



Endovenous Cyanoacrylate Super-Glue to Treat Varicose Veins: How I Perform VenaSeal™ Ablation – Tips & Tricks Gained From Ablating Over 300 Truncal Saphenous Veins

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Abstract

The treatment of incompetent truncal veins has been innovated by the introduction of minimally invasive non-thermal non-tumescent (NTNT) techniques. One of these consists of the use of cyanoacrylate glue (CAG) to occlude the vein lumen by means of the VenaSeal™ device. This device has been shown to be safe in the published trials in patients and an efficacious innovative technique comparable to the current gold standard of endothermal ablation (EVTA), which has been around in the endovenous arena for over 20 years. CAG is proving to be popular amongst venous surgeons because it is less invasive and traumatic to the patient than EVTA and can be performed theoretically with one puncture and takes less time to perform because no tumescence is required with this technique. The aims of this paper is to explain in detail of “How I do” the ablation of the truncal vein using this product, how I select and work up patients for this procedure and the tips and tricks I have picked up with my experience of having blocked over 300 truncal saphenous veins with this device in Singapore.

Keywords: VenaSeal™ Closure System; Endovenous; Cyanoacrylate glue; Varicose vein; CVI

Introduction

Varicose veins are common and are known to affect at least one third of the population [1]. Chronic venous insufficiency (CVI) has been shown to have a negative impact on patients’ quality of life (QoL) and treatment of varicose veins has been demonstrated to lead to improvement [2].

Over the past two decades, the management of CVI and varicose veins has been revolutionized by the introduction of minimally invasive endovenous thermal ablation techniques to occlude the pathological refluxing superficial saphenous vein. Currently, both the UK National Institute of Health and Clinical Excellence (NICE) and the Society for Vascular Surgery/American Venous Forum recommend endothermal ablation as the first-line treatment for truncal vein incompetence [3,4]. The safety and efficacy of endothermal ablation of truncal saphenous veins have been demonstrated [5] and recent unrivalled 15-year follow-up data using radiofrequency ablation (RFA) have shown excellent durable long-term technical success [6]. However, thermal techniques such as radiofrequency and laser ablation, require the use of peri-venous tumescence to provide anaesthesia and to protect surrounding tissues from thermal injury. Tumescence administration, although generally well-tolerated, requires multiple injection sticks along the course of the saphenous vein, which can cause both intra-procedural and post-operative discomfort [7] as well as adverse events such as haematoma and ecchymosis. Furthermore, thermal-related complications such as skin burns, nerve injury and endothermal heat-induced thrombosis may occur. This may also preclude treatment of below knee great saphenous vein incompetence, often present in the Asian population, due to the proximity of the saphenous nerve to the superficial vein.

Non-thermal, non-tumescent (NTNT) endovenous technologies have been introduced as a natural evolution of minimising surgical trauma further, to eliminate the need for tumescent infiltration and to address the limitations of endothermal ablation. NTNT techniques are thought to help further enhance the patient’s peri-operative experience, especially as outcomes become more patient-centric and satisfaction-based. The decision to intervene in the majority of cases is ultimately based on symptomatology and QoL issues.

The VenaSeal™ Closure System™ (VSCS) (Medtronic Plc, Dublin, Ireland) is a NTNT ablative device that induces endovenous closure by delivery of cyanoacrylate glue (CAG)

