VENASEAL: Non-thermal endovascular options for treatment of superficial venous insufficiency

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Disclosure

Speaker name:

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I have the following potential conflicts of interest to report:

- [ ] Consulting
- [ ] Employment in industry
- [ ] Stockholder of a healthcare company
- [ ] Owner of a healthcare company
- [ ] Other(s)

- I do not have any potential conflict of interest
OUTLINE

Chronic Venous Insufficiency

What is Venaseal?

Venaseal Data

UMMC CVI and Venaseal experience

How I do it?

Conclusion
Chronic Venous Insufficiency

Venous disease affects half of adult population.

- 80% have reticular or spider varicose veins
- 30-50% have truncal varicose veins
- 5-10% have skin changes of chronic venous insufficiency (CVI)
- 1% have chronic venous ulcer (CVI)

VERY COMMON CONDITION!
Epidemiology
During relaxation:
The pressure fall and the blood from superficial veins enter to the deep veins.

During contraction:
The veins which has valves pump the blood to the heart.
Pathophysiology

Normal Venous Blood Flow

- Valves

Sustained Venous Hypertension

- Venous reflux
- Valve dysfunction
- Distention of capillary walls (varicose veins)

- Extravasation of fluid (edema) and macromolecules (i.e., fibrinogen, hemosiderin)

- Fibrinogen → pericapillary fibrin cuffs

- White cell trap phenomenon (↑ local inflammatory mediators)
### Aetiology & Risk Factors

<table>
<thead>
<tr>
<th>AETIOLOGY</th>
<th>EXAMPLE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Superficial venous reflux</td>
<td>Long saphenous/short saphenous varicosities</td>
</tr>
<tr>
<td>Deep venous insufficiency</td>
<td>Valvular damage e.g. post DVT</td>
</tr>
<tr>
<td>Venous outflow obstruction</td>
<td>Stenosis/occlusion e.g. post DVT, venous cannulation</td>
</tr>
<tr>
<td>Calf muscle pump failure</td>
<td>Immobility, obesity, prolonged sitting</td>
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</tbody>
</table>
Classification

C0: No visible or palpable signs of venous disease
C1: Telangiectases or reticular veins
C2: Varicose veins
C3: Oedema
C4: a. Pigmentation and/or eczema
   b. Lipodermatosclerosis and/or atrophie blanche
C5: Healed venous leg ulcer
C6: Active venous ulcer
Managements

Conservative
• Compression stockings/bandage
• Pharmacotherapy (Daflon)
• Leg elevation, physio and massage

Operative
• Open surgery (HSVL +/- phlebectomy)
• Endovenous Ablation
  • Thermal + tumescent – EVLT, RFA
  • Non-thermal Non-tumescent – MOCA, Foam Sclerotherapy, Cyanoacrylate Ablation (VENASEAL)
VENASEAL

Indication
Intended for the permanent, complete, endovascular adhesive closure of the great saphenous vein (GSV) and associated varicosities in the treatment of venous reflux disease.

Contraindication
Not intended for use in patients with the following conditions:
Previous hypersensitivity reactions to the VA or Cyanoacrylate
Acute superficial thrombophlebitis
Thrombophlebitis migrans
Acute Sepsis

CE marked, FDA Approved
VENASEAL

- Eliminate need for tumescent anesthesia
- Eliminate need for compression stockings
- Significantly reduce post-procedure pain and bruising
- Improve current treatment closure rate of >90%

Images courtesy of M. Madsen
VENASEAL

- Proprietary formulation of advanced medical cyanoacrylate-based adhesive
- Proprietary catheter engineered to be inert to adhesive
- Proprietary dispenser gun designed to deliver adhesive precisely

CAUTION: Federal (USA) law restricts these devices to sale by or on the order of a physician. Please reference the instructions for use for a complete listing of indications, contraindications, warnings and precautions, adverse effects and a full set of instructions for the procedure.
Adhesives In Medicine

