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Interventions for great saphenous vein incompetence (Review)

Whing J, Nandhra S, Nesbitt C, Stansby G

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[Intervention Review]

Interventions for great saphenous vein incompetence

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ABSTRACT

Background

Great saphenous vein (GSV) incompetence, causing varicose veins and venous insufficiency, makes up the majority of lower-limb superficial venous diseases. Treatment options for GSV incompetence include surgery (also known as high ligation and stripping), laser and radiofrequency ablation, and ultrasound-guided foam sclerotherapy. Newer treatments include cyanoacrylate glue, mechanochemical ablation, and endovenous steam ablation. These techniques avoid the need for a general anaesthetic, and may result in fewer complications and improved quality of life (QoL). These treatments should be compared to inform decisions on treatment for varicosities in the GSV. This is an update of a Cochrane Review first published in 2011.

Objectives

To assess the effects of endovenous laser ablation (EVLA), radiofrequency ablation (RFA), endovenous steam ablation (EVSA), ultrasound-guided foam sclerotherapy (UGFS), cyanoacrylate glue, mechanochemical ablation (MOCA) and high ligation and stripping (HL/S) for the treatment of varicosities of the great saphenous vein (GSV).

Search methods

The Cochrane Vascular Information Specialist searched the Cochrane Vascular Specialised Register, CENTRAL, MEDLINE, Embase, CINAHL, and AMED databases, and World Health Organization International Clinical Trials Registry Platform and ClinicalTrials.gov trials registers to 2 November 2020. We undertook reference checking to identify additional studies.

Selection criteria

We included randomised controlled trials (RCTs) treating participants for varicosities of the GSV using EVLA, RFA, EVSA, UGFS, cyanoacrylate glue, MOCA or HL/S. Key outcomes of interest are technical success, recurrence, complications and QoL.

Data collection and analysis

Two review authors independently selected trials, applied Cochrane's risk of bias tool, and extracted data. We calculated odds ratios (ORs) with 95% confidence intervals (CIs) and assessed the certainty of evidence using GRADE.

Main results

We identified 11 new RCTs for this update. Therefore, we included 24 RCTs with 5135 participants. Duration of follow-up ranged from five weeks to eight years. Five comparisons included single trials. For comparisons with more than one trial, we could only pool data for 'technical success' and 'recurrence' due to heterogeneity in outcome definitions and time points reported. All trials had some risk of bias concerns. Here we report the clinically most relevant comparisons.

EVLA versus RFA

Technical success was comparable up to five years (OR 0.98, 95% CI 0.41 to 2.38; 5 studies, 780 participants; moderate-certainty evidence); over five years, there was no evidence of a difference (OR 0.85, 95% CI 0.30 to 2.41; 1 study, 291 participants; low-certainty evidence). One study reported recurrence, showing no clear difference at three years (OR 1.53, 95% CI 0.78 to 2.99; 291 participants; low-certainty evidence), but a benefit for RFA may be seen at five years (OR 2.77, 95% CI 1.52 to 5.06; 291 participants; low-certainty evidence).

EVLA versus UGFS

Technical success may be better in EVLA participants up to five years (OR 6.13, 95% CI 0.98 to 38.27; 3 studies, 588 participants; low-certainty evidence), and over five years (OR 6.47, 95% CI 2.60 to 16.10; 3 studies, 534 participants; low-certainty evidence). There was no clear difference in recurrence up to three years and at five years (OR 0.68, 95% CI 0.20 to 2.36; 2 studies, 443 participants; and OR 1.08, 95% CI 0.40 to 2.87; 2 studies, 418 participants; very low-certainty evidence, respectively).

EVLA versus HL/S

Technical success may be better in EVLA participants up to five years (OR 2.31, 95% CI 1.27 to 4.23; 6 studies, 1051 participants; low-certainty evidence). No clear difference in technical success was seen at five years and beyond (OR 0.93, 95% CI 0.57 to 1.50; 5 studies, 874 participants; low-certainty evidence). Recurrence was comparable within three years and at 5 years (OR 0.78, 95% CI 0.47 to 1.29; 7 studies, 1459 participants; and OR 1.09, 95% CI 0.68 to 1.76; 7 studies, 1267 participants; moderate-certainty evidence, respectively).

RFA versus MOCA

There was no clear difference in technical success (OR 1.76, 95% CI 0.06 to 54.15; 3 studies, 435 participants; low-certainty evidence), or recurrence (OR 1.00, 95% CI 0.21 to 4.81; 3 studies, 389 participants; low-certainty evidence). Long-term data are not available.

RFA versus HL/S

No clear difference in technical success was detected up to five years (OR 5.71, 95% CI 0.64 to 50.81; 2 studies, 318 participants; low-certainty evidence); over five years, there was no evidence of a difference (OR 0.88, 95% CI 0.29 to 2.69; 1 study, 289 participants; low-certainty evidence). No clear difference in recurrence was detected up to three years (OR 0.93, 95% CI 0.58 to 1.51; 4 studies, 546 participants; moderate-certainty evidence); but a possible long-term benefit for RFA was seen (OR 0.41, 95% CI 0.22 to 0.75; 1 study, 289 participants; low-certainty evidence).

UGFS versus HL/S

Meta-analysis showed a possible benefit for HL/S compared with UGFS in technical success up to five years (OR 0.32, 95% CI 0.11 to 0.94; 4 studies, 954 participants; low-certainty evidence), and over five years (OR 0.09, 95% CI 0.03 to 0.30; 3 studies, 525 participants; moderate-certainty evidence). No clear difference was detected in recurrence up to three years (OR 1.81, 95% CI 0.87 to 3.77; 3 studies, 822 participants; low-certainty evidence), and after five years (OR 1.24, 95% CI 0.57 to 2.71; 3 studies, 639 participants; low-certainty evidence).

Complications were generally low for all interventions, but due to different definitions and time points, we were unable to draw conclusions (very-low certainty evidence). Similarly, most studies evaluated QoL but used different questionnaires at variable time points. Rates of QoL improvement were comparable between interventions at follow-up (moderate-certainty evidence).

Authors' conclusions

Our conclusions are limited due to the relatively small number of studies for each comparison and differences in outcome definitions and time points reported. Technical success was comparable between most modalities. EVLA may offer improved technical success compared to UGFS or HL/S. HL/S may have improved technical success compared to UGFS. No evidence of a difference was detected in recurrence, except for a possible long-term benefit for RFA compared to EVLA or HL/S. Studies which provide more evidence on the breadth of treatments are needed. Future trials should seek to standardise clinical terminology of outcome measures and the time points at which they are measured.

PLAIN LANGUAGE SUMMARY

Which procedures are best for treating varicose veins in the leg?

Key messages

We are uncertain about which treatments are best for varicose veins because we found only a small number of studies that compared the different types of treatment, and because studies differed in how they measured results.

- All currently available varicose vein treatments are similar in terms of whether the treatment fully destroys the vein, or stops blood from pooling in the legs, or both (technical success).

- We need studies that provide more evidence on all the available treatments.

