GSV and small saphenous veins (SSV). Also, in obese and older patients, significant advantages can be seen in using the VenaSeal procedure.[19]

A 2021 study by Tang et al evaluated CAC for refluxing truncal veins. Duplex ultrasonography was used to evaluate truncal vein occlusion. The revised VCSS and 3 quality of life (QoL) questionnaires were used to measure improvement in venous disease-related symptoms. Trunk closure rates observed at 6 and 12 months were 99.3% and 97.9%, respectively. The revised VCSS and QoL questionnaire scores remained stable between the 3-month and 12-month follow-up without further significant improvements. No significant adverse events were noted. Based on the findings at 12 months, CAC was considered a safe and effective vein ablation method. It has demonstrated a high success rate in closing the target vein, leading to a sustained improvement in the patient's QoL.[36]

In another 2021 study, Tang et al evaluated the efficacy of CAC in treating varicose veins in a prospective cohort of Singaporean Asian individuals of various racial origins. The study focused on early clinical outcomes and patient satisfaction after the CAC intervention, measured at 3 months. The research included 100 patients who underwent CAC treatment between April and December 2018. There was 100% technical success in the CAC procedure. Patients showed good procedural tolerance and experienced minimal pain during the procedure. Three months after the procedure, there was a significant improvement in various assessment scores. It was concluded through the study that CAC is a safe and effective approach for obstructing the refluxing truncal veins in Asian patients during the initial postoperative follow-up period. Patients reported high levels of satisfaction and low postoperative pain. In addition, there was a significant and sustained improvement in their QoL after 3 months of assessment.[32]

VenaSeal Procedure

Based on the patient's medical condition or individual choice, general anesthesia, spinal anesthesia, regional anesthetic blocks, or local anesthesia can be used.[13] Application of the VenaSeal system should begin at a distance of 1 cm to 1.5 cm from the saphenofemoral junction, and the adhesive should be carefully applied at different sites with a regular 2 cm to 3 cm gap, taking into account the diameter, flow, and pressure of the vein. Before the adhesive material is inserted into the vein, the pressure is assessed using an intravenous catheter. Large side branches connected to auxiliary vessels may require additional treatment involving a single application of adhesive.[19] Two injections of adhesives are given along with providing compression proximal to GSV using an ultrasound probe. Local compression is given after the injection. Unless the treatment of the entire length of the designated vein is complete, the process is repeated. Duplex ultrasound can be used to verify target vein occlusion.[13] After the procedure is complete, the catheter is removed and pressure is applied to the catheter entry point to stop the bleeding.[12] One small bandage should be used after the procedure; no compression stockings or bandages are necessary.[25,26] According to a study, on average, 2.95 ± 0.42 mL of cyanoacrylate adhesive is used per limb.[11]

VenaSeal Advantages

VenaSeal's advantages compared with laser and radio wave therapy are reduced side effects and an almost negligible pain score.[19] A generator is required in laser or radiothermal ablation, and the procedure can cause postoperative complications such as pain and bruising.[28] Some degree of pain might be experienced in more than 70% of limbs after ELT, and more than 50% might require analgesics for pain management. A study reported that after ELT, the pain scores range between 2.2 to 2.6 on a scale of 0 to 5.[31,37,38] According to a different study, the postoperative pain score after CAC is around 0.3 ± 0.6, whereas the same after SS is 1.1 ± 1.5.[13] The VenaSeal procedure can be done in 1 visit to the clinic.[33] According to a study, patients can leave between 30 and 120 minutes after the VenaSeal procedure,[19] whereas radiofrequency ablation takes more time due to its lengthy pullback procedure.[31] Other advantages of VenaSeal include, but are not limited to, an extremely rare occurrence of skin pigmentation, no phlebitis, no hypesthesia, no paresthesias, improved patient QoL, significantly lower rates of secondary procedures, and less post-procedure ecchymosis. During the whole procedure, tumescent anesthesia does not need to be used so the patient can avoid its associated burden.[19,25,26,33] A study reported that after performing ELT, ecchymosis was observed in many patients, most probably due to vein perforation by laser energy or the usage of tumescent anesthesia. Moreover, complications after ELT are not limited to ecchymosis, and it has been reported that there is a good chance of thrombophlebitis and paresthesia occurrence after performing an ELT.31,37 Even after the VenaSeal procedure, compression stockings are not required, which are often associated with low patient compliance.[25] A study aimed to analyze the medical indication and use of elastic compression stockings stated that patients