<table>
<thead>
<tr>
<th>Adhesive</th>
<th>Date</th>
<th>Use</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cyanoacrylate Adhesives</td>
<td>1950s</td>
<td>Wound adhesives</td>
</tr>
<tr>
<td>Histoacryl Blue™ *</td>
<td>1980s</td>
<td>Skin incisions</td>
</tr>
<tr>
<td>Dermabond™ *</td>
<td>1998</td>
<td>Skin incisions/lacerations</td>
</tr>
<tr>
<td>Ethicon OMNEX™ *</td>
<td>1998</td>
<td>Surgical adhesives</td>
</tr>
<tr>
<td>Trufill™ *</td>
<td>2000</td>
<td>Liquid embolic system, AVM embolization</td>
</tr>
<tr>
<td>Indermil™ *</td>
<td>2002</td>
<td>Skin incisions/lacerations</td>
</tr>
</tbody>
</table>

Cyanoacrylate Use

- Vascular closing agent for:
  - Cerebral arteriovenous malformations (AVM)
  - Pelvic congestion syndrome and varicoceles
  - Gastric varices
  - Aortic aneurysms
Proprietary formulation of advanced medical cyanoacrylate-based adhesive designed to coapt and close the vein
**CYANOACRYLATE POLYMERIZATION STRUCTURE**

- **High viscosity**
  - to prevent embolization outside the treatment area and allow good contact with the intimal surface

- **Quick polymerization**
  - to prevent embolization outside the treatment area

- **Soft and elastic after polymerization**
  - to prevent the ability to feel the adhesive after implantation

- **Strong bond formation**
  - to prevent recanalization and the requirement for post-treatment compression stockings
POTENTIAL ADVERSE EFFECTS
ASSESSMENT PERFORMED TO DETERMINE ADVERSE REACTIONS THAT ARE UNIQUE TO CYANOACRYLATES

- Allergic reactions to cyanoacrylates, such as hives, asthma, hay fever and anaphylactic shock
- Arteriovenous fistula
- Bleeding from the site of access
- Deep vein thrombosis (DVT)
- Edema in the treated leg
- Embolization, including pulmonary embolism (PE)
- Hematoma
- Hyperpigmentation
- Infection at the access site
- Non-specific mild inflammation of the cutaneous and subcutaneous tissue
- Pain
- Paresthesia
- Phlebitis
- Superficial thrombophlebitis
- Urticaria or ulceration may occur at the site of injection
- Vascular rupture and perforation
- Visible scarring

As noted within the IFU the use of the VenaSeal™ closure system is contraindicated when the following conditions exist:
- Previous hypersensitivity reactions to the VenaSeal™ adhesive or cyanoacrylates
- Acute superficial thrombophlebitis
- Thrombophlebitis migrans
- Acute sepsis exists

For the purpose of this discussion we will highlight those potential adverse reactions that are unique to cyanoacrylates. This will include the important distinction between Hypersensitivity and Phlebitis.
HYPERSENSITIVITY VS. PHLEBITIS

Hypersensitivity
- Itching and redness
- 48-72 hours post-procedure

Phlebitis
- Redness and pain
- 4-6 days post-procedure

Allergic reactions to cyanoacrylates include: Hives, asthma, hay fever and anaphylactic shock\(^2\)

Hypersensitivity is typically classified as types 1-4.\(^1\)
Itchy rash is typically associated with type 4 hypersensitivity, whereas hives and more systemic reactions are more characteristic of type 1 hypersensitivity.\(^1\)

\(^1\) Reidl, M and Casillas A, Adverse Drug Reactions: Types and Treatment Options, Am Fam Phys, Nov 2003; 68(9):1781-90
\(^2\) VenaSeal™ Closure system IFU
The Evidence

ESCHAR Trial
• Open surgery plus compression better for recurrent ulcer prevention

EVRA Trial

A Randomized Trial of Early Endovenous Ablation in Venous Ulceration

Manjit S. Gohal, M.D., Francine Haslett, B.Sc., Xin rex Liu, Ph.D., Andrew Bradbury, M.D., Richard Bulbulia, M.D., Nicky Cullum, Ph.D., David M. Epstein, Ph.D., Isaac Nyamekye, M.D., Keith R. Podd, M.D., Sophie Renton, M.S., Jane Warnick, Ph.D., and Alan M. Davies, D.Sc., for the EVRA Trial Investigators

ABSTRACT

BACKGROUND
Venous disease is the most common cause of leg ulceration. Although compression therapy improves venous ulcer healing, it does not treat the underlying cause of venous hypertension. Treatment of superficial venous reflux has been shown to reduce the rate of ulcer recurrence, but the effect of early endovenous ablation of superficial venous reflux on ulcer healing remains unclear.