What are varicose veins?

Varicose veins are bulging, twisty veins close to the skin's surface that usually occur in the legs. They are caused by chronic venous insufficiency, which is when your veins do not manage to help blood to flow back up to your heart efficiently, and blood pools in your legs. About one-third of adults are thought to have chronic venous insufficiency. Women are more likely than men to have varicose veins.

Varicose veins can be painful, itchy and unsightly, especially when standing and walking. Occasionally, they may result in skin changes or sores (ulcers) on the leg that take more than two weeks to heal.

How are varicose veins treated?

Varicose veins can be treated using a variety of procedures.

Traditionally, surgery was used to remove the main surface vein (called the 'great saphenous vein', which runs from the groin to the ankle) and any connected varicose veins through small openings in the leg. People having this procedure (known as 'high ligation and stripping') need to have a general anaesthetic to make them unconscious and stop them from feeling pain or moving while the surgery is done.

More recently, several treatments have emerged where the procedure is done inside the vein (endovenous), using a very fine tube. These treatments involve sealing the main vein in the thigh by deliberately damaging the vein wall. There are two main types of treatment:

- heat-based, where heat energy from lasers, radio waves or steam, is used to damage the vein wall;

- chemical-based, where chemicals (including foam or glue) are used to damage and consequently seal the vein.

These newer treatments are done using a local anaesthetic, meaning you do not feel pain in your legs during the procedure but you remain awake.

What did we want to find out?

We wanted to compare all the currently available treatments for varicose veins to find out which is best in terms of:

- short- and long-term technical success (whether the treatment fully destroys the vein, or stops blood from pooling in the legs, or both);

- stopping varicose veins from returning (recurrence);

- avoiding unwanted effects; and

- improving people's well-being.

What did we do?

We searched for studies that compared treatments for varicose veins in men and women of any age.

We compared and summarised the results of the studies and rated our confidence in the evidence, based on factors such as study methods and sizes.

What did we find?

We found 24 studies that involved 5135 people with mild to severe varicose veins. The studies followed people for between 5 weeks to 8 years after their treatment. The majority of the people in the studies were women.

The studies took place in private and public clinics and hospitals in 10 different countries: Austria, Denmark, Egypt, Finland, France, Germany, the Netherlands, Turkey, the United Kingdom and the USA.

The studies we found did not investigate all possible treatments for varicose veins, especially newer treatments.

Main results

Technical success

Most treatments are equally likely to fully destroy the vein or prevent blood pooling in the legs, or both. However:

- heat-based endovenous treatment with a laser may be more successful than traditional surgery;

- both heat-based laser treatment and surgery may be more successful than chemical-based endovenous treatment with a foam chemical.

Recurrence rates

Most treatments were similarly successful at stopping varicose veins from recurring.

Heat-based radio wave endovenous treatment may be better than both laser endovenous treatment and surgery at preventing varicose veins from recurring in the longer term.

Unwanted effects

Unwanted effects were generally low for all treatments. The studies reported very few serious unwanted effects requiring treatment, both in the short and long term.

Well-being

People in the studies said they had improved well-being regardless of the treatment they received.

What are the limitations of the evidence?

Our confidence in the evidence ranges from moderate to very low because of:

- concerns over how the studies were carried out (people in most of the studies were aware of which treatment they were getting, as were the researchers assessing treatment data, which could affect the studies' results);

- similar studies did not get the same results; and

- only a small number of studies contributed data to each result.

We were not able to reach firm conclusions about which of the treatments compared is best.

How up to date is this evidence?

This Cochrane Review updates our previous review. The evidence is current to November 2020

Summary of findings 1. Endovenous laser ablation (EVLA) compared to radiofrequency ablation (RFA) for great saphenous vein (GSV) incompetence

EVLA compared to RFA for GSV incompetence

Patient or population: people with GSV incompetence
Setting: hospital
Intervention: EVLA
Comparison: RFA

Outcomes	Anticipated absolute effects * (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with RFA	Risk with EVLA				
Technical success (< 5 years)	Study population 975 per 1000	974 per 1000 (940 to 989)	OR 0.98 (0.41 to 2.38)	780 (5 studies)	⊕⊕⊕⊖ **moderate** [a]	
Technical success (> 5 years)	Study population 952 per 1000	944 per 1000 (857 to 980)	OR 0.85 (0.30 to 2.41)	291 (1 study)	⊕⊕⊖⊖ **low** [b]	
Recurrence (< 5 years)	Study population 116 per 1000	167 per 1000 (93 to 281)	OR 1.53 (0.78 to 2.99)	291 (1 study)	⊕⊕⊖⊖ **low** [b]	
Long-term recurrence (> 5 years)	Study population 129 per 1000	291 per 1000 (184 to 429)	OR 2.77 (1.52 to 5.06)	291 (1 study)	⊕⊕⊖⊖ **low** [b]	
Complications (up to 8 years)	See comment				⊕⊖⊖⊖ **very low** [c]	Analysis was prevented as studies reported minor and major complications using different definitions and at varying time points. Results of individual studies were inconsistent with each other so we are not able to draw any conclusions.

QoL (up to 8 years)	See comment	⊕⊕⊖⊖ **moderate** [a]	The majority of studies for this comparison showed no difference in QoL scores between the two variables. Nordon 2011 showed no difference in improvement using AVVQ and EQ-5D at three months. There was no difference in AVVQ or SF-12 (in either the physical or mental component SF-12) at 6 months in Shepherd 2010. Rasmussen 2011 found no difference in SF-36 at 1 month or AVVQ at 3 years. Recovery 2009 reported improved global QoL scores in RFA at 7 and 14 days post-operation but comparable by 1 month. Syndor 2017 did not measure QoL.

* **The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: confidence interval; **EVLA:** endovenous laser ablation; **GSV:** great saphenous vein; **OR:** odds ratio; **QoL:** quality of life; **RFA:** radiofrequency ablation

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

[a]We downgraded by one level due to risk of bias concerns.
[b]We downgraded by two levels due to risk of bias concerns and possible imprecision.
[c]We downgraded by three levels due to risk of bias concerns, inconsistency, imprecision and possible publication bias.

