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Non-Compounded Polidocanol 1% Endovenous Microfoam (Varithena) or Thermal Ablation: A Network Meta-Analysis

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VEITH SYMPOSIUM

Disclosure

Consultant: InVera, MedVasc

Speakers Bureau: Angiodynamics, Boston Sci, BD, InVera

Research: Boston Sci, BD, InVera, Amsel

Royalties: Angiodynamics

Comparative effectiveness of non-compounded polidocanol 1% endovenous microfoam (Varithena) ablation versus endovenous thermal ablation utilizing a systematic review and network meta-analysis

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Objective: We compared the effectiveness and safety of polidocanol 1% endovenous microfoam ablation vs endovenous thermal ablation with radiofrequency or laser energy for treatment of venous insufficiency caused by lower extremity truncal vein incompetence via network meta-analysis of published comparative evidence.

Methods: We conducted a systematic literature review following best practices, including a prospective protocol. We screened studies published in English from 2000 to 2023 for randomized and nonrandomized studies reporting direct or indirect comparisons between polidocanol 1% endovenous microfoam and endovenous thermal ablation. Thirteen studies met our eligibility criteria for the network meta-analysis. The co-primary effectiveness outcomes were the closure rate ≥3 months after procedure and the average change in the Venous Clinical Severity Score. For the subgroup of venous ulcer patients, the ulcer healing rate was the primary effectiveness outcome. The secondary outcomes included safety and patient-reported outcomes. Network meta-analyses were conducted on outcomes having sufficient data. Categorical outcomes were summarized using odds ratios (ORs) with 95% confidence intervals (CIs). Sensitivity tests and estimates of network inconsistency were used to investigate the robustness of our meta-analysis.

Results: We found that polidocanol 1% endovenous microfoam was not significantly different statistically from endovenous thermal ablation for venous closure (OR, 0.65; 95% CI, 0.36-1.18; P = .16). Although not the primary aim of the study, the network meta-analysis also provided evidence to confirm our supposition that polidocanol 1% endovenous microfoam was significantly differentiated statistically from physician-compounded foam, with higher odds for vein closure (OR, 2.91; 95% CI, 1.58-5.37; P < .01). A sensitivity analysis using the longest available time point for closure in each study, with a minimum of 12 months of follow-up (median, 48 months; range, 12-72 months), showed results similar to those of the main analysis. No association was found between the risk of deep vein thrombosis and the treatment received. The available data were insufficient for a network meta-analysis of Venous Clinical Severity Score improvement and ulcer healing rates.

Conclusions: Polidocanol 1% endovenous microfoam was not significantly different statistically from endovenous thermal ablation for venous closure and deep vein thrombosis risk for chronic venous insufficiency treatment, based on a network meta-analysis of published evidence. Polidocanol 1% endovenous microfoam was significantly differentiated statistically from physician-compounded foam, with higher odds of vein closure. A sensitivity analysis found venous closure findings were robust at follow-up intervals of 12 months or greater and for up to 6 years. New evidence meeting the inclusion criteria for this review will be incorporated at regular intervals into a living network meta-analysis.

2024

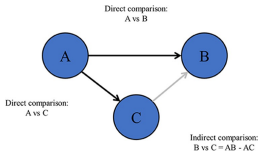
Study Objective

The objective of this study was to compare the effectiveness and safety of polidocanol 1% endovenous microfoam ablation (PEM) versus radiofrequency or laser energy (ETA) in the treatment of adult patients with lower extremity truncal vein incompetence.

The study design (we employed) was a systematic review of the published comparative evidence (randomized or non-randomized studies) incorporated into a network meta-analysis

Network Meta-analysis

- **A network meta-analysis pools and synthesizes evidence from both direct and indirect comparisons to provide more generalizable evidence on the relative effects of medical treatments, especially when head-to-head studies are few**
- **The primary effectiveness outcomes were:**
  - **Closure rate at time points of at least 3 months post-procedure**
  - **Venous Clinical Severity Score: Mean or median change**
  - **VLU healing rate outcome (subgroup analysis)**
- **Secondary outcomes**
  - **Safety (particularly deep venous thrombosis, DVT**
  - **Patient-reported outcomes, including quality**



Methods for Network Meta-Analyses

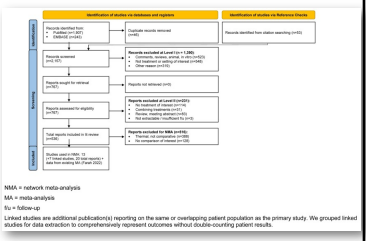
Network meta-analyses were conducted on outcomes having sufficient data for PEM and ETA, which included Closure Rate and DVT

Closure Rate and DVT were summarized with odds ratios (OR) with 95% confidence intervals (CI)