METHODS
In a trial conducted at 20 centers in the United Kingdom, we randomly assigned 460 patients with venous leg ulcers to receive compression therapy and undergo early endovenous ablation of superficial venous reflux within 2 weeks after randomization (early-intervention group) or to receive compression therapy alone, with consideration of endovenous ablation deferred until after the ulcer was healed or until 6 months after randomization if the ulcer was unhealed (deferred-intervention group). The primary outcome was the time to ulcer healing. Secondary outcomes were the rate of ulcer healing at 24 weeks, the rate of ulcer recurrence, the length of time free from ulcers (ulcer-free time) during the first year after randomization, and patient-reported health-related quality of life.

RESULTS
Patient and clinical characteristics at baseline were similar in the two treatment groups. The time to ulcer healing was shorter in the early-intervention group than in the deferred-intervention group; most patients had healed ulcers with early intervention (hazard ratio for ulcer healing, 1.38, 95% confidence interval [CI], 1.13 to 1.68).

CONCLUSIONS
Early endovenous ablation of superficial venous reflux resulted in faster healing of venous leg ulcers and more time free from ulcers than deferred endovenous ablation.
## The Evidence

<table>
<thead>
<tr>
<th>Study</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Feasibility Study</strong></td>
<td>38 Patients, enrollment completed Aug. 2011</td>
</tr>
<tr>
<td></td>
<td>1, 3, 6, 12, 24 and <strong>36 month</strong> follow-ups</td>
</tr>
<tr>
<td><strong>eSCOPE</strong></td>
<td>70 patients, enrollment completed Sept. 2012</td>
</tr>
<tr>
<td>(European multicenter study)</td>
<td>2 day, 1, 3, 6, 12, 24 and <strong>36 month</strong> follow-ups</td>
</tr>
<tr>
<td><strong>VeClose</strong></td>
<td>242 patients, enrollment completed Sept. 2013</td>
</tr>
<tr>
<td>(U.S. pivotal randomized control study)</td>
<td>3 day, 1, 3, 6, 12, 24, <strong>36 mo f/up, extension to 60 mos</strong></td>
</tr>
<tr>
<td><strong>WAVES</strong></td>
<td>50 patients, single site, enrollment completed Dec. 2015</td>
</tr>
<tr>
<td>Post Market Study</td>
<td>Follow-up at 1 week, 1, 3, &amp; <strong>12 months.</strong></td>
</tr>
</tbody>
</table>
CONCLUSION

VECLOSE 36 MONTH RESULTS:

- VenaSeal™ closure rate of 94.4% with continued, non-inferiority to RFA (P=0.005) through 36 months.

- Statistically significant improvement from baseline for VCSS, AVVQ, and EQ-5D; sustained results with no difference between treatment groups out to 36 months.

- No reported DVT’s, allergic reactions, or other SAE’s through 36 months. Early events were mild and self-limiting; delayed events were uncommon.

- The VeClose RCT study, with its high level of clinical evidence and rigor continued to demonstrate the following for VenaSeal:
  - Safe, reliable, non-thermal, non-tumescent treatment option
  - Strong, consistent and durable results through 36 months
CONCLUSIONS

- Closure rate remains high at 12 months, despite including large veins (up to 20 mm), multiple segments, and the SSV

- Patients had continued improvement in VCSS, AVVQ and EQ-5D between 3 and 12 months

- New adverse events were infrequent between 3 and 12 months

- Patient satisfaction was high

- Extent of adjunctive procedures needed at 3 months less than predicted by treating physicians, and few additional procedures were performed between 3 and 12 months
UMMC CVI Experience