Summary of findings 2. Endovenous laser ablation (EVLA) compared to ultrasound-guided foam sclerotherapy (UGFS) for great saphenous vein (GSV) incompetence

EVLA compared to UGFS for GSV incompetence

Patient or population: people with GSV incompetence
Setting: hospital
Intervention: EVLA
Comparison: UGFS

Outcomes	Anticipated absolute effects * (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with UGFS	Risk with EVLA				

Technical success (< 5 years)	Study population 802 per 1000	961 per 1000 (799 to 994)	OR 6.13 (0.98 to 38.27)	588 (3 studies)	⊕⊕⊖⊖ **low** [a]	
Technical success (> 5 years)	Study population 626 per 1000	915 per 1000 (813 to 964)	OR 6.47 (2.60 to 16.10)	534 (3 studies)	⊕⊕⊖⊖ **low** [a]	
Recurrence (< 5 years)	Study population 186 per 1000	134 per 1000 (44 to 350)	OR 0.68 (0.20 to 2.36)	443 (2 studies)	⊕⊖⊖⊖ **very low** [b]	
Long-term recurrence (> 5 years)	Study population 232 per 1000	246 per 1000	OR 1.08 (0.40 to 2.87)	418 (2 studies)	⊕⊖⊖⊖ **very low** [b]	
Complications (up to 8 years)	See comment				⊕⊖⊖⊖ **very low** [c]	All three studies reported on this outcome but using different definitions and at varying time points. Rasmussen 2011 reported more phlebitis and hyperpigmentation rates amongst the UGFS group. In Vernermo 2016, skin pigmentation was more common in the UGFS group but haematomas were seen more often after EVLA compared to UGFS at 1 month. Magna 2013 reported two cases of hyperpigmentation in EVLA participants compared to one case in UGFS at 3 months.
QoL (up to 8 years)	See comment				⊕⊕⊕⊖ **moderate** [d]	Magna 2013 reported no significant differences between EVLA and UGFS at 3 months and 1 year in CIVIQ2 and EQ-5D scores. In Rasmussen 2011, UGFS was deemed to be better for bodily pain and physical functioning in the SF-36 score initially. AVVSS showed no difference between comparisons at 1 month. Vernermo 2016 found no significant difference in median AVVSS between the treatment groups at 1 year

* **The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: confidence interval; **EVLA**: endovenous laser ablation; **GSV**: great saphenous vein; **OR:** odds ratio; **QoL:** quality of life; **UGFS**: ultrasound-guided foam sclerotherapy

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

[a]We downgraded by two levels due to risk of bias concerns and inconsistency.
[b]We downgraded by three levels due to risk of bias concerns, inconsistency and imprecision.
[c]We downgraded by three levels due to risk of bias concerns, inconsistency, imprecision and possible publication bias.
[d]We downgraded by one level due to risk of bias concerns.

Summary of findings 3. Endovenous laser ablation (EVLA) compared to SFJ ligation and stripping (HL/S) for great saphenous vein (GSV) incompetence

EVLA compared to HL/S for GSV incompetence

Patient or population: people with GSV incompetence
Setting: hospital
Intervention: EVLA
Comparison: HL/S (surgery)

Outcomes	Anticipated absolute effects * (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with HL/S (surgery)	Risk with EVLA				
Technical success (< 5 years)	Study population		OR 2.31 (1.27 to 4.23)	1051 (6 studies)	⊕⊕⊖⊖ **low** [a]	
	933 per 1000	970 per 1000 (947 to 983)				
Technical success (> 5 years)	Study population		OR 0.93 (0.57 to 1.50)	874 (5 studies)	⊕⊕⊖⊖ **low** [a]	
	917 per 1000	911 per 1000				

		(863 to 943)				
Recurrence (< 5 years)	Study population		OR 0.78 (0.47 to 1.29)	1459 (7 studies)	⊕⊕⊕⊖ **moderate** [b]	
	179 per 1000	146 per 1000 (93 to 220)				
Long-term recurrence (> 5 years)	Study population		OR 1.09 (0.68 to 1.76)	1267 (7 studies)	⊕⊕⊕⊖ **moderate** [b]	
	328 per 1000	347 per 1000 (249 to 462)				
Complications (up to 8 years)	See comment			-	⊕⊖⊖⊖ **very low** [c]	Analysis was prevented as studies reported minor and major complications using different definitions and at varying time points. Slightly higher rates of early haematomas and wound problems were possibly seen with HL/S (surgery); and EVLA may be associated with slightly more phlebitis.
QoL (up to 8 years)	See comment			-	⊕⊕⊕⊖ **moderate** [b]	Rates of improvement in QoL were comparable between both treatment groups in all studies.

* **The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: confidence interval; **EVLA**: endovenous laser ablation; **GSV**: great saphenous vein; **HL/S**; SFJ ligation and stripping; **OR:** odds ratio; **QoL:** quality of life; **UGFS**: ultrasound-guided foam sclerotherapy

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

[a]We downgraded by two levels due to risk of bias concerns and imprecision.
[b]We downgraded by one level due to risk of bias concerns.
[c]We downgraded by three levels due to risk of bias concerns, inconsistency, imprecision and possible publication bias.

Summary of findings 4. Radiofrequency ablation (RFA) compared to mechanochemical ablation (MOCA) for great saphenous vein incompetence

RFA compared to MOCA for GSV incompetence

Patient or population: people with GSV incompetence
Setting: hospital
Intervention: RFA
Comparison: MOCA

Outcomes	Anticipated absolute effects * (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with MOCA	Risk with RFA				
Technical success (< 5 years)	Study population		OR 1.76 (0.06 to 54.15)	435 (3 studies)	⊕⊕⊖⊖ **low** [a]	
	983 per 1000	990 per 1000 (776 to 1000)				
Technical success (> 5 years)	See comment		-	-	-	Data for this time point are not yet available.
Recurrence (< 5 years)	Study population		OR 1.00 (0.21 to 4.81)	389 (3 studies)	⊕⊕⊖⊖ **low** [a]	
	117 per 1000	117 per 1000 (27 to 390)				
Long-term recurrence (≥ 5 years)	See comment		-	-	-	Data for this time point are not yet available.
Complications (up to 1 year)	See comment		-	-	⊕⊖⊖⊖ **very low** [b]	Analysis was prevented as studies reported minor and major complications using different definitions and at varying time points, but rates were similar between treatment groups.
QoL (AVVQ, EQ-5D) (up to 1 year)	See comment		-	-	⊕⊕⊕⊖ **moderate** [c]	No differences detected between groups at any time point during the studies.

* **The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: confidence interval; **GSV**; great saphenous vein; **MOCA**: mechanochemical ablation; **OR:** odds ratio; **QoL:** quality of life; **RFA**: radiofrequency ablation

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

[a]We downgraded by two levels due to risk of bias concerns and inconsistency.
[b]We downgraded by three levels due to risk of bias concerns, inconsistency and possible publication bias.
[c]We downgraded by one level due to risk of bias concerns.

Summary of findings 5. Radiofrequency ablation (RFA) compared to SFJ ligation and stripping (HL/S) for great saphenous vein (GSV) incompetence

RFA compared to HL/S for GSV incompetence

Patient or population: people with GSV incompetence
Setting: hospital
Intervention: RFA
Comparison: HL/S (surgery)

Outcomes	Anticipated absolute effects * (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with HL/S (surgery)	Risk with RFA				
Technical success (< 5 years)	Study population		OR 5.71 (0.64 to 50.81)	318 (2 studies)	⊕⊕⊖⊖ **low** [a]	
	974 per 1000	995 per 1000 (960 to 999)				
Technical success (> 5 years)	Study population		OR 0.88 (0.29 to 2.69)	289 (1 study)	⊕⊕⊖⊖ **low** [b]	
	958 per 1000	952 per 1000 (868 to 984)				
Recurrence (< 5 years)	Study population		OR 0.93 (0.58 to 1.51)	546 (4 studies)	⊕⊕⊕⊖ **moderate** [c]	
	147 per 1000	138 per 1000				

		(91 to 206)				
Long-term recurrence (> 5 years)	Study population		OR 0.41 (0.22 to 0.75)	289 (1 study)	⊕⊕⊖⊖ **low** [b]	
	268 per 1000	130 per 1000 (74 to 215)				
Complications (up to 8 years)	See comment				⊕⊖⊖⊖ **very low** [d]	Analysis was prevented as studies reported minor and major complications using different definitions and at varying time points. Overall the number of complications was low, but surgery may be associated with slightly higher rates of wound problems, haematomas and saphenous nerve injuries and more phlebitis was seen after RFA.
QoL (up to 8 years)	See comment				⊕⊕⊕⊖ **moderate** [c]	None of the studies detected a difference between treatment arms by four months.

