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Cyanoacrylate adhesive perforator embolization (CAPE) of incompetent perforating veins of the leg, a feasibility study

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Abstract

Consideration of treating incompetent perforating veins remains a conundrum based on scientific evidence available till date. While subfascial endoscopic perforator surgery (SEPS) proved to be a worthy alternative for open surgery, other even less invasive techniques were being introduced by the late nineties of the last century. Percutaneous thermo-ablation techniques are still being used today and seem more effective than non-thermal techniques. However, thermal techniques require anaesthesia and potentially may cause inadvertent damage to surrounding tissues such as nerves. Cyanoacrylate adhesive has a proven record, but not for the treatment of chronic venous disease of the leg. Innovation has led to the development of the VenaSeal® Sapheon Closure System which has been designed to use a modified cyanoacrylate glue as a new therapy for truncal vein incompetence. This paper explores the feasibility of ultrasound guided cyanoacrylate adhesive perforator embolization (CAPE). Results show a 76% occlusion rate of incompetent perforating veins without serious complications leading to the conclusion that further investigation with a dedicated delivery device in a larger patient population is warranted.

Keywords

Cyanoacrylate, VenaSeal®, Sapheon, perforating vein, embolization, ultrasound

Background

Based on the current level of evidence, the treatment of incompetent perforating veins (IPV) remains an enigma. The call for more reliable randomised controlled trials (RCTs) remains unanswered till date.[1,2] As matters stand, there does seem to be a consensus about the rules of engagement. Former guidelines of the American Venous Forum (AVF) on the management of incompetent perforating veins with open and endoscopic surgery have proposed to abandon the modified open Linton procedure due to the associated morbidity, based on strong evidence. Further recommendations to treat perforator incompetence in patients with advanced venous disease to improve venous hemodynamic and clinical outcomes, specifically for those with primary valvular incompetence and less so in those with a post-thrombotic syndrome, are based on weak evidence of moderate quality.[3] This leaves ample room for conjecture about the when and how to treat IPV.[4] The desire to employ minimally invasive treatment techniques as an alternative for open surgery, has seen subfascial endoscopic perforator surgery (SEPS) already being surpassed by even less invasive methods by the end of the nineties. Percutaneous coil embolization[5] proved to be ineffective while transluminal occlusion of perforators (TRLOP), later reinvented as perforator ablation procedures (PAPS), involving thermo-ablation[6,7], is still being used. During the current reign of thermo-ablation devices, other non-thermal therapies such as

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cryoperforator surgery[8] seem futile and ultrasound guided sclerotherapy appear effective on the basis of repetitive sessions.[9] In the quest to present another non-thermal, non-tumescent and potentially more effective possibility, this paper explores the feasibility of ultrasound guided cyanoacrylate adhesive perforator embolization (CAPE).

Methods

Patients

On the basis of written informed consent, patients suffering from one or more symptomatic IPV with C_3-C_6 (CEAP classification) were eligible for treatment. Duplex ultrasound (DUS) was used to identify perforator incompetence defined as efflux lasting for more than 0.35 seconds[10,11] with at least a diameter of 3 mm measured at the level of the fascia. Exclusion criteria were age <18 years, gravid, immobility, deep venous obstruction, or concomitant truncal incompetency of the ipsilateral leg. All patients had undergone previous treatment and were diagnosed as having residual or recurrent venous pathology related solely to the presence of IPV.

Procedure

The procedures were performed in an academic tertiary hospital operating room (OR) of the Maastricht University Medical Centre day care centre. Peroperative DUS (MyLab^{TM}Alpha, Esaote Benelux) was used to identify the IPV. The ideal line of approach for perforator access, according to the anatomy and location of the perforator, was marked on the skin with the patient in a normal upright standing position.

Depending on the position of the IPV, the patient was asked to lie either supine or prone, with the table in reversed Trendelenburg. A rapid deflatable occlusion cuff (VBM tourniquet 4500) was employed on the upper leg, cranial to the IPV and inflated to 70 mmHg, This was to ensure maximum dilation of the venous system as well as venostasis. The reason for this was twofold, firstly to improve venous accessibility and secondly, to avoid involuntary migration of introduced cyanoacrylate into the deep venous system.