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commonly referred to as “super glue”. CAG has been safely and widely used intravascularly to embolise intracranial arterio-venous malformations and aneurysms and to manage pelvic varicoceles and gastric varices. CAG triggers an acute inflammatory reaction in the vessel wall via a polymerization reaction leading to encapsulation and vein fibrosis. The high viscosity and polymerization properties of the adhesive allow precise placement within the vein [8]. VSCS received *ConformiteEuropeene*(CE) mark in September 2011 and was approved by the Food and Drug Administration (FDA) in the US for superficial truncal vein closure in February 2015. Since receiving its CE mark in 2011, VSCS has been in clinical use in Europe, Australia, Canada, Dubai, South Korea, Malaysia, South Korea and Hong Kong. It was first introduced into Singapore in January 2016 and is a *Health Sciences Authority* (HSA) approved medical device. It has been shown to be safe and efficacious in its initial trials in the US [9-11] and Europe [12]. The first published VSCS outcome data from Asia was from Hong Kong, where there was some variation in the technique of CAG delivery and concentrated on treating a cohort of patients with only bilateral varicose veins (predominantly C2/C3 disease) because of cost concerns [13]. Park recently reported that CAG was safe and efficacious in a cohort of South Korean patients with refluxing saphenous veins and demonstrated good venous ablation without paraesthesia for veins treated below the knee and in the suprafascial plane [14].

The aim of this paper is to report the author’s technique for using the VSCS and the experience he has gained from using the device and document procedural tips learnt during treatment of over 300 truncal veins to date.

Patient Selection

Patients with varicose veins and or chronic venous insufficiency symptoms undergo a focused history and clinical examination at the specialist vascular outpatient clinic of one consultant vascular surgeon (TYT), who has a large endovenous practice and regularly performs not only VenaSeal™ vein closure but also mechano-chemical ablation (MOCA) (ClariVein™, *Vascular Insights LLC*, Madison, CT, US), foam sclerotherapy (FS) and RFA (Venefit™, *Medtronic Plc*, Dublin, Ireland) to treat varicose veins and/or CVI.

Assessment includes clinical signs for great saphenous vein (GSV) and/or small saphenous vein (SSV) reflux, CEAP (clinical, aetiological, anatomical and pathophysiological elements) classification [15] and baseline Venous Clinical Severity Score [16] (VCSS) evaluation of the index leg.

A deep and superficial duplex ultrasound evaluation, which included colour and spectral Doppler in addition to B-mode using the Philips iU22 or EPIQ 7G (*Philips Healthcare Solutions*, WA, US) devices, is performed independently by one of our dedicated certified vascular sonographers prior to any decision for surgery. Reflux is determined at the saphenofemoral (SF)/sapheno-popliteal (SP) junction in the standing position and due consideration is taken for truncal vein tortuosity and whether it traverses out of the encompassing fascia sheath. When you start using the device, pick the relatively straight truncal GSV that remains in its fascial sheath because manoeuvring the relatively stiff system up to the SFJ, in and out from the fascia, can be quite difficult, which may require ultimately a double puncture technique. Saphenous vein reflux as documented by ultrasound is defined and considered significant as retrograde flow of > 0.5 seconds [17]. GSV diameter is measured with

the patient supine at three levels (proximal thigh near SFJ, mid thigh, and distal thigh just above the knee.

Inclusion criteria for use of the VSCS are:

1. Age > 21 years old and ability to give informed consent for the procedure
2. CEAP class C2-C6 varicose veins
3. Symptomatic primary or recurrent GSV, SSV and/or ATV incompetence with reflux > 0.5 seconds on colour Duplex including one or more of the following symptoms: aching, throbbing, heaviness, fatigue, pruritus, night cramps, restlessness, generalized pain or discomfort, swelling
4. Patients who have GSV/SSV diameters of 3mm to 12mm in the standing position and contain a refluxing segment of at least 10cm.

Patients are excluded from having this procedure if they are pregnant, lactating, allergic or had a previous hypersensitivity reaction to cyanoacrylate, peripheral arterial disease (ABPI<0.8), acute venous thrombo-embolism or sepsis, history of hypercoagulability and if their GSV/SSV are severely tortuous. Recurrent varicose veins, previous superficial thrombophlebitis (not active), which have recanalized and are incompetent and patients on anticoagulation with warfarin are not specifically excluded. Recently, I have noticed that those with multiple drug allergies are more likely to develop phlebitis with glue ablation even with anti-inflammatory (NSAID) cover and I have begun to shy away from using the device in these patients, especially if the patient cannot take NSAID post-procedure.