* **The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: confidence interval; **GSV**; great saphenous vein; **HL/S**; SFJ ligation and stripping; **OR:** odds ratio; **QoL:** quality of life; **RFA**: radiofrequency ablation

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
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[c]We downgraded by one level due to risk of bias concerns.
[d]We downgraded by three levels due to risk of bias concerns, inconsistency, imprecision and possible publication bias.

Summary of findings 6. Ultrasound-guided foam sclerotherapy (UGFS) compared to SFJ ligation and stripping (HL/S) for great saphenous vein (GSV) incompetence

UGFS compared to HL/S for GSV incompetence

Patient or population: people with GSV incompetence

Setting: hospital
Intervention: UGFS
Comparison: HL/S (surgery)

Outcomes	Anticipated absolute effects * (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with HL/S (surgery)	Risk with UGFS				
Technical success (< 5 years)	Study population		OR 0.32 (0.11 to 0.94)	954 (4 studies)	⊕⊕⊖⊖ **low** [a]	
	888 per 1000	718 per 1000 (467 to 882)				
Technical success (> 5 years)	Study population		OR 0.09 (0.03 to 0.30)	525 (3 studies)	⊕⊕⊕⊖ **moderate** [b]	
	929 per 1000	542 per 1000 (283 to 798)				
Recurrence (< 5 years)	Study population		OR 1.81 (0.87 to 3.77)	822 (3 studies)	⊕⊕⊖⊖ **low** [c]	
	168 per 1000	267 per 1000 (149 to 431)				
Long-term recurrence (≥ 5 years)	Study population		OR 1.24 (0.57 to 2.71)	639 (3 studies)	⊕⊕⊖⊖ **low** [c]	
	380 per 1000	432 per 1000 (259 to 624)				
Complications (up to 8 years)	See comment			639 (3 studies)	⊕⊖⊖⊖ **very low** [d]	Analysis was prevented as studies reported minor and major complications using different definitions and at varying time points.
QoL (up to 8 years)	See comment			930 (4 studies)	⊕⊕⊕⊖ **moderate** [b]	None of the five included studies showed evidence of a difference in QoL scores between the two treatment groups.

* **The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: confidence interval; **GSV**; great saphenous vein; **HL/S:** SFJ ligation and stripping; **OR:** odds ratio; **QoL:** quality of life; **UGFS**: ultrasound-guided foam sclerotherapy

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

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[a]We downgraded by two levels due to risk of bias concerns and inconsistency.
[b]We downgraded by one level due to risk of bias concerns.
[c]We downgraded by two levels due to risk of bias concerns and inconsistency.
[d]We downgraded by three levels due to risk of bias concerns, inconsistency and possible publication bias.

BACKGROUND

Varicose veins of the lower limbs are dilated, tortuous, superficial veins. They can be painful, itchy or unsightly, especially when standing and walking. Occasionally, they may result in skin changes or leg ulcers. Varicose veins have been previously treated with surgery to remove the veins, by stripping them to the level of the knee (high ligation and stripping (HL/S)). Newer, less invasive treatments seal the main leaking vein in the thigh by using heat, chemical irritants (sclerosants) or adhesives (glue). These techniques potentially result in less pain after the procedure, fewer complications, and a quicker return to work and normal activities with improved quality of life. They also avoid the need for a general anaesthetic. The results of these newer treatments need to be compared to high ligation and stripping (HL/S) and to one another.

Description of the condition

The great saphenous vein (GSV) and small saphenous vein (SSV) are the main components of the superficial veins of the leg. The GSV runs from the ankle to the saphenofemoral junction in the groin and is responsible for the majority of varicose veins. The normal venous system relies on a complex mechanism consisting of valves, muscle pumps and pressure changes to overcome the forces of gravity, positional changes and pressure changes within the thorax and abdomen. Disruption of the normal function of the deep or superficial venous system will result in retrograde flow, also known as venous incompetence. Venous incompetence is thought to occur through a number of mechanisms. The ascending valvular incompetence theory describes the failing of valves and the loss of antegrade flow (from the ankle to the heart), of blood from the high-pressured venous system, venous pooling and resulting venous hypertension (Corcos 1996; Corcos 2000; Trendelenburg 1890). There are other associated mechanisms at play, such as raised ankle venous pressure, inflammation and leakage of blood constituents into the surrounding tissue. These make up the vicious cycle of venous disease as inflammation leads to further venous disruption and failure of the venous mechanisms (Jones 2009; Labropoulos 2005; Pascarella 2005; Takase 2004).

The Clinical, Etiological, Anatomical and Pathophysiological (CEAP) classification for chronic venous disease is used to standardise its reporting. The clinical classes of the CEAP classification are shown in Table 1. The tool is validated in clinical practice and focuses primarily on clinical classification (Carpentier 2003).

The commonest manifestation of superficial venous incompetence (SVI) is palpable, tortuous, dilated vessels known as varicose veins. Longstanding incompetence, sometimes termed chronic venous insufficiency (CVI), is estimated to affect one third of the adult population (NICE 2013b), 60% to 70% of which is due to saphenofemoral, or GSV, valvular incompetence (Labropoulos 1994). Prevalence of CVI increases with age and risk factors including trauma, history of deep vein thrombosis (DVT), multiple pregnancies, obesity and occupations involving prolonged periods of standing. People may be asymptomatic or complain of mild symptoms such as aching, pain and poor cosmetic appearance. Rabe 2010 reported that in the Bonn Vein Study II 31.8% of people with GSV reflux and C2 disease progressed to more severe disease during 6.6 years of follow up but were not shown to progress to ulcers during the available follow-up.

Description of the intervention

The traditional treatment of GSV incompetence is by open surgery (Sarin 1992). This involves a small groin incision to perform flush ligation of the saphenofemoral junction (SFJ) and ligation of any tributaries. The GSV is then removed by a process called 'stripping' using a wire or flexible PIN-stripper. Phlebectomies (small stab incisions) can also then be performed with a vein hook (or through transilluminated powered phlebectomy) to remove any visible or preoperatively-marked varicosities of the truncal or non-saphenous veins within the calf or GSV branches within the thigh (Darwood 2008; Nesbitt 2014; Subramonia 2010). The exact role and impact of phlebectomies on the overall outcome for people with venous incompetence are important, but the treatment of choice per se is beyond the scope of this review.

