

## Comparative Clinical and Patient-Reported Outcomes for Endovenous Laser Ablation *vs.* Cyanoacrylate Ablation in Chronic Venous Insufficiency: A Systematic Review and Meta-Analysis

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### ABSTRACT

The approach treatments to manage Chronic Venous Insufficiency (CVI) has evolved from surgery to minimally invasive techniques such as Endovenous Thermal Ablation (EVLA) with complications persist. The literature search was performed through databases including PubMed, Scopus, ProQuest, and ScienceDirect up to April 2025. The primary outcome was occlusion rates in 12 months. Other outcomes included Venous Clinical Severity Score (VCSS) improvement and adverse events. Nine studies were included as final data analysis. The occlusion rates for CVI after EVLA and CAA of 92.85% and 87.27%, respectively. After 12 months follow-up, both groups showed similar improvement in Venous Clinical Severity Scores (VCSS). Overall, adverse events were more common with EVLA, while the CAA group had lower rates. Both EVLA and CAA procedures demonstrated high occlusion rates. The improvement in quality of life after both EVLA and CAA procedure is similar. However, EVLA has more complications than CAA while maintaining similar effectiveness.

## INTRODUCTION

Patients with chronic venous disease (CVD) often seek treatment due to a range of symptoms and clinical signs that can significantly affect their quality of life. Common symptoms include leg pain, discomfort, and heaviness, while visible signs of CVD include varicose veins, edema, skin discoloration, lipodermatosclerosis, and in severe cases, venous ulceration. The condition is classified based on clinical severity, ranging from C0 (no visible signs) to C6 (advanced venous ulceration), with progression often leading to increased complications and a greater impact on daily life. CVD is a widespread condition that affects approximately 83.6% of the global population. Varicose veins in the lower limbs are the primary cause of chronic venous insufficiency (CVI). Additionally, as many as 30% of varicose veins can advance to more severe stages of CVI.

The approach to manage varicose veins has evolved significantly in recent years, yet the optimal treatment remains uncertain. Historically, surgical ligation and stripping under general anesthesia were the standard methods. However, modern minimally invasive techniques using local anesthesia such as endovenous thermal ablation—have become more prevalent due to their lower procedural morbidity, faster recovery times, and improved patient comfort. Among these, endovenous laser ablation (EVLA) is widely recommended as a first-line therapy by the European Society for Vascular Surgery. These modern approaches have been associated with reduced peri-procedural pain and a quicker return to daily activities, making them an attractive alternative to traditional surgery. However, these procedures are associated with side effects due to thermal energy, which can damage the venous wall and lead to pain, pigmentation, skin burns, nerve injury or paresthesia and arteriovenous fistula formations. To minimize these limitations, nonthermal, non-tumescent (NTNT) methods such as cyanoacrylate ablation (CAA), mechanochemical ablation (MOCA), and ultrasound-guided foam sclerotherapy have been introduced.

Despite the growing use of these advanced interventions, particularly EVLA and CAA, the comparative effectiveness and safety profiles of these techniques remain a matter of ongoing debate. Studies to date have yielded inconsistent and sometimes conflicting results regarding procedural success, complication rates, and patient-reported outcomes. Furthermore, while the Venous Clinical Severity Score (VCSS) and other disease-specific tools have been used to evaluate treatment impact also have a lack of high-quality comparative evidence synthesizing data from multiple studies to guide optimal clinical decision-making. The comparative effectiveness of EVLA and CAA techniques for treating superficial venous incompetence remains debatable, as existing studies report conflicting findings. To provide a clearer understanding, this meta-analysis was conducted to systematically evaluate and compare the outcomes of EVLA and CAA, with the goal of providing clearer evidence to support treatment selection.