A conventional 7F introducer sheath was placed in the IPV using an ultrasound guided Seldinger technique with 1% lidocaine local anaesthesia at the site of introduction. The guidewire visible with sonography makes it possible to extend the range of the to be treated subfascial tract, ever so slightly, when compared to a direct through needle approach. The sheath is advanced to the tip of the dilator before the dilator is removed. Backbleeding through the sheath was confirmation of intraluminal positioning. Multiple introducer sheaths were placed (Figure 1) if more than one IPV was to be treated prior to unpackaging the VenaSeal® Sapheon Closure System (Sapheon Inc, Morrisville, North Carolina, USA) cyanoacrylate delivery device.

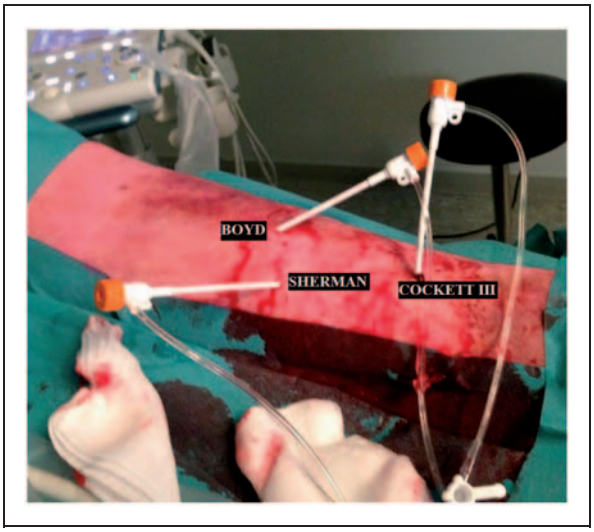

Figure 1. Access of more than one IPV using 7F introducer sheaths.

The delivery device has been specifically designed to treat incompetent truncal veins such as the great and small Saphenous veins. Once a 3 ml syringe is mounted and locked into the dispenser gun, a full 3 seconds trigger pull will eject a total of 0.09 ml (range 0.06–0.12 ml) adhesive. The adhesive has to travel through a 5F 92 cm length catheter. Normally when treating truncal veins, this catheter is mounted through a 7F 80 cm length introducer sheath involving employment of a 180 cm J-guidewire and a 5F 86 cm length dilator. The sheer length of the guidewire, the 6 cm discrepancy in length of the dilator and catheter make the set impractical for the treatment of IPV.

Bench testing the device prior to adapting it for CAPE, it was found that the 5F 92 cm length catheter to have a volume of 1.5 ml. This catheter has been ingeniously designed so that the catheter tip can be easily recognised on ultrasound in the transverse plane when the tip is perpendicular to the ultrasound transducer as is the scenario when treating truncal veins. However when the tip is at an angle to the transducer, as often is the case with perforating veins, this beneficial property is somewhat compromised (Figure 2). As ultrasound positioning of the catheter tip was deemed vital, it was proposed to leave air in the catheter tip over a distance of 5 mm. Actually the normal protocol for priming the catheter in the treatment of truncal veins is advancing the adhesive up to