SFJ ligation and stripping (HL/S) is usually performed as a day case procedure, usually under general anaesthesia, within an operating theatre setting. Post-operative recovery and return to work is usually between two and three weeks; however, in some cases, this may be prolonged up to six weeks (HELP-1 2011; Subramonia 2010). Overall complication rates following SFJ ligation and stripping are reported as between 17% to 20% (Critchley 1997; HELP-1 2011). Recognised complications include pain, dysaesthesia, paraesthesia, bruising, haematoma, wound infection, lymphatic leaks, venous thromboembolism (deep vein thrombosis (DVT) and pulmonary embolus (PE)) and damage to major veins, arteries and nerves (CLASS 2014; Critchley 1997; Subramonia 2010). The need for general anaesthesia or spinal anaesthesia also subjects individuals to further risk of complications (i.e. allergic reaction to anaesthetic agents, damage to teeth during intubation, post-operative nausea and vomiting).

Endovenous treatments

In the past two decades, endovenous procedures for treating SVI have emerged. These procedures rely on a catheter or device inserted into the vein under ultrasound guidance. They are minimally invasive, utilise local anaesthesia and do not require surgical incisions or exposures. These procedures potentially offer more acceptable treatments for GSV varicosities if outcomes are equivalent to or better than conventional surgery. These techniques can be divided into thermal tumescent treatments and non-thermal non-tumescent treatments.

Thermal treatments rely on the use of heat energy to damage the vein wall and lead to occlusion and fibrosis. Non-thermal interventions predominantly rely on the use of a chemical sclerosant or, more recently, a glue that causes inflammatory and chemical damage to the vein wall, which can also be used in combination with mechanical agitation and maceration of the intima.

Thermal tumescent interventions

Endovenous thermal ablation is the use of heat to close the vein. The devices available are endovenous laser ablation (EVLA), radiofrequency ablation (RFA) or steam ablation (EVSA). There are a number of manufacturers, designs and differences within each of these categories. However, for clarity, we have adopted umbrella terminology in this review.

EVLA, RFA and EVSA are performed using tumescent anaesthesia, where local anaesthetic is injected under ultrasound guidance

along the length of the vein. The benefit of this approach is four-fold: (1) analgesia (pain relief): provided during and after the procedure; (2) compression: the perivenous dilute anaesthetic solution compresses the vein wall onto the endovenous catheter due to the increased hydrostatic pressure within the saphenous sheath; (3) hydrodissection: simultaneously, perivenous nervous structures are moved away from heat within the vein by means of hydrodissection, to protect adjacent structures such as nerves; and (4) heat sink: as the fluid is typically cool, it acts as a heat sink, reducing the risk of neurological sequelae and burns (Joh 2014).

Endovenous laser ablation (EVLA) and radiofrequency ablation (RFA) are established interventions with an improved complication profile and reduced recovery time compared to open surgery (CLASS 2014; HELP-1 2011; LAST 2014; Subramonia 2010). In addition, they do not require general anaesthesia. In 2013, the National Institute for Health and Care Excellence (NICE) recommended the use of endovenous ablation as the first line treatment intervention for duplex ultrasound-confirmed varicose veins and truncal incompetence (NICE 2013a).

Various types of laser fibres, wavelengths and radial tips are available for EVLA. For the purposes of this clinically-orientated review, we have grouped these under one category, accepting that there may be nuanced advantages and disadvantages for each laser type. In EVLA, the GSV is cannulated under ultrasound guidance at the most distal point of reflux with an optical laser fibre. This is then advanced to just below the SFJ. The proximity to the junction varies by manufacturer but is typically 2 cm. Tumescent anaesthesia is then infiltrated, surrounding the EVLA catheter under duplex ultrasound (DUS) guidance. Ablation of the vessel occurs as the laser is activated and then slowly withdrawn retrograde (the rate varies depending on manufacturer recommendation). The operator simultaneously compresses the vein, delivering between 60 and 80 J/cm (Darwood 2008). EVLA can be performed using sedation, local or general anaesthesia in addition to tumescence. Complications include phlebitis, pain, bruising, burns and sensory disturbances. Min 2003 showed 93% duplex ultrasound-proven occlusion at two years following EVLA for GSV varicosities, with all recurrences occurring within the first nine months.

RFA is performed under a similar principle to EVLA; however, luminal occlusion is induced through heat from radiofrequency energy controlled by a thermocouple. As in EVLA, the GSV is cannulated distally and the catheter electrode is positioned just below the SFJ then surrounded with tumescent anaesthesia. The catheter is then withdrawn by segments along the length of the vein whilst under compression. Normal activity following the procedure is encouraged. Complications such as phlebitis, sensory disturbance and burns are uncommon and have reduced since the introduction of tumescence. Arteriovenous fistulation is a recognised but rare complication (< 0.15%) (Rudarakanchana 2012; Weiss 2019).

Endovenous steam ablation (EVSA) works in a similar way to EVLA and RFA, where a catheter is advanced under ultrasound guidance into the target vein. This then allows 'superheated' steam (pressurised) to be pumped into the vein once tumescent has been infiltrated. The result is venous occlusion through thermal damage to the vein wall. Histological examination post intervention shows vein wall fibrosis and inflammation, destruction of endothelium, alterations of elastic and collagen fibres and reduction of the lumen (LAST 2014). Proposed benefits of steam sclerosis include use of lower temperatures (120 ºC) compared to EVLA (temperatures of up to 600 ºC reported), with fewer thermal injuries and reduced post-operative pain (LAST 2014). EVSA is reported to not produce potentially harmful exogenous substances and some data on cost-effectiveness exist (LAST 2014). The catheter in EVSA is also more flexible than those used in RFA and EVLA, which enables access to more tortuous vessels and perforator branches (Van den Bos 2011). Occlusion rates are reported to range from 85 to 100% (Woźniak 2015).

Non-thermal, non-tumescent interventions (NTNT)

The initial technique of non-thermal interventions for GSV incompetence was that of ultrasound-guided foam sclerotherapy (UGFS). UGFS is the recommended second line technique in the United Kingdom (UK) for the treatment of varicose veins as per NICE guidance (NICE 2013a). Under ultrasound guidance, the vein is cannulated and a foam sclerosant is injected, causing inflammation of the endothelial and subendothelial layers of the wall and hence fibrosis and obliteration of the vein. Various types of foam are available. However, initial success rates have been reported as low and repeated treatments are frequently required (Devereux 2014; Proebstle 2015). The procedure may be associated with poor post-procedural cosmesis, with skin staining and 'lumpiness' reported. There is also a risk of visual disturbances and very low risk of stroke (NICE 2013b). People are also required to wear compression stockings following the procedure. The major advantage of non-thermal interventions over thermal interventions is that they can be performed in outpatient departments and without any systemic analgesia. In addition, in those with lipodermatosclerosis or ulceration, UGFS can be useful as the infiltration of perivenous tumescence is not required.