## **THEORETICAL REVIEW**

Chronic venous disease (CVD) represents a significant public health burden, affecting up to 83.6% of the global population, with varicose veins as a common manifestation. Progression to chronic venous insufficiency (CVI) often results in debilitating symptoms and reduced quality of life. Over recent decades, the treatment landscape for superficial venous incompetence has evolved from invasive surgical techniques to minimally invasive endovenous procedures. Particularly EVLA has become a widely adopted first-line therapy for treating saphenous vein reflux, supported by guidelines such as those from the European Society for Vascular Surgery (ESVS). EVLA utilizes thermal energy to induce endothelial damage and vein closure. To mitigate the limitations of thermal-based approaches, nonthermal, non-tumescent (NTNT) technologies have been introduced, with cyanoacrylate adhesive ablation (CAA) emerging as a promising alternative. CAA involves the use of medical glue to occlude the target vein, eliminating the need for tumescent anesthesia or thermal energy. Therefore this difference approach to treat CVI, this study is to decide which treatment approach can show the better outcomes for patient. The study adhered to the 2020 PRISMA guidelines for Systematic Reviews and Meta-Analyses throughout its duration. Systematic searches were performed in PubMed, Scopus, ProQuest, and ScienceDirect up to April 2025. RevMan 5.4 was utilized for information investigation

## **METHODOLOGY**

This meta-analysis adhered to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. The protocol is registered with the International Prospective Register of Systematic Reviews (PROSPERO) under the registration number CRD420251030623.

### ***Literature Searching and Screening***

The search strategy utilized specific terms to identify relevant studies concerning R.D.P.W and N.T.A: ((Endovenous thermal ablation) OR (laser ablation)) AND ((cyanoacrylate) OR (cyanoacrylate glue)) AND ((Varicose veins) OR (Venous insufficiency)). The titles and abstracts were initially reviewed independently to identify studies that met the inclusion criteria. Following this, the full texts of the selected articles were thoroughly assessed for eligibility.

### ***Eligibility Criteria***

The selection of studies commenced with examining the titles and abstracts of full-text articles according to the established inclusion and exclusion criteria. The studies were subsequently reviewed and assessed by all two authors (R.D.P.W and N.A.H) to evaluate their eligibility. The authors reviewed the titles and abstracts of all retrieved studies according to the specified eligibility criteria:

- (1) Ages between 18 and 75 years
- (2) A reflux time of GSV > 0.5 seconds on duplex scanning
- (3) Normal GSV diameter > 5.5 mm
- (4) Symptoms of the patients (pain, cramps, leg swelling, etc.)
- (5) Clinical-Etiology-Anatomy-Pathophysiology (CEAP) C2-C6
- (6) English language full-text
- (7) Eligible studies should have reported at least one of our outcomes interest

This study excluded a history of DVT, pregnancy, coagulopathy, breastfeeding, and also duplicate publication, using data from non-human studies (animal), review articles, case reports, and foreign language. The endpoint outcomes comprised occlusion rates, VCSS improvements, and adverse events.

### *Data Extraction and Quality Assessment*

Two authors (R.D.W.P. and N.T.A.) used a pre-established table to extract data for the included studies. A third author (P.O.) addressed disagreements. The collected data comprised general study information and comprehensive patient demographics, including age and gender. The quality of the studies was assessed using the Newcastle-Ottawa Scale (NOS) assessment tool. Quality ratings were reviewed as good, adequate, or poor.

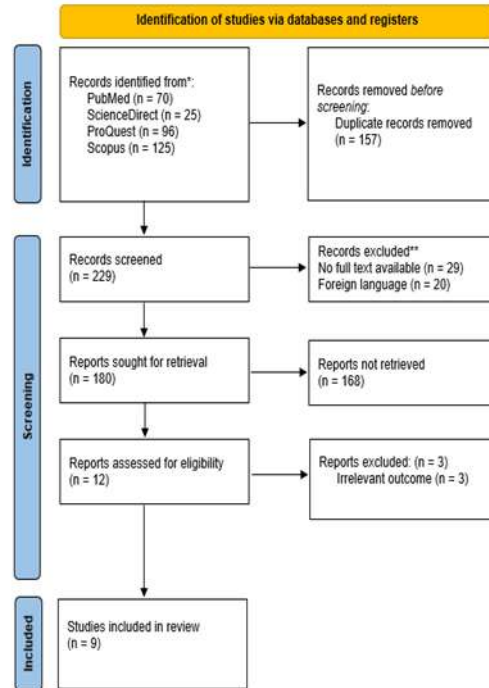
### *Data Synthesis and Analysis*

A meta-analysis was performed employing standard methodologies. Due to the considerable variability among studies stemming from differing research method and participant characteristics, we employed random effects to pool the data for each outcome. The  $I^2$  statistic was used to assess statistical heterogeneity across the studies.  $I^2$  values of 25%, 50%, and 75% correspond to low, moderate, and high heterogeneity, respectively. All results included p-values and 95% confidence intervals (CI). The evaluation of publication bias was conducted through the use of a funnel plot.