Sensitivity tests and estimates of network inconsistency using local and global approaches were employed to investigate model robustness

Systematic Review Results

- Systematic literature review using best practices, including a prospective protocol
- Screened more than **2,000 studies** published in English from 2000 to 2023
- Many not comparative or did not report on a treatment of interest
- **13 studies** met our eligibility criteria for the network meta-analysis
- **6 randomized trials** and **7 non-randomized** comparative studies
- CEAP-Clinical was most often C2-C6; truncal veins treated primarily GSV
- We incorporated a previous meta-analysis (Farah, *et al.* 2022, conducted for SVS/AVF/AVLS guidelines) for ETA vs. surgery data



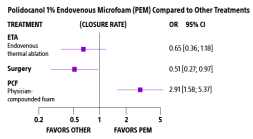
NMA = network meta-analysis
MA = meta-analysis
f/u = follow-up
Linked studies are additional publication(s) reporting on the same or overlapping patient population as the primary study. We grouped linked studies for data extraction to comprehensively represent outcomes without double-counting patient results.

Results of Network Meta-Analysis
Closure Rate

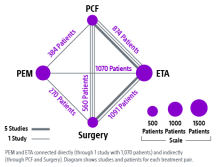
- 9 studies, supplemented by 3 ETA versus surgery studies from the Farah 2022 meta-analysis, supplied data on the primary endpoint of vein closure at a median timepoint of 12 months (range 3-72 months)
- PEM was not statistically different from ETA for vein closure (OR 0.65, 95% CI 0.36 to 1.18, P=0.16).
- PEM was directly and indirectly connected to ETA in the network for this outcome, as shown in the network diagram.
- In the indirect comparison node of the network that included physician-compounded foam (PCF), PEM was statistically significantly differentiated from PCF with higher odds of vein closure (OR 2.91, 95% CI 1.58 to 5.37, P<0.01)
- A sensitivity analysis using the longest available time point for closure in each study showed similar results

PEM (Varithena) had higher odds for vein closure and was statistically significantly differentiated from PCF from 3 months up to 6 years

A sensitivity analysis found venous closure findings were robust at follow-up intervals of 12 months or greater and up to 6 years



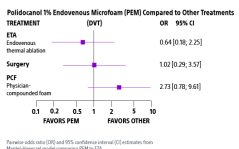
Pairwise odds ratio (OR) and 95% confidence interval (CI) estimates from random-effects model comparing PEM to ETA.



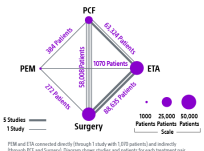
PEM and ETA connected directly (through 1 study with 1,070 patients) and indirectly (through PCF and Surgery). Diagram shows studies and patients for each treatment pair.

*As of July 1, 2024

There is no evidence that Varithena is associated with an increased risk of DVT compared to endovenous thermal ablation or PCF treatment



Pairwise odds ratio (OR) and 95% confidence interval (CI) estimates from Mantel-Haenszel model comparing PEM to ETA.



PEM and ETA connected directly (through 1 study with 1,070 patients) and indirectly (through PCF and Surgery). Diagram shows studies and patients for each treatment pair.

*As of July 1, 2024

Conclusions

PEM was not statistically different from ETA for vein closure and DVT risk for chronic venous insufficiency treatment

PEM was statistically significantly differentiated from PCF with higher odds for vein closure, based on a network meta-analysis of published evidence.

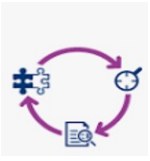
For vein closure, a sensitivity analysis showed findings were robust at standard follow up intervals of 12 months or greater and up to 6 years.

New evidence will be incorporated into a living network meta-analysis [https://www.varithena.com/en-us-hcp/clinical-evidence/living-meta-analysis.html] as it becomes available

The living network metanalysis will be presented later today

What is a living Systematic Review?

A Systematic review which is continually updated, incorporating relative new evidence as it becomes available.

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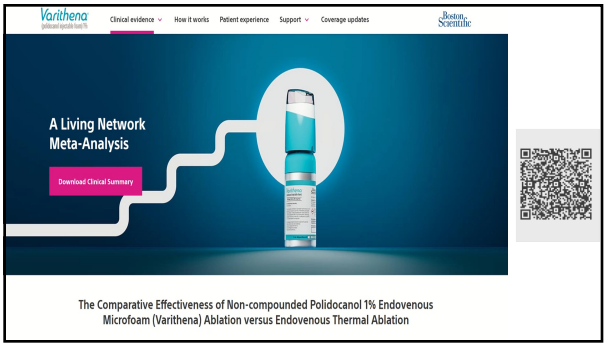
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The Comparative Effectiveness of Non-compounded Polidocanol 1% Endovenous Microfoam (Varithena) Ablation versus Endovenous Thermal Ablation