All patients receive a procedure-specific information leaflet produced by the device company in their native language, which explains the technique including risks and side-effects. Patients who do not want to be treated with VSCS are routinely offered treatment with RFA, MOCA, FS or open surgery. There is no deliberate selection bias to only perform the operation with favourable saphenous vein anatomy and all treatment options, if deemed appropriate, were offered to the patient. CAG was applied more liberally, with broader inclusion criteria of patients than the previous reported studies.

VenaSeal™ Technique

The VenaSeal™ Closure system technique has been previously described [9], which is generally adhered to but with local modifications, which will be summarized.

In keeping with local preference, patients are given the choice to have the procedure performed either under a Regional Anaesthetic (RA), sedation, General (GA) or Local Anesthetic (LA). However, it is my usual practice to routinely do this procedure purely under LA, with or without sedation unless concomitant phlebectomies are required in which case a RA or GA is employed. Antibiotics at induction are routinely given. The patient is positioned supine with a body warmer and with a sandbag under the knee to enhance access to the GSV. The SSV is treated with the patient placed in the prone position with the foot hanging off the edge of the operating table to allow foot dorsiflexion and easier percutaneous venous access of the SSV at the ankle.

The index leg is disinfected with either chlorhexidine prep (no phlebectomies) or with povidone-iodine (concomitant phlebectomies) and sterile drapery is applied. After injection of local anaesthetic (1%

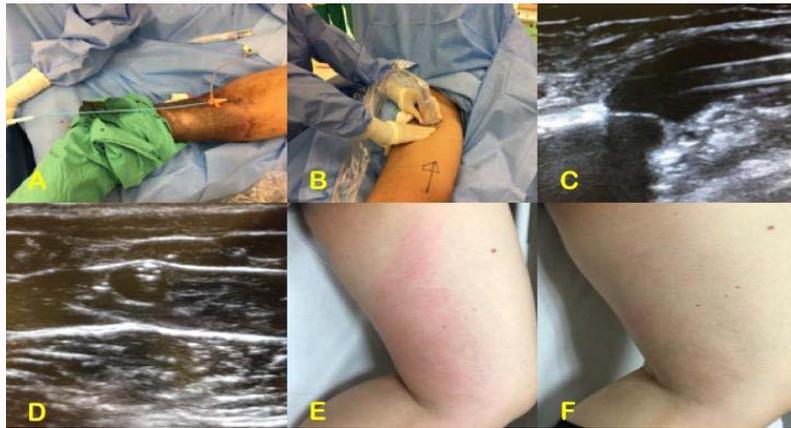


Figure 1: **A:** Panel A shows that the venous puncture is made typically just above the skin changes and at the lowest point of truncal reflux. **B:** Panel B shows temporary compression using the ultrasound probe and manual compression to control the migration of CAG cranially and allow the vein to collapse onto the catheter and glue to improve the coarptation process. **C:** Panel C shows the importance of good visualisation of the catheter in relation to the sapheno-femoral junction and that the tip of the final introducer-delivery catheter complex is placed 5cm caudal to the SFJ. **D:** Panel D shows the “Crown of Thorns” sign. This shows the tip of the introducer-delivery complex that should be placed 5cm caudal to the SFJ. **E:** Panel E shows the “VenaSeal Red reaction”. This is likely a type IV hypersensitivity reaction and not a true phlebitis reaction. In this patient the symptoms and signs came on 2 weeks after the procedure causing pain, pruritus and oedema along the ablated GSV. The patient was treated with a further course of NSAIDS. **F:** Panel F shows the resolution of the reaction 3 weeks after presentation. This is usually self-limiting and does not require a course of steroids. Patients should be asked for a history of cyanoacrylate glue allergy.