## **RESULTS**

### *Study selection*

The keyword search initially identified 316 studies. After removing duplicates and screening titles and abstracts, 12 articles were selected for full review. Following the exclusion of 3 irrelevant studies, data from nine studies were ultimately included. The selection process is detailed in the PRISMA flow diagram provided (**Fig. 1**).



\*Consider, if feasible to do so, reporting the number of records identified from each database or register searched (rather than the total number across all databases/registers).

\*\*If automation tools were used, indicate how many records were excluded by a human and how many were excluded by automation tools.

**Figure 1. Preferred Reporting Items for Systematic Reviews and Meta-Analyses flow diagram**

### *Quality of assessment*

Nine retrospective cohort studies were evaluated using the NOS assessment tool that includes eight items across three domains: patient selection, comparability, and outcomes. Studies scoring 7-9 were deemed high quality, 4-6 moderate quality, and 0-3 low quality. Any scoring discrepancies were resolved through discussion until consensus was achieved.

### *Study characteristics*

Nine studies were identified, involving 1439 CVI outpatients in the EVLA group and 1299 patients in the CAA glue group. All studies included in this review were retrospective cohort studies. Most studies were conducted in Turkey, and two were from the Czech Republic and Poland.

Venous occlusion or obliteration is an anatomical term referring to the narrowing of a vein-circulating channel. The occlusion rate of venous treatments defined the percentage of treated veins that remain successfully closed and the absence of reflux on duplex ultrasonography (DUS) after a specific period following procedures such as EVLA and CAA after 12 months-follow up. The VCSS is a standardized tool used to assess the severity of CVD. This provides a quantitative evaluation of disease progression followed by evaluating various clinical sign and symptoms: pain, varicose veins, edema, pigmentation, inflammation, induration, ulcer size, number of ulcers, ulcer duration, and compression stocking use. A decrease in VCSS score, particularly in this study

after 12 months-follow up. Each component is rated on a scale from zero to three, representing absent (score = 0), mild (score = 1), moderate (score = 2), and severe levels (score = 3), with a maximum possible score of 30 points.<sup>21</sup> The adverse events refer to any unintended or harmful reaction due to the procedure. These events can range from mild to severe and may affect the patient's recovery or treatment outcome.

Table 1. Characteristics of the included studies

No	References	Country	Study Design	Intervention		Age, years (Mean±SD)		Gender		Vein treated	GSV Diameters		Pain Score	
				EVLA	CAA	EVLA	CAA	Male	Female		EVLA	CAA	EVLA	CAA
				1	Kubat <sup>3</sup>	Turkey	R	109	79		47.4±11.4	50.6±11.68	77	111
2	Kilic <sup>4</sup>	Turkey	R	77	73	51.2±10.8	49.3±14.0	74	76	GSV	7.1±1.6	7.2±2.2	5.1±2.9	2.4±2.6
3	Koramaz <sup>7</sup>	Turkey	R	189	150	45.09±12	47.08±11	169	170	GSV	7.15±1.77	6.88±1.80	N/A	N/A
4	Cem <sup>10</sup>	Turkey	R	412	431	46.24±11.31	42.21±8.02	172	671	GSV	7.14±1.07	6.73±1.67	N/A	N/A
5	Eroglu <sup>11</sup>	Turkey	R	139	168	45.9±10.4	47.7±11.9	136	171	GSV, SSV	8.0±1.9	7.6±1.9	N/A	N/A
6	Sahin <sup>11</sup>	Turkey	R	146	54	49.0±11.2	53.7±9.1	122	78	GSV	8.3±1.9	8.7±2.2	N/A	N/A
7	Bozkurt <sup>12</sup>	Turkey	R	156	154	40.2±11.2	42.5±13.1	152	158	GSV	7.1±1.6	7.2±1.8	N/A	N/A
8	Balaz <sup>9</sup>	Turkey	R	42	27	56.5±14.0	43.5±12.0	30	51	GSV, SSV	5.6±1.1	5.7±1.2	2.0±0	2.0±0
9	Wilczko <sup>14</sup>	Czech	R	46	43	42.5±11.2	46.1±14.4	28	61	AASV, GSV, SSV	7.6±1.5	7.4±1.8	2.9±2.4	4.3±2.4