Indications:
• CEAP 3-6

Late 2017-Current

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Count</th>
</tr>
</thead>
<tbody>
<tr>
<td>MOCA</td>
<td>43</td>
</tr>
<tr>
<td>Venaseal</td>
<td>5</td>
</tr>
<tr>
<td>EVLA</td>
<td>2</td>
</tr>
<tr>
<td>RFA</td>
<td>1</td>
</tr>
<tr>
<td>Foam</td>
<td>16</td>
</tr>
<tr>
<td>HSVL</td>
<td>7</td>
</tr>
<tr>
<td>MSA</td>
<td>13</td>
</tr>
</tbody>
</table>
### UMMC VENASEAL Early Experience

<table>
<thead>
<tr>
<th>Age</th>
<th>Sex</th>
<th>Clinical Stage</th>
<th>Veins ablated</th>
<th>Total Length Ablated (cm)</th>
<th>Total Cyanoacrylate used (ml)</th>
<th>Target vessel occlusion</th>
<th>Pain Score (1-10)</th>
<th>Early recurrence</th>
<th>Post-op DVT</th>
</tr>
</thead>
<tbody>
<tr>
<td>50</td>
<td>M</td>
<td>3</td>
<td>GSV</td>
<td>62</td>
<td>2.3</td>
<td>100%</td>
<td>0</td>
<td>N</td>
<td>N</td>
</tr>
<tr>
<td>64</td>
<td>M</td>
<td>6</td>
<td>b/l GSV</td>
<td>81</td>
<td>4</td>
<td>100%</td>
<td>0</td>
<td>Y (due to ATV reflux)</td>
<td>N</td>
</tr>
<tr>
<td>50</td>
<td>M</td>
<td>4</td>
<td>b/l GSV</td>
<td>88</td>
<td>4</td>
<td>100%</td>
<td>0</td>
<td>N</td>
<td>N</td>
</tr>
<tr>
<td>68</td>
<td>F</td>
<td>6</td>
<td>GSV, SSV</td>
<td>65</td>
<td>4 (double dose)</td>
<td>100%</td>
<td>0</td>
<td>N</td>
<td>N</td>
</tr>
<tr>
<td>80</td>
<td>F</td>
<td>6</td>
<td>GSV</td>
<td>60</td>
<td>2.5</td>
<td>100%</td>
<td>0</td>
<td>N</td>
<td>N</td>
</tr>
</tbody>
</table>
HOW I DO IT?
Preparing the leg
Dry and Wet Table

- Adhesive, 5cc, Qty. 1
- Dispenser assembly, Qty. 1
- (Gray) Dilator, 5 Fr, Qty. 1
- (White) Delivery Catheter, 5 Fr, Qty. 1
- (Blue) Introducer, 7 Fr, Qty. 1
- Syringes, 3cc, Qty. 2
- J-wire Guide Wire, 0.035 inch, 180 cm, Qty. 1
- Dispenser Tips, 14 Gauge, Qty. 2
GSV Puncture and Wiring
Catheter Insertion and Placement
Catheter Insertion and Placement

SFJ Measurement Point

Delivery Catheter Tip

Green cone = safe
Yellow cone = warning area
Red cone = not advisable

5 cm

From Zygmunt, Venous Ultrasound, a volume in the Practical Phlebology series. © 2013 CRC Press. With permission.
GSV Ablation

Inject 0.10 cc adhesive into the vein, pull back 1 cm, inject 0.10 cc pull back 3 cm

Compress 3 minutes

Inject 0.10 cc, pull back 3 cm, compress for 30 seconds

Repeat process throughout vein
GSV Ablation

Confirm tip position

Probe Transverse and compress vein cephalad to catheter

Depress Trigger completely & hold 3 seconds

Pull back 3 cm

Maintain transducer compression, and add light compression with free hand for 30 sec.
End procedure

CHECK for DVT & GSV occlusion
Conclusion

Lower limb chronic venous insufficiency is a very common condition and surgical treatment or intervention can significantly improve quality of life.

Endovenous Ablation is as effective as traditional surgery and has less complications.

VENASEAL is an excellent option of endovenous ablation which has short learning curve, good safety profile with evidence based outcome.
THANK YOU
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