lignocaine) at the designated puncture site (usually at the lowest point of saphenous vein reflux Figure 1A.), a Seldinger technique is used to introduce a micro-catheter 4Fr introducer sheath (*Angiodynamics Inc*, Queensbury, NY, US) into either the GSV or SSV under ultrasound guidance, exchanged for a short 7Fr sheath, which is copiously flushed with saline. This aids dilatation of the vein to allow easier passage of the subsequent wire and introducer/delivery catheters. The 0.035” proprietary guidewire is passed just into the SFJ and over this, the long 5Fr proprietary introducer sheath is placed just caudal to the SFJ. The dilatator is removed and the sheath is flushed with saline and pulled back a distance of 10cm. The patient is deliberately placed into a steep head-down position in order to collapse and empty the saphenous vein of blood. On a separate sterile dry preparatory trolley, the CAG is drawn up into the proprietary 5ml syringe without air and is attached to the disperser gun. The 5Fr delivery catheter is connected to the syringe and is primed with adhesive up to the black mark 3cm from the tip end. It is important not to flush the delivery catheter with saline prior to avoid polymerization of the adhesive inside the catheter and to avoid over shooting the black mark with CAG as this can inadvertently allow the glue to be dispersed closer to the SFJ/SPJ later during initial deployment. After one final copious flush with saline to disperse the blood near the tip of the introducer catheter, the primed delivery catheter is now placed inside the introducer sheath and married up. The tip of the introducer sheath/delivery catheter complex is advanced to the SFJ so that it is placed accurately 5cm caudal to the junction using ultrasound guidance (Figure 1B). With regards to the SPJ, the tip is never placed past the fascial curve whether it is longer than the 5cm cut off distance from the SPJ proper, in order to minimize spillage of CAG into the deep system. This can be seen clearly by the “crown of thorns” sign on ultrasound (Figure 1D).

The ultrasound probe is now turned transversely and is used to apply pressure just 2cm cephalad to the tip of the catheter complex to occlude and close the vein just caudal to the SFJ. The first dosage of CAG is applied by pressing and holding the trigger of the disperser gun for 3 seconds. The device is immediately pulled back 1cm and another

glue shot is discharged for the same duration followed by a 3 minute period of compression. The hand not holding the ultrasound is used to compress the vein/catheter directly caudal to the probe (Figure 1D). After 3 minutes, the proximal GSV near the SFJ is interrogated with ultrasound to check for potential proximal extension of the glue and whether the vein had become incompressible. Following this, repeated 3cm-spaced injections with 30-second ultrasound probe/manual compression sequences are applied until the entire length of the target vein is treated. The 7Fr sheath is removed when there is 15cm treatment length left otherwise you run the risk of glueing inside the sheath. Removing the 7fr sheath under a LA procedure is usually the most painful part of the procedure and the patient should be warned prior to removal to minimize the pain process. The last dose of glue is administered 3cm from the access site and subsequently the device is removed swiftly with glue being administered continuously to seal the subcutaneous tract and minimize bleeding. As the complex is removed from the access site, the glue is snapped off the tip. Each injection disperses approximately 0.1cc of adhesive. However, it is important not to get glue in the access site at all. This has caused some infections and access site issues such as pain and even glue rejection. Allergists and users of the product I have spoken to encourage users to avoid getting CAG into the subcutaneous space or near the access site in fear of causing an immune reaction. The SC space has a high number of immune cells and potentially CAG may trigger a hypersensitivity reaction, which may explain the relatively high rate of phlebitis like reaction following the procedure.

This basically follows the device instructions for use (IFU) but after the first 10 cases performed, I decided to inject 2 x 0.1cc aliquots of CAG after the first 1cm pullback (double dosing technique), if the proximal vein diameter were > 6.6mm in view of Chan et al. [18] finding that a median GSV diameter of ≥ 6.6 mm was a predictor for late recanalization [18]. Furthermore where the truncal vein was focally dilated and at the level where branches came off and where incompetent perforators were located, a double dosing regime was undertaken to deliberately allow spillage of glue into these tributaries.

A completion Duplex ultrasound scan is routinely performed after the procedure to confirm the patency of the common femoral vein and the deep venous system and to ascertain whether there is any flow within the truncal vein and whether it is still compressible. The ipsilateral foot is dorsi- and plantar-flexed in order to minimize deep venous stasis at the end of the procedure. Concomitant phlebectomies are then performed as necessary using the standard Oesch hook technique. Subcutaneous heparin is routinely given after the procedure to minimize the risk of deep vein thrombosis.