R; Retrospective study, EVLA; Endovenous Laser Ablation, CAA; Cyanoacrylate Ablation, GSV; Great Saphenous Vein, SSV; Small Saphenous Vein, AASV; Anterior Accessory Saphenous Vein, N/A; Not Available

Table 1. Continued

No	Reference	CEAP CLASSIFICATION							
		EVL				CAA			
		CEA P 2	CEA P 3	CEA P 4	CEA P 5	CEA P 2	CEA P 3	CEA P 4	CEA P 5
1	Kubat <sup>8</sup>	69	28	7	5	47	23	6	3
2	Kilic <sup>6</sup>	51	20	6	0	51	19	3	0
3	Koramaz <sup>7</sup>	22	93	64	10	20	66	54	10
4	Cem <sup>10</sup>	155	181	68	8	167	222	34	8
5	Eroglu <sup>13</sup>	4	77	58	0	4	93	71	0
6	Sahin <sup>11</sup>	61	69	16	0	18	33	3	0
7	Bozkurt <sup>12</sup>	119	33	4	0	104	38	12	0
8	Balaz <sup>9</sup>	12	17	1	0	8	32	3	2
9	Wilczko <sup>14</sup>	32	10	4	0	34	6	3	0

CEAP; Clinical-Etiology-Anatomu-Pathologic Classification

CEAP 2; Varicose veins with/without any symptoms

CEAP 3; Swollen ankle (edema) due to varicose veins

CEAP 4; Skin damage due to varicose veins

CEAP 5; Healed venous leg ulcer

**Patient Characteristics**

The mean age of patients in the studies analyzed was  $45.79 \pm 2.81$ , with a total of 2510 patients. A total of 62% of patients undergoing CVI were female. Regarding the CEAP classification, 39% of the outpatients were categorized as CEAP 2, 42.3% as CEAP 3, 16.7% as CEAP 4, and 1.8% as CEAP 5. The great saphenous vein (GSV) was the most commonly treated vein across nine studies. Three studies focused on the small saphenous vein (SSV), while two studies examined the anterior accessory saphenous vein (AASV) (Table 1).

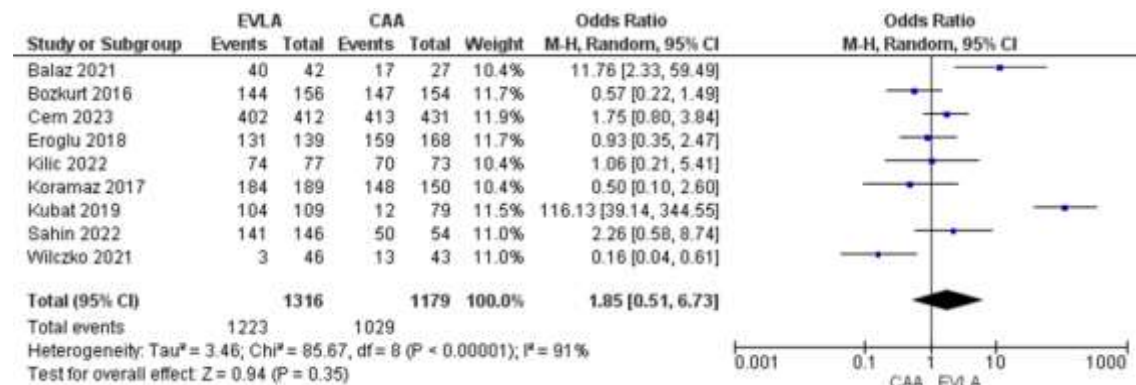
**Clinical Outcomes**

**Occlusion Rates in 12 months**

Nine studies<sup>8-14</sup> reported overall occlusion rates for CVI after EVLA and CAA of 92.85% and 87.27%, respectively. A random effect model meta-analysis did not show a statistically significant difference (OR 1.85, 95% CI 0.51 - 6.73,  $p = .35$ ,  $I^2 = 91\%$ ) (Fig. 2).