More recently, there has been increasing use of other non-thermal treatments for GSV insufficiency. These also do not require the use of tumescence (which can be painful and itself cause complications). Additionally, they do not subject individuals to the risk of thermal injury and are therefore known as non-tumescent non-thermal (NTNT) techniques (Leung 2016; Shepherd 2010).

Mechanochemical ablation (MOCA) is a NTNT technique which obliterates the venous lumen through the use of a rotating catheter tip, causing vasospasm and mechanical damage to endothelial cells. Further chemical injury is induced through the concomitant injection of a liquid sclerosant (Leung 2016; Tang 2017). The procedure only requires local anaesthesia and individuals are encouraged to mobilise immediately following the procedure. MOCA is reported to have lower rates of post-procedural pain and enhanced recovery times in comparison with other endovenous techniques (Leung 2016). Tang 2017 reported a complication rate of 4.3% (which predominantly consisted of superficial self-resolving phlebitis), and no major complications were reported. Occlusion rates between 94% to 97% are reported (Tang 2017).

Cyanoacrylate embolisation consists of the injection of cyanoacrylate glue within the vein via a hand-held delivery gun. Under ultrasound guidance, the incompetent GSV is cannulated distally and a catheter inserted to 5 cm below the SFJ. Cyanoacrylate is then injected with alternating compression and pullback every few minutes for the length of the vein. Cyanoacrylate achieves immediate occlusion by chemically bonding the opposing vein walls together (Morrison 2015). The glue causes fibrotic degradation of the vein via a granulomatous foreign body and

inflammatory vein wall reaction (Proebstle 2015). Tumescent anaesthesia is not required and manufacturers state that there no need for people to wear compression stockings post intervention. As the procedure is intraluminal, there is reduced risk of damage to perivenous nervous structures. Side effects predominantly consist of self-limiting phlebitic reactions and wound infections (Gibson 2017). However, thrombus extension into the deep venous system has been reported with the consequent risk of migration to pulmonary vasculature (Proebstle 2015).

How the intervention might work

All the interventions aim to occlude the incompetent great saphenous vein (GSV). The endovenous interventions outlined above all broadly rely on endoluminal venous damage by means of: thermal energy (EVLA/RFA/EVSA) (Goode 2010; Khilnani 2010; Van den Bos 2011); chemical irritation (UGFS/MOCA) (Mueller 2013; Tessari 2001; Van Eekeren 2014); or adhesion (cyanoacrylate) (Lane 2017).

The outcome is venous endothelial damage which results in venous inflammation and subsequent sclerosis and scarring as the vein heals following the endothelial obliteration. This leads to venous occlusion. All methods described require the application of DUS to enable cannulation of the GSV at the lowest point of reflux, and each method is suitable for the majority of axial venous incompetence.

There has been a large increase in the uptake of these methods and their application in routine practice continues in both the NHS and private sector. The advent of the 2013 NICE guidelines has facilitated a paradigm shift in the management of GSV incompetence (Coughlin 2015; NICE 2013a). Surgery by means of open ligation and stripping is still performed but it is no longer the gold standard intervention. Surgical treatment aims to physically disconnect the GSV from its junction and then remove the length of GSV by stripping. This is an effective treatment but carries a greater morbidity in terms of the need for general anaesthesia, post-operative complications and a longer recovery.

Why it is important to do this review

This is an update of a Cochrane Review first published in 2011, and previously updated in 2014 (Nesbitt 2011; Nesbitt 2014). Since the previous version of this Cochrane Review was published, new UK NICE guidance (NICE 2013a) and subsequent European guidance on the management of chronic venous incompetence (Wittens 2015) have been published. Furthermore, the development of newer endovenous devices has resulted in a wider range of technologies that can be used to treat this disease. As outlined above, these have varying levels of supporting evidence, and they differ in their underlying application and treatment methods. This has sparked an increase in venous literature comparing existing treatments with newer interventions and reporting on long-term outcomes. This Cochrane Review considers the full breadth of treatment options for GSV incompetence and compares these options. Therefore, this review has a wider scope compared to previous versions of this review (Nesbitt 2011; Nesbitt 2014). We present the current evidence to provide the venous practitioner and wider healthcare community an up-to-date resource to enable accurate, evidence-based decision-making that can be tailored to individuals. The review is aimed at highlighting the strengths and weaknesses within the entire field of GSV interventions (open surgery, endovenous thermal and endovenous non-thermal techniques) in order to answer key questions of day-to-day venous practice: which method is currently the most technically effective and which method offers long-term benefits and lowest recurrence rates.

OBJECTIVES

To assess the effects of endovenous laser ablation (EVLA), radiofrequency ablation (RFA), endovenous steam ablation (EVSA), ultrasound-guided foam sclerotherapy (UGFS), cyanoacrylate glue, mechanochemical ablation (MOCA) and high ligation and stripping (HL/S) for the treatment of varicosities of the great saphenous vein (GSV).

METHODS

Criteria for considering studies for this review

Types of studies

We included randomised control trials (RCTs) which compared interventions for treating varicosities of the great saphenous vein (GSV). We excluded studies which:

- included participants who underwent a combination of interventions (for instance, endovenous laser ablation (EVLA) or radiofrequency ablation (RFA) with high ligation and stripping (HL/S));
- treated all other axes of superficial venous incompetence such as small saphenous vein (SSV), perforating veins or varicosities of tributaries, anterior thigh or accessory GSV veins (AAGSV);
- treated telangiectasias or thread veins;
- did not provide data (subgroup analysis) for participants who had both GSV and SSV varicosities treated;
- included recurrent treatment (i.e. participants underwent previous treatment for GSV varicosities);
- included participants who received simultaneous treatment of bilateral GSV insufficiency with different interventions (e.g. one limb treated with EVLA and the other limb with ultrasound-guided foam sclerotherapy (UGFS);
- involved CHIVA and ASVAL, as these are axial-preserving techniques.

Types of participants

We included men and women of any age, with duplex ultrasound-proven varicosities of the great saphenous system, who were suitable to undergo any of the treatment interventions. The focus of this review was on the management of C2 to C4 grade varicose veins. People with varicose veins with healed leg ulcer (C5) or active leg ulcer (C6) were excluded from this Cochrane Review. Endovenous thermal ablation for treating venous leg ulcers is evaluated in a separate Cochrane Review (Samuel 2013).

Types of interventions

We included these interventions:

- endovenous laser ablation (EVLA);
- radiofrequency ablation (RFA);
- endovenous steam ablation (EVSA);
- ultrasound-guided foam sclerotherapy (UGFS);

- cyanoacrylate glue;
- mechanochemical ablation (MOCA);
- SFJ ligation and stripping (surgery) (HL/S).