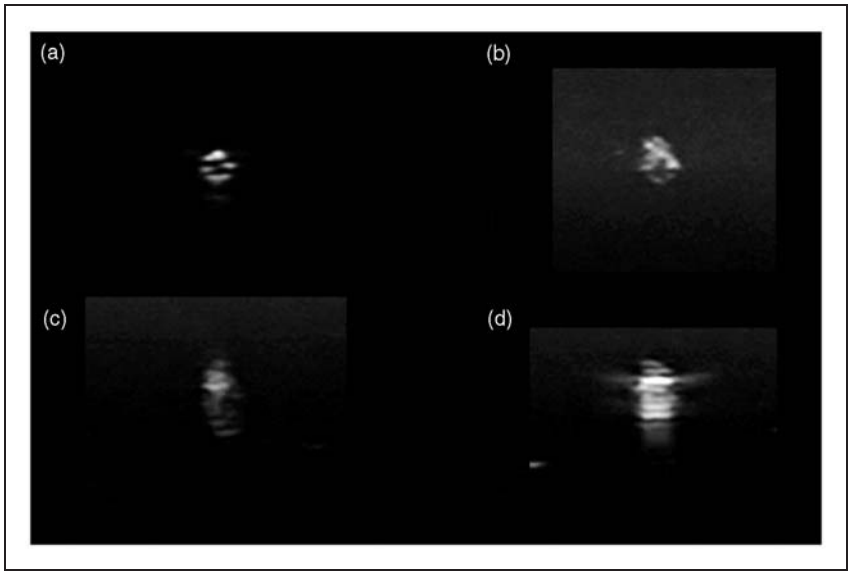

Figure 2. The Sapheon Venaseal catheter tip in tranverse plane, with ingenious patented design to ensure a characteristic ultrasound signature when scanned perpendicularly (a), but beginning to become distorted at an insonation angle of 45° (b), an unrecognisible at an angle of 60° (c). The tip still blurred at 60°, becomes more echogenic with an air bubble at the tip, enabling safer positioning (d).

30 mm (range 10–50 mm), but the volume of air would be excessive and detrimental for IPV imaging.. A small air 'bubble' at the catheter tip can easily be identified with ultrasound independent of the insonation angle, allowing for accurate tip placement.

An increment of 0.09 ml cyanoacrylate adhesive may not seem much however with the catheter tip closely situated to the deep venous system, delivery of smaller safer volumes is desirable. Also with the syringe loaded in the dispenser gun, aspiration is not possible. On this basis, it was decided to discard the use of the dispenser gun and use the syringe in a conventional manner. It was shown that smaller volumes of glue could be injected in this way.

Thus priming the delivery device was simplified. The primed Sapheon catheter was passed through the introducer sheaths, which were removed directly after the tip was satisfactorily situated in the IPV. The glue was then advanced with the slightest increment under ultrasound guidance, and allowed to polymerise for an initial period of 3 minutes without hardly withdrawing the catheter tip. The echolucent adhesive becomes echogenic with time. On introduction of the second drop of adhesive, the occlusion cuff is released unless there were multiple IPVto be treated. Venostasis was maintained until this phase was reached in the last IPV. Polymerisation of the second increment was followed by a third drop after 90 seconds with the slightest possible withdrawal of the catheter tip. When it was clear that fresh adhesive was accumulating at tip without migration towards the deep venous system, slightly larger volumes were introduced while withdrawing the tip more visibly, millimetres at a time and periods of polymerisation brought down to a minimum of 30 seconds per increment. When ultrasound confirmed that the tip was exiting the vein the catheter was withdrawn. The total amount of adhesive was registered per perforator.

Patients were ambulatory after normal wound dressing. No postoperative compression therapy was applied.

Outcome

Patients were asked to return after three months. DUS examination was used to determine the outcome of treatment. Occlusion with the clear termination of IPV efflux was scored as a successful endpoint.

Results

A total of 33 IPV (Table 1) in 27 legs (12 right, 15 left) of 23 patients (12 ♂, 11 ♀ mean age 52 years range 31–81) were treated. Procedures were carried out without complications. On the follow-up DUS, occlusion without efflux was seen in 25 (76%) whereas 8 (24%) of the treated IPV had persistent efflux. A mean of 0.7 ml of cyanoacrylate adhesive was used per IPV both in the successful group as in the group with failed closure. 2 (9%) patients suffered from wound infections at the access point, 1 (4%) had a thrombophlebitis. No patients had deep venous thrombosis (DVT) nor was any form of neurological damage reported.

Table 1. Distribution of treated perforating veins and results of CAPE.