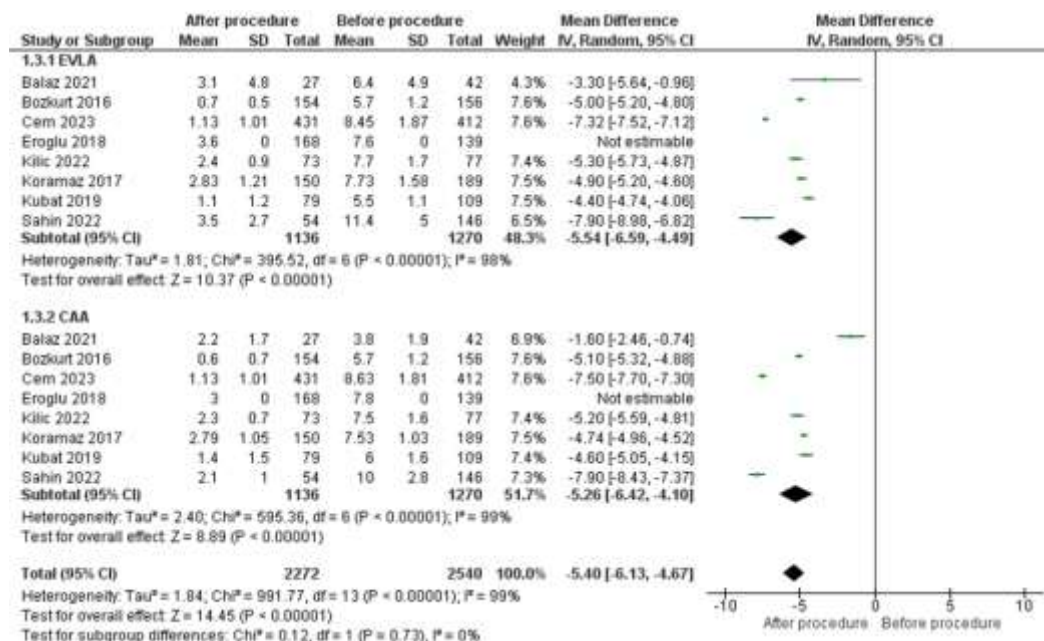
**Venous Clinical Severity Score (VCSS)**

A total of VCSS comparisons from eight studies involving 4812 participants were gathered to analyze the effects of VCSS after EVLA and CAA. After 12 months follow-up, the EVLA group showed improvement from  $7.88 \pm 2.87$  to  $2.03 \pm 1.88$  and the CAA group from  $7.65 \pm 2.13$  to  $1.71 \pm 1.27$ . The analysis results after EVLA and CAA were MD -5.54 [95% CI -6.59 - -4.49],  $p < .0001$ ,  $I^2 = 98\%$  and MD -5.26 [95% CI -6.42 - -4.10],  $p < .0001$ ,  $I^2 = 99\%$ . The overall effect test was significant ( $p = .0001$ ). Based on the funnel plot, there is no indicated publication bias (Fig. 3).



EVLA vs CAA occlusion rates after 12 months procedure performed were 92.85% vs 87.27% ( $P = 0.35$ ). The solid squares indicate the odd ratio (OR), the horizontal lines depict the 95% confidence intervals (CIs), and the diamond represents the overall pooled ratio. M-H, Mantel-Haenszel.

**Figure. 2 Forest plot of occlusion rates comparing Endovenous Laser Ablation (EVLA) vs Cyanoacrylate Ablation (CAA) procedure.**



The subgroup difference was insignificant ( $P = 0.73$ ). The solid squares indicate the odd ratio (OR), the horizontal lines depict the 95% confidence intervals (CIs), and the diamond represents the pooled mean difference. *M-H*, Mantel-Haenszel.

**Figure. 3 Forest plot of Venous Clinical Severity Score (VCSS) before and after procedure showed improvement change in 12 months for EVLA vs CAA group.**

### Adverse Events

#### Paresthesia

Six studies<sup>6-8,10-11,13</sup> reported clinical findings related to paresthesia events during the procedure. The overall incidence of paresthesia was 2.2% after EVLA and 0.21% after CAA. A meta-analysis using a random-effects model revealed a statistically significant for the EVLA procedure (OR 4.50, 95% CI 1.61 - 12.60,  $p = .004$ ,  $I^2 = 0\%$ ) (Fig. 4).