We planned to include these comparisons:

- endovenous laser ablation versus radiofrequency ablation;
- endovenous laser ablation versus endovenous steam ablation;
- endovenous laser ablation versus ultrasound-guided foam sclerotherapy;
- endovenous laser ablation versus cyanoacrylate glue;
- endovenous laser ablation versus mechanochemical ablation;
- endovenous laser ablation versus SFJ ligation and stripping;
- radiofrequency ablation versus endovenous steam ablation;
- radiofrequency ablation versus ultrasound-guided foam sclerotherapy;
- radiofrequency ablation versus cyanoacrylate glue;
- radiofrequency ablation versus mechanochemical ablation;
- radiofrequency ablation versus SFJ ligation and stripping;
- endovenous steam ablation versus ultrasound-guided foam sclerotherapy;
- endovenous steam ablation versus cyanoacrylate glue;
- endovenous steam ablation versus mechanochemical ablation;
- endovenous steam ablation versus SFJ ligation and stripping;
- ultrasound-guided foam sclerotherapy versus cyanoacrylate glue;
- ultrasound-guided foam sclerotherapy versus mechanochemical ablation;
- ultrasound-guided foam sclerotherapy versus SFJ ligation and stripping;
- cyanoacrylate glue versus mechanochemical ablation;
- cyanoacrylate glue versus SFJ ligation and stripping;
- mechanochemical ablation versus SFJ ligation and stripping.

Types of outcome measures

Primary outcomes

- Early technical success: defined as complete anatomical obliteration, or absence of reflux, within the GSV at around six weeks, on duplex ultrasound (DUS) (standard criterion of one second of reflux was used)
- Long-term technical success: defined as complete anatomical obliteration, or absence of reflux, within the GSV on DUS at five years or more

Secondary outcomes

- Recurrence: clinical definition as reported by the clinician or participant at least one year following intervention. We expanded this outcome to include the term recanalisation. We have outlined the definition where reported by the included studies.
- Post-operative complications within three months (early) and beyond three months (late)
  - Minor complications are defined as those not requiring intervention, such as wound or thigh haematoma, saphenous nerve injury, thermal injury, bruising and phlebitis.
  - Major complications are defined as those requiring intervention, such as venous thromboembolism (VTE), respiratory distress and wound complications.
- Quality of life (QoL): measured by generic QoL scores pre- and post-intervention (e.g. Aberdeen Varicose Vein Symptom Severity score (AVVSS, also referred to as the Aberdeen Varicose Vein Questionnaire, AVVQ), Short Form 36 (SF-36))
- Pain: participant-reported pain post-operatively. This could be reported via visual analogue scales or number of analgesic tablets taken.
- Venous Clinical Severity Score (VCSS) pre- and post-intervention
- Length of procedure
- Hospital stay: whether the intervention was performed as a day case procedure or required an inpatient admission
- Return to normal activities or work (days)

Search methods for identification of studies

Electronic searches

The Cochrane Vascular Information Specialist conducted systematic searches of the following databases for randomised controlled trials and controlled clinical trials without language, publication year or publication status restrictions.

- Cochrane Vascular Specialised Register via the Cochrane Register of Studies (CRS-Web searched on 2 November 2020).
- Cochrane Central Register of Controlled Trials (CENTRAL) Cochrane Register of Studies Online (CRSO 2020, Issue 10).
- MEDLINE (Ovid MEDLINE Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE Daily and Ovid MEDLINE) (searched from 1 January 2017 to 2 November 2020).
- Embase Ovid (searched from 1 January 2017 to 2 November 2020).
- CINAHL Ebsco (searched from 1 January 2017 to 2 November 2020).
- AMED Ovid (searched from 1 January 2017 to 2 November 2020).

The Information Specialist modelled search strategies for other databases on the search strategy designed for CENTRAL. Where appropriate, they were combined with adaptations of the highly sensitive search strategy designed by the Cochrane Collaboration for identifying randomised controlled trials and controlled clinical trials (as described in the *Cochrane Handbook for Systematic Reviews of Interventions* Chapter 6, Lefebvre 2011). Search strategies for major databases are provided in Appendix 1 and Appendix 2.

The Information Specialist searched these trials registries on 2 November 2020:

- World Health Organization International Clinical Trials Registry Platform (who.int/trialsearch);
- ClinicalTrials.gov (clinicaltrials.gov).

Searching other resources

We cross-checked reference lists from relevant RCTs and meta-analyses to ensure the inclusion of all appropriate studies.

Data collection and analysis

Selection of studies

Two review authors (JW and SN) independently screened the trials identified by the literature search for eligibility. We resolved disagreements by consulting a third review author (GS).

Data extraction and management

Two review authors (JW and SN) independently extracted data. A third review author (CN) then cross-checked data extraction.

We extracted the following data from the included RCTs.

- Methods: aim of study, study design, unit of allocation, start and end date, duration, country, intention-to-treat analysis, ethical approval.
- Participants: setting, consent, number of participants randomised, number of participants analysed, exclusions post-randomisation, loss to follow-up, age (median), sex, co-morbidities, number of bilateral limbs, inclusion and exclusion criteria.
- Interventions: treatment, control, duration, timing, delivery, providers.
- Outcomes: primary and secondary outcomes, time points measured and recorded, outcome definition, person measuring, unit of measurement, power.
- Other: funding, conflicts of interest.

Assessment of risk of bias in included studies

Two review authors (JW and SN) independently assessed the included studies using Cochrane's risk of bias tool (Higgins 2011). This tool assesses bias in seven different domains (random sequence generation, allocation concealment (selection bias), performance bias, detection bias, attrition bias, reporting bias and other bias), with each domain being assessed as being at high, low or unclear risk of bias, depending on each review author's judgement. We resolved any disagreements through discussion with a third review author (GS).

Measures of treatment effect

We used odds ratios (OR) with 95% confidence intervals (CI) as the measure of effect for each of the dichotomous outcomes. When data were available, we planned to used mean difference (MD) and standard deviation (SD) to report outcomes with continuous scales of measurement. We also planned to attempt to standardise and combine data where different studies used different scales (i.e. using standardised mean difference (SMD) and SD). We carried out analyses at different time points, as reported by the trials. We based our calculations on an intention-to-treat approach.

Unit of analysis issues

We intended to use the participant as the unit of analysis. Where studies used 'legs or limbs' as their unit of analysis, we contacted study authors to clarify the number of participants. If we were unable to obtain this information, we used 'legs/limbs' as the unit of analysis for technical success, recurrence and VCSS. QoL was reported using a variety of QoL assessment tools.

Dealing with missing data

We contacted study authors to request missing data or answer queries where required.

Assessment of heterogeneity

We noted and explored heterogeneity in the data, using previously identified characteristics of the studies, particularly assessments of risk of bias. The I^2 statistic was used to determine heterogeneity. We considered I^2 values greater than 50% to indicate the possible presence of heterogeneity, as in the previous version of this review (Nesbitt 2014), and as suggested by the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011).

Assessment of reporting biases

We planned to construct funnel plots to evaluate reporting bias, for meta-analyses including 10 or more studies (Higgins 2011).

Data synthesis

We calculated a summary statistic for each outcome (where there were sufficient data), using Review Manager 5 (Review Manager 2014). We used a fixed-effect model unless heterogeneity was detected (I^2 values greater than 50%), in which case, we planned to use a random-effects model.