IPV type and location	Number	CAPE occlusion	CAPE Failure
Posterior tibial			
Cockett II	3	2	1
Cockett III	10	7	3
Paratibial			
Boyd	3	2	1
Sherman	2	1	1
Midthigh			
Dodd	1	1	
Hunter	3	3	
Popliteal fossa			
	9	7	2
Medial Gastrocnemius			
Gillot	2	2	
Total	33	25 (76%)	8 (24%)

Discussion

The current AVF guidelines[12] with regards to the treatment of IPV may have a stifling effect on development, as practitioners may avoid being unorthodox. The very fact that properly conducted RCTs are scarce should actually endorse entrepreneurship. Pilot studies with small patient numbers can be valuable, as researchers can be pointed in the right direction. For example, it has been proven that the treatment of IPV with coil embolization[5] or cryoperforator surgery[8] as inadvisable. Despite the lack of grade one strong evidence, one may ask whether therapists should postpone treatment of IPV until a $C_{5,6}$ clinical stage. Valid papers have been published about the intricate roles of IPV setting a platform for verification and further investigation[13,14]. This paper is not meant to determine when IPV should be treated, rather it explores another possibility of how IPV can be treated.

Cyanoacrylate adhesive has proven effective in various fields such as brain arteriovenous embolization, retinal repair, and wound and tissue closure[15]. In fact the concept of using cyanoacrylate to treat IPV is not novel, as it has been used to occlude gastro-enterological perforating veins. Adverse events have been reported which may give an indication as to safe dosage. Kazi et al. reported that when patients developed a pulmonary embolism (PE), a mean volume of >4.2 ml of cyanoacrylate was administered compared to 1.8 ml for those without PE[16]. In our study the volumes used were well below the safety margin.

There are encouraging short term and preliminary reports on developing the application of cyanoacrylate adhesives for superficial venous disease of the lower limb.[17–21] It is being emphasized that using cyanoacrylate adhesive abolishes the necessity for tumescent anaesthesia and subsequently reduce the risk of thermally induced paraesthesia. In this respect, our findings concur with those till date. In this study no link could be attributed to possible failure and anticoagulation as has been previously described.[22]

The current VenaSeal® Sapheon protocol for the treatment of the GSV, advises not to leave the catheter in position after infusing adhesive as to avoid polymerisation with the catheter tip itself, and instructions describe withdrawing the catheter over a distance of 3 cm after delivery of 0.09 ml (range 0.06–0.12 ml) using the dispenser gun. However the dimensions of IPV do not allow for this. During CAPE dragging and tugging of the administered adhesive could be seen on ultrasound. It was also observed that the adhesive properties of the hydrophobic catheter tip were less than that of the surrounding tissue and that during infusion fresh adhesive would tend to envelope older cyanoacrylate. This remains a point for further scrutiny.

Keeping in mind that the used VenaSeal® Sapheon Closure System has been designed to treat truncal incompetence, as well as the inherent learning curve, an occlusion rate of 76% at 3 months follow up can be considered to be acceptable. Patients in our study had no concomitant venous disease which makes comparing our results to other papers somewhat difficult. Authors[23–25] claiming higher occlusion rates, often have a biased selection as treatment of perforating veins has been combined with the incompetent truncal veins. It is known that the treatment of truncal veins in itself may lead to the readjustment of efflux in perforating veins.[26]

When the results of CAPE are compared to authors who similarly have omitted patients with truncal incompetency, it is prudent to state that CAPE is as good as thermoablation. Van den Bos et al[27] had an occlusion rate of 64% at 3 months, Hingorani et al[28] 88% at 1 month with radiofrequency and Hissink et al.[29] 78% at 3 months with a bare fibre laser.

Conclusion

CAPE of incompetent perforating veins is feasible and as effective as endovenous thermo-ablative techniques without the risks of potential inadvertent thermal lesion. Further investigation with a dedicated delivery device in a larger patient population is warranted.

Conflict of interest

The authors have no commercial association which may constitute as a conflict of interest in relation to the contents of this manuscript.

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