#### Pigmentation

Five studies<sup>6-8,10,13</sup> reported that pigmentation events after the procedure were 2.86% for EVLA and 1.01% for CAA. Pooled analysis showed no significant difference between both procedures (OR 1.85, 95% CI 0.84 - 4.05,  $p = .13$ ,  $I^2 = 0\%$ ) (Fig. 4).

#### Ecchymosis

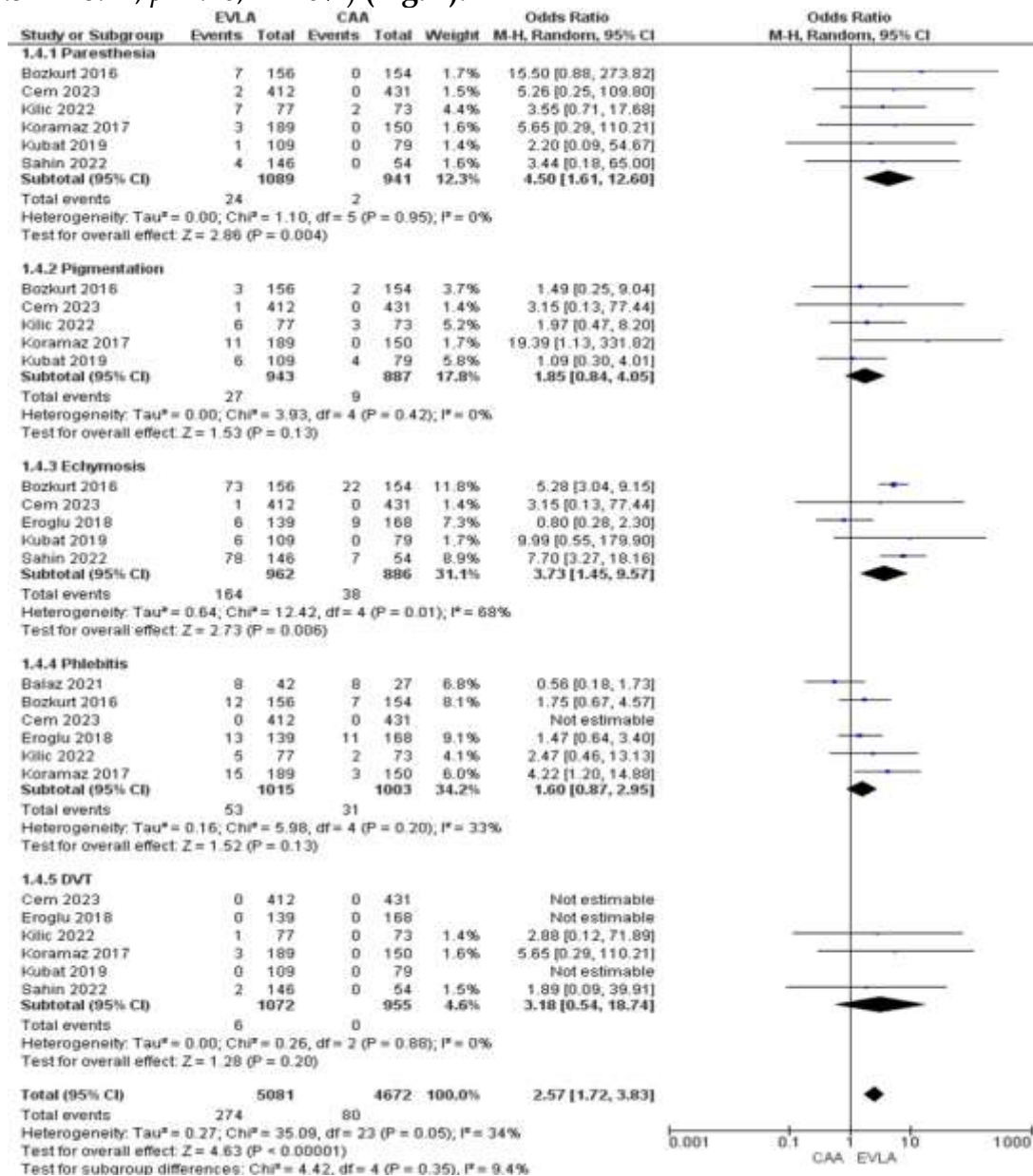
Of the included studies<sup>8,10-13</sup> reported ecchymosis was encountered in 17.04% of patients in the EVLA group and 4.28% in the CAA group. A meta-analysis showed statistically significant differences higher in patients undergoing EVLA procedure (OR 3.73, 95% CI 1.45 - 9.57,  $p = .006$ ,  $I^2 = 68\%$ ) (Fig. 4).