A full length compression bandage (Class II; Coband lite™) is applied to the treated limb(s) from the foot to the groin only if concomitant phlebectomies or FS are also performed and removed after 24 hours. The patient is then advised to undertake light exercise (3 x 15 minute walks on the same day), once they felt well enough to do so. The patients are prescribed a one week's course of 60mg po od Arcoxia™ (Merck & Co., NJ, US) to minimize the risk of developing phlebitis and advised to return to their work and normal activities as soon as they felt capable to do so. All patients are scheduled for a follow-up assessment at 2 weeks, including physical examination and a targeted duplex ultrasound to check for deep vein thrombosis and that the target vein has been obliterated successfully.

Discussion

In my experience, about 10% of patients necessitated the use of a double puncture technique to allow the catheter to be manoeuvred up to the SFJ, mainly due to the tortuosity of the vein in the below knee segment of the GSV and also due to angulation of the vein at the level of the distal thigh, where the vein was suprafascial, before diving acutely into its normal surrounding anatomical fascia. There is a significant number of asian patients (approximately 30-40%) who have their GSV come out of its fascial envelope during its course (supra-fascial extension) and traversing up to the skin surface. In my experience with the VenaSeal™ device, a double puncture technique may be essential to successfully navigate the epifascial component of the truncal vein, especially if tortuous and small, as the 5Fr introducing catheter can be rather stiff to manoeuvre up even over a 0.035" wire, unlike the lower profile mechano-chemical ablation ClariVein™ catheter, which my group has previously shown to be flexible enough to better navigate the venous curves [19]. However this has not compromised the anatomical occlusion rate [20]. In order to seal the remnant intervening vein segment (< 3cm) just caudal to the proximal sheath puncture, which has been reported to be the site of recurrences [21], we have modified the IFU for CAG injection by placing the proprietary delivery catheter through the most distal sheath as close to the proximal sheath insertion site as possible and giving a double dose of CAG (0.2cc). By giving a double dose at this point, we allow the glue to travel proximally to seal the intervening vein segment once the proximal GSV has been treated and proximal sheath has been removed.

I have also found that the VSCS can be used in a retrograde fashion i.e. access at the knee level, the catheter can be passed distally to under an ulcer bed and injected directly into the veins, which feed the ulcer or unhealthy area of skin near the ankle. I have found that making the venous puncture at the knee is easier technically than at the ankle where the skin and surrounding tissue are desmoplastic and tougher to cannulate the vein in CEAP 4b/5/6 disease and the experience is that you can get right under the ulcer bed if you are approaching it from a retrograde position. Another group has shown that this technique can expedite wound healing in the venous ulcer

setting albeit with a different ablative device [22]. All ulcers I have treated in this manner have healed by 3 months follow-up.