complained about pain, discomfort, a burning sensation, and leg edema after using compression stockings. Another problem with these compression stockings is that patients do not prefer to buy them due to high prices, face difficulty in finding them, and remain dissatisfied with the appearance of the stockings. It is difficult for people living in tropical regions to wear these stockings compared with people living in cooler regions, considering comfort.[39] According to a 2022 study by Shah et al, after completing the VenaSeal procedure, health related QoL symptoms improved significantly.[25,26]

VenaSeal Complications

Complications of the VenaSeal procedure are usually minor and include endovenous glue-induced thrombosis (EGIT), complex hypersensitivity and irritation reaction (CHAIR), numbness, tightness, pigmentation, and distal thrombosis. A study used the term "abnormal phlebitis-like reaction" to describe a complication called CHAIR.[13,18] Furthermore, no association has been reported between the type of ablation performed (GSV, SSV, or GSV/SSV combined) and phlebitis incidence.[33] Phlebitis can be mild and transient and can be treated with over-the-counter analgesics.25 A 2013 study by Almeida et al found that patients might also show thread-like thrombus extensions into the common femoral vein, but they can be resolved spontaneously without anticoagulation.[26]

Complications from other treatments of varicose veins include a high recurrence rate, disfigurement from scarring, paresthesia, and hematoma. High saphenous ligation and stripping are linked to high recurrence rates, posing financial burdens on both patients and healthcare systems. Even if we keep aside the cost factor, RVV operations are comparatively more complicated. A randomized clinical trial documented a 62% recurrence prevalence at an 11-year follow-up after saphenofemoral ligation, whether performed with or without stripping. The study noted a lack of statistically significant distinction between the cohorts undergoing ligation-only and stripping procedures. The trial also stated that stripping the GSV is recommended as part of routine varicose vein surgery as it reduces the risk of reoperation by 60%. However, it could not reduce the rate of visible recurrent veins. It has been reported that up to 70% of patients develop RVV following open surgery, of which 26% develop varicose veins worse than before the operation. Complications such as more varicose veins, continuing symptoms, thread veins, recurrent phlebitis, and eczema may occur after conservative management, sclerotherapy, and surgery. There has been an expectation that regular use of preoperative Doppler and duplex might reduce recurrence rates. However, 1 study with a year of follow-up has not shown any apparent benefit from adding duplex scanning to assessment.25,40-45 Radiofrequency ablation can cause paresthesia as localized patches in the treated limbs in many patients. It can also cause thrombophlebitis, characterized by a pain sensation and visible reddening along the course of the treated vein.[31]

VenaSeal Limitations

Despite the advantages of the VenaSeal procedure, it remains a new technique, and only a few studies are available to reflect its long-term advantages, which leads to uncertainty surrounding potential long-term risks associated with its usage. This uncertainty limits the use of the VenaSeal procedure. Another limitation of this technique is its high cost, making it out of reach for many patients.[21,46]

Conclusion

VenaSeal is an efficacious and safe approach for varicose vein treatment. It has demonstrated a high success rate in closing the target vein, leading to a sustained improvement in patient QoL. Patients generally report high levels of satisfaction and low postoperative pain. Only minimal complications are reported during or after the procedure. Despite these advantages, the VenaSeal procedure is less cost-efficient, and a lack of studies showing its long-term usage raises suspicion about its long-term effects. Hence, more studies need to be conducted to show the long-term effects of the VenaSeal procedure. ■

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Related Article

When Is the VenaSeal Closure System Appropriate for Patients With Ulcers and Combined Arterial and Venous Disease? An Interview With Michael Shao, MD

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