#### Phlebitis

The findings from six studies<sup>6-8,10-12</sup> on phlebitis events after the CVI procedure showed no significant differences between the EVLA and CAA groups (OR 1.60, 95% CI 0.87 - 1.95,  $p = .13$ ,  $I^2 = 33\%$ ) (Fig.). After procedures in the EVLA and CAA groups, Phlebitis rates were 5.22% and 3.09%, respectively (Fig. 4).

**DVT (Deep Vein Thrombosis)**

Six studies<sup>8-12,14</sup> reported DVT complications after the procedure. The overall rates using EVLA and CAA were 0.5% and 0%, respectively. Meta-analysis results showed no statistically significant difference (OR 3.18, 95% CI 0.54 - 18.74,  $p = .20$ ,  $I^2 = 0\%$ ) (Fig. 4).



The solid squares indicate the odd ratio (OR), the horizontal lines depict the 95% confidence intervals (CIs), and the diamond represents the overall pooled ratio. M-H, Mantel-Haenszel.

**Figure. 4 Forest plot results adverse events comparing Endovenous Laser Ablation (EVLA) vs Cyanoacrylate Ablation (CAA) regard to paresthesia, pigmentation, ecchymosis, phlebitis, and deep vein thrombosis (DVT) rates.**

**DISCUSSION**

Our discussion focuses on the evolving treatment options for CVI, which have progressed beyond traditional stripping techniques to include advanced modalities such as EVLA and CAA. These technological advancements have generated significant interest among both patients and vascular surgeons. The

effectiveness of EVLA and CAA as minimally invasive techniques for varicose vein treatment is the main goal of this review. While CAA has gained popularity, it presents both advantages and disadvantages. Notably, upon contact with intravascular tissue, CAA undergoes rapid polymerization, leading to vein occlusion through an inflammatory response. This inflammatory reaction plays a crucial role in initiating vein closure, highlighting both the potential and limitations of CAA as a treatment modality.

A retrospective study, with a total of 538 patients, found that CAA achieved a 99.4% occlusion rate at the 12 months. Another study<sup>9</sup> showed that the occlusion rates in CAA and EVLA groups in 12 months were 98.6% and 97.3%, respectively. However, our study found that CAA had lower occlusion rates (87.2%) compared to EVLA (92.9%) and indicated no statistically significant difference between both procedures. A previous systematic review and meta-analysis also revealed occlusion rates after CAC and EVLA procedures did not show a significant difference. Study by Poulouse et al. demonstrated that CAA mixed with lipiodol led to rapid vein obliteration in rabbit models, with the effect occurring almost immediately.<sup>20,21</sup> The study also found that within 2-3 months, the glue had largely disappeared and replaced by fibrotic tissue. Similarly, study by Sahin et al. revealed that patients treated with CAC showed immediate vein obliteration by Doppler USG with no hardness detected upon palpation of the GSV site in one month follow-up.

The WAVES study was the first to establish the effectiveness of CAC in treating GSV, SSV, and AASV with diameters of up to 20 mm and reported complete vein occlusion at the one-month follow-up. However, an analysis by Chan et al. of 108 GSV cases, with diameters ranging from 2.3 to 11.4 mm, suggested that a mean GSV diameter greater than 6.6 mm could be a significant predictor of recanalization and highlights the potential influence of vein size on treatment outcomes. Additionally, veins with a diameter greater than 7 mm had significantly longer remnant stump lengths than smaller veins. This suggests that larger veins may influence the distribution and effectiveness of the adhesive used in the procedure. Meanwhile, in our review, GSV diameters  $7.84 \pm 2.36$  for the EVLA procedure and  $7.40 \pm 2.40$  for the CAA procedure were not statistically significant.