VenaSeal™ is similar to other endovenous procedures, in that it is performed using catheters and wires using the Seldinger technique. Therefore, if the treating physician is used to performing other endovenous procedures, this is an easy transition to make and is a fast learning curve. When performing heat-based procedures, most endovenous specialists generally gain venous access at the knee level to avoid risk of nerve injury lower down the calf. With VenaSeal™, I have tended to gain access much lower in the calf or at the lowest point of reflux (Figure 1A). I believe that one of the most important parts of the procedure is to ensure that the tip of the delivery catheter is placed 5 cm from the SFJ and clear visualisation with the ultrasound is mandatory. Once I have verified appropriate catheter placement, the ultrasound probe is placed transversely 2 cm proximal to the catheter tip to occlude the saphenous vein at this point. This is how we maintain proximal control of the adhesive. It is important to give some space for the adhesive to deploy. If the ultrasound probe were placed right at the tip of the catheter or just below the SFJ, there may be some migration of the adhesive proximal towards the SFJ, which is undesirable. It is important to wait the full 3 minutes after the administration of the first 2 aliquots of the adhesive. The reason for failure with this procedure is due to the proximal high pressure zone. If you tried to shortcut this first 3 minute compressive hold, you run the risk of having a proximal section recanalize, which may result in a re-opening of the whole vein. After the top section is adequately treated, we can move fairly quickly through the remainder of the truncal vein treatment. Although the IFU calls for treating up to 12 mm diameter veins, larger diameter veins (up to 20mm) and aneurysmal sections have been treated with good results. The important aspect for these large diameter veins is to put the head down as much as possible to help collapse the vein onto the catheter and allow sealing and apposition of the vein walls with glue. Furthermore using this double dosing technique described above for larger diameter veins allows a more secure seal to form. If there is a large branch varicosity or perforating vein coming into the saphenous vein, I have used additional aliquots of adhesive at this point with success. I have noticed for the smaller varicosities, that double dosing with glue and manually manipulating the glue from the truncal vein towards these side branches is effective and minimises the number of phlebectomies later required. The most challenging part of the procedure is the situation when treating multiple veins. Whenever initially priming the adhesive in the delivery catheter, the adhesive moves quite slowly. When we are priming the catheter for the second vein to be treated, there has already been adhesive in the catheter, and the adhesive moves quicker during the priming process. I have had experience when getting ready to treat the second leg, the adhesive had migrated through the entire length of the delivery catheter and into the sheath, resulting in occlusion of the sheath. I was not able to advance the delivery catheter into the vein. In this situation, I had to abort this part of the procedure, and open a new kit and start the process again. It is also important to flush out the blood from the introducer sheath prior to marrying up with the delivery catheter to prevent blood/glue polymerisation. Also if the glue has passed the 3cm black safety mark on the delivery catheter, care has to be taken during injection especially near the junction as the adhesive can shoot forward more than expected. Another difficulty I have faced is the use of the J 0.035" supporting wire in small tortuous GSVs, which sometimes can get stuck during passage up the leg. What I have found is that if you reverse the wire and send in the straight stiffer end of the

wire with care it negotiate the curves better to the SFJ bearing in mind the higher risk of venous perforation. The cost of CAG is expensive (there is a rider of approximately S\$2000 for the device in Singapore). Therefore opening another packet would not be cost-effective. For bilateral and multi truncal vein ablation and using a double dosing technique, this can use up the CAG quite quickly. Remember the delivery catheter is lined with approximately 1.3ml of glue, which can be pumped out effectively by drawing up the empty syringe with air. A key point is to hold the gun trigger down for longer than 3 secs to allow a similar amount of glue to be expressed at this stage.

Transient phlebitis is the only common minor complication after this procedure (approx. 10%) despite all patients being routinely prescribed a week's post-operative course of NSAIDs. Whether this is a true phlebitis reaction is currently controversial because onset can vary from within a few days to over 2 weeks following the procedure. This has been recently described as an "abnormal red skin reaction" after CAG embolization thought to be a delayed hypersensitivity reaction secondary to foreign body (glue) (Figure 1E) [23]. This is defined as any abnormal skin finding such as erythema, itching, pain, oedema and tenderness over the treated vein area. Although it looks like phlebitis it is generally more-wide spread, occurring 7-14 days post-procedure with predilection in the great saphenous vein location and females. The course is self-limiting and is treated with anti-inflammatories and/or steroids (Figure 1F). In my experience, phlebitis tended to occur along the course GSV and not along the tributaries. There was no predilection for females and those with higher BMI (>25) as previously described [14].

Conclusions

CAG is a safe and efficacious modality to ablate the great and short saphenous veins in asian patients in the short-term (1 year). The procedure can be safely expanded to bilateral procedures and multiple truncal veins in the same leg, which are well tolerated. There is no hardware to buy, loan or upkeep and the technique can be quickly performed on an outpatient basis if required, thereby reducing overhead and procedural costs. There is a high satisfaction rate and peri-procedural pain is low.

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