Vascular Diseases and Therapeutics

Editorial

ISSN: 2399-7400

Cyanoacrylate glue using the VenaSeal™ Closure System for varicose veins may not be the panacea endovenous ablation device-more complications than you think

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Editorial

The last twenty years has seen an explosion in the number of medical devices available for the management of varicose veins. Whereas previously, decision making revolved around whether to operate or not, the question of which procedure is best has become the subject of much competition and debate.

Radiofrequency and endovenous laser ablation (RFA/EVLA) are two of the most popular minimally invasive treatments and having come to the market earlier, they have a well-established safety record and are the current gold standard for comparison. Recent unrivalled 15-year follow-up data using RFA have shown excellent durable long-term technical success [1]. However, there are still significant adverse events and the concerns of skin burns and endovenous heat induced thrombosis (EHIT) (3-5%) [2,3] are unique to these thermal techniques.

Mechanical obstruction and Chemical Ablation (MOCA) avoids the risks of thermal and nerve injuries and obviates the need for tumescent anaesthesia. Use of a single introducer sheath and puncture site, means a single injection of local anaesthetic is sufficient in the majority of cases. However there have been concerns recently of a higher recurrence rate at one year follow-up with this device in different geographical settings [4,5].

Cyanoacrylate glue (CAG) ablation, marketed as VenaSeal (Medtronic Plc, Galway, Ireland), or VariClose™ (Biolas) is also non-thermal non-tumescent in nature, and has been shown to be safe and effective in the short-term [6-9]. Metanalysis has shown greater anatomic recurrence rates at one year compared to MOCA. These results, though not directly compared, are also inferior to RFA and EVLA though superior to foam sclerotherapy [10]. It is important to note however that clinical recurrence does not always match anatomic recurrence [10,11].

Though significant adverse events are no more common in the literature, phlebitis rates from 11.4-20% [12,13] have been reported using the VenaSeal™ device, which are higher than all the other modalities previously described. Of particular note, is a condition which is similar to phlebitis, occurring beyond the treatment zone called the VenaSeal™ Red reaction [9]. It is likely many of these patients display a form of abnormal cutaneous erythema, which is a distinct entity from phlebitis. It has now been widely described, and is an adverse event thought to be a delayed type IV hypersensitivity reaction to the glue itself [14]. This seems to have a predilection along the course of the great saphenous vein (GSV) and in females [15]. Patch testing has been performed suggestive that it may be a allergic contact dermatitis to CAG and that it is a delayed hypersensitivity reaction to the acrylate component of the compound [16]. 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 [17]. Allergists and users of the product encourage proceduralists to avoid getting CAG into the subcutaneous space (SC) 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. It is important to avoid offering this option of venous ablation to patients with multiple drug allergies as hypersensitivity reaction is more likely in these types of patients [18].

The true incidence of phlebitis, and this cyanoacrylate-related reaction is difficult to estimate due to a lack of differentiated reporting of the two entities. More research into the immunology of this reaction is required to understand which patients should and should not be offered this treatment because the phlebitis type reaction can be severe and prolonged requiring treatment with steroids and antihistamines [19].

Another problem patients have encountered followed VenaSeal™ treatment is the pulling of the fibrosed truncal vein when they flex and extend their leg. This is particularly more pronounced when the GSV has a suprafascial component and is nearer the skin surface [11]. From a technical viewpoint, about 10% of patients necessitated the use of a double puncture technique to allow the catheter to be manoeuvred up to the sapheno-femoral junction , 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 patients (approximately 30%) who

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Received: June 27, 2020; **Accepted:** August 10, 2020; **Published:** August 13, 2020

have their GSV come out of its fascial envelope during its course (supra-fascial extension) and traversing up to the skin surface. In our 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 may be more flexible to navigate the venous curves [20]. We have also developed a retrograde cannulation technique using this device to counter these small angulated deep seated veins [21].

Embolisation of the glue, and the potential for devastating pulmonary embolism (PE) with no hope of thrombolysis is a legitimate concern despite the manufacturer's reassurances. Multiple case reports exist of PE, including fatal PE, after cyanoacrylate embolisation in other vascular beds [22,23]. Many of the trials and early feasibility studies quote zero percent deep vein thrombosis (DVT) rate and this has been used as a unique selling point to attempt to gain market share, but this is misleading. From the beginning, Almeida's first in man study showed thread-like extension into the common femoral vein [8] and while no PE resulted from this, they have been reported in subsequent series [7,11,24,25]. Less common adverse events of any kind require particular vigilance, and the small numbers in early studies showing no DVT means insufficient power to detect rare but potentially devastating complications.

Venaseal therefore is a new technique with a good safety profile in trials, but which has not yet been proven in widespread use. A current RCT is ongoing to compare MOCA against CAG and is designed to determine which method causes less pain and is more efficacious [26].

Proper monitoring of outcomes and especially rare but significant complications needs to begin in earnest, allowing us to determine what the right treatment is for each patient. At the very least, surgeons need to be mindful of the uncertainty that accompanies every device to the market, and rather than trying it and assume that one device fits all, ask what is its role, and what can it do that existing technologies can't? If neither of these questions has a clear answer then why experiment?

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