In our study, the VCSS showed a significant improvement after one year from  $7.88 \pm 2.87$  to  $2.03 \pm 1.88$  in the EVLA group and  $7.65 \pm 2.13$  to  $1.71 \pm 1.27$  in the CAA group. Similarly, study by Bootun et al. showed a significant improvement of VCSS score for the CAA group, decreasing from 6.1 at baseline to 1.5 after one year. Furthermore, Goda et al. revealed significant VCSS scores improvement from  $7.76 \pm 1.49$  to  $2.59 \pm 1.03$  in 12 months. Balaz et al. (2021) demonstrated that although recanalization rate of CAA was high, patients experienced some symptomatic relief, as reflected in the improved VCSS scores, though the improvement was less pronounced compared to the EVLA group. These may be attributed to the presence of residual adhesive material within the lumen even after recanalization, which could reduce the severity of reflux and contribute to partial clinical improvement. In general, endovenous techniques resulted in less pain compared to conventional surgery for treating GSV

insufficiency. Nevertheless, many studies reported that the EVLA procedure was associated with higher pain scores. In line with these findings, our study also observed higher VAS scores with EVLA compared to CAC, however there were no significant differences between the two procedures.

The rate of complications following CVI treatment has shown variation due to the absence of standardized protocols. Regarding the incidence of paresthesia, few studies revealed that paresthesia occur more frequent in the EVLA group compared to the CAA group. A statistically significant difference was noted in the frequency of ecchymosis, with CAA exhibiting a lower occurrence than EVLA. The possible reason for paresthesia and ecchymosis appears frequently in thermal ablation methods is because it requires multiple injections for tumescent anesthesia, whereas NBCA eliminates this need.

The other adverse events such as DVT, phlebitis, and pigmentation were found frequently in the patients receiving EVLA compared to CAA, yet no significant difference between both. Study by Turner et al. (2023) stated no substantial difference in DVT rates among various endovenous closure techniques has been consistently shown and no correlation between the intervention type and DVT occurrence. Established risk factors for thrombotic events after ablation may have a greater impact on individuals with a history of DVT. These factors include previous superficial thrombophlebitis, advanced age, inherited thrombophilia, larger GSV diameter, and concurrent venous procedures, especially microphlebectomy. Phlebitis, including redness, pain, and local swelling in the treated area, were hypersensitivity reactions leading to phlebitis-like signs and symptoms in veins treated with cyanoacrylate glue. Recent studies reported histological analysis of a type IV hypersensitivity reaction to the glue as a foreign body. This differs from the phlebitis observed following thermal ablation. The exact cause of hyperpigmentation remains uncertain. Potential explanations include direct thermal damage, considering the relatively superficial location of the vein. Although sufficient tumescent anesthesia was administered and effectively displaced the vein deeper, this may not have adequately absorbed the heat. Another possibility is the migration of melanin pigment. However, identifying the exact cause would be challenging without histological analysis. The overall complication mostly appeared, CAA procedure was associated with lower incidences of paresthesia, ecchymosis, phlebitis, skin pigmentation, and DVT compared to EVLA.

## **CONCLUSIONS AND RECOMMENDATIONS**

EVLA and CAA are effective and minimally invasive options for CVI treatment. Both techniques demonstrated high occlusion rates, with no statistically significant difference among them. The VCSS scores significantly improved in both groups, indicating substantial clinical benefits. However, EVLA was associated with a higher incidence of adverse events such as paresthesia, ecchymosis, and pigmentation, likely due to its reliance on thermal ablation. In contrast, CAA demonstrated a lower complication rate while maintaining similar effectiveness. The choice between these methods should consider individual patient characteristics, procedural risks, and clinician expertise.

## FURTHER STUDY

This study has limitations and it is necessary to conduct further research related to the topic "Comparative Clinical and Patient-Reported Outcomes for Endovenous Laser Ablation *vs.* Cyanoacrylate Ablation in Chronic Venous Insufficiency". Future prospective, randomized controlled trials with larger sample sizes and long-term follow-up are recommended to better assess durability, recurrence rates, and quality-of-life outcomes beyond 12 month. Cost-effectiveness analyses and assessments of procedural efficiency may further guide practical adoption in various healthcare settings.

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