Subgroup analysis and investigation of heterogeneity

We planned to undertake subgroup analyses to examine the stability of the results in relation to a number of factors, including participant type. However, due to the lack of outcome data reported by categories of interest, we did not perform subgroup analysis at this time.

Sensitivity analysis

We planned to exclude from meta-analysis those studies deemed to have a high risk of bias in four or more bias domains.

Summary of findings and assessment of the certainty of the evidence

We created summary of findings (SOF) tables using the GRADEpro Guideline Development Tool to present the main findings of the review for the time point at which the most relevant data were available from the included studies (Atkins 2004; GRADEpro GDT). The population consisted of people with varicosities of the great saphenous vein (GSV) system. We created one SOF table for comparisons of most clinical relevance and which included data from more than one study. We included in our SOF tables the main outcomes listed under Types of outcome measures that we considered essential for decision-making; namely, technical success (under and over five years), recurrence (under and over five years), complications, and quality of life. We evaluated the certainty of the evidence using the GRADE approach (Guyatt 2008). We assigned one of four levels of certainty: high, moderate, low or very low, based on overall risk of bias, directness of evidence, inconsistency of results, precision of estimates, and risk of publication bias, as previously described (Higgins 2011).

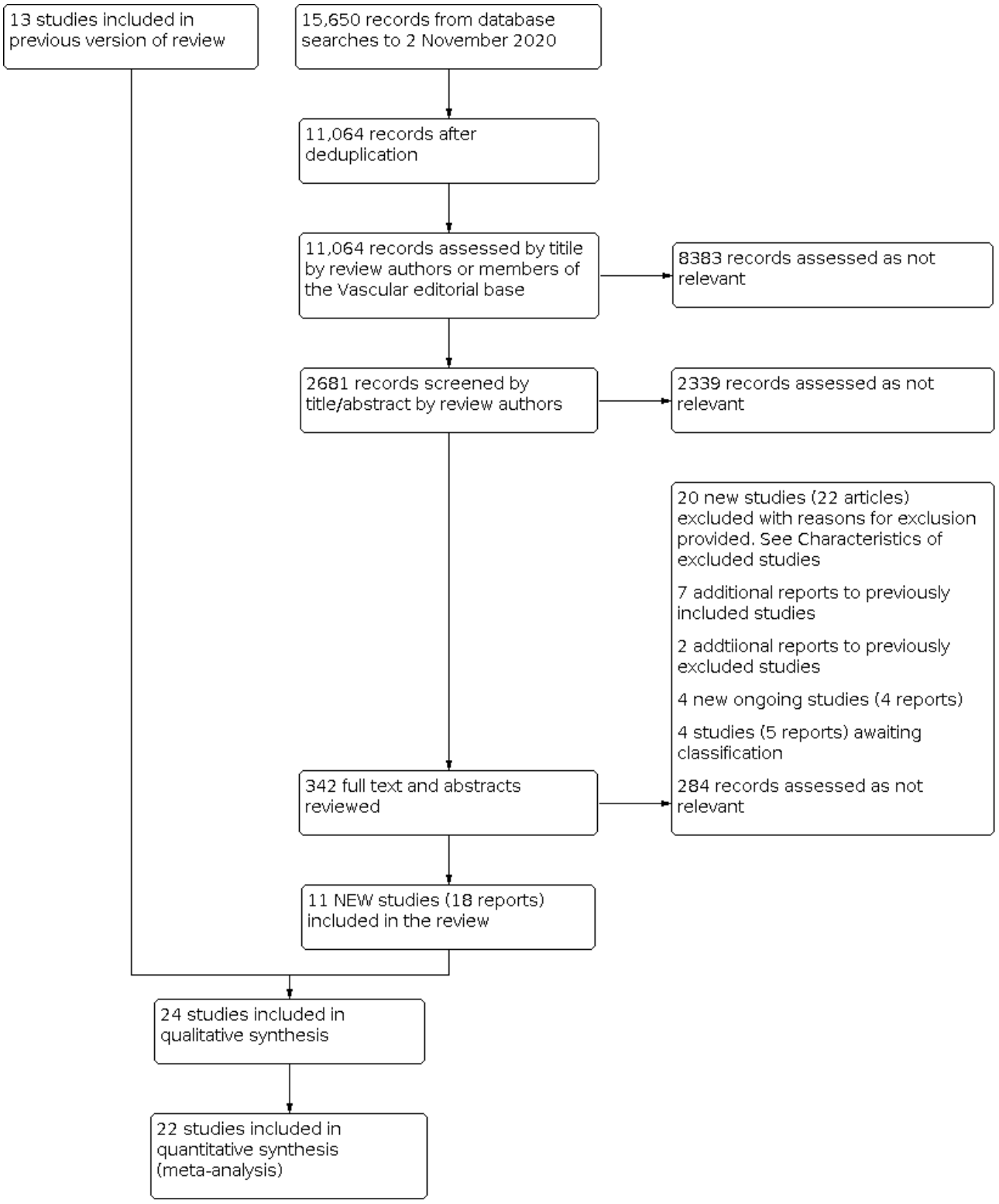
RESULTS

Description of studies

Results of the search

See Figure 1.

Figure 1. Study flow diagram



Included studies

We included a total of 24 studies in this review. This includes 11 new studies (18 reports) (Calik 2019; Lane 2017; LAST 2014; MARADONA 2019; Morrison 2015; Nordon 2011; Recovery 2009; Shepherd 2010; Syndor 2017; Vähäaho 2019; Vernermo 2016), in addition to the 13 from the previous version of the review (Darwood 2008; EVOLVeS 2003; Flessenkämper 2013; FOAM 2010; Helmy ElKaffas 2011; HELP-1 2011; Magna 2013; Pronk 2010; Rasmussen 2007; Rasmussen 2011; Rautio 2002; RELACS 2012; Subramonia 2010). We also included additional reports of the long-term follow-

up (greater than five years) for this update for seven studies (Flessenkämper 2013; FOAM 2010; HELP-1 2011; Magna 2013; Pronk 2010; Rasmussen 2011; RELACS 2012). See the Characteristics of included studies tables.

All studies were RCTs in single, double and multi-centre settings. Trials were conducted in a variety of private and public clinics and hospitals in countries including Turkey, Egypt, UK, USA, Finland, Germany, Denmark, Netherlands, Austria and France. The unit of analysis was considered to be the 'participants' in the majority of studies, with six studies reporting 'limbs' or 'legs' as the unit of analysis (Darwood 2008; EVOLVeS 2003; LAST 2014; Magna 2013; Pronk 2010; Rasmussen 2011). Calik 2019 involved a small number of bilaterally treated participants and refers to 'procedures' as their unit of analysis.

The studies included in this review randomised a total of 5135 participants and analysed 4422. Sample sizes in the studies ranged from 33 (Rautio 2002), to 500 participants (Rasmussen 2011); see sample study size in Table 2. In keeping with the epidemiology of venous insufficiency, a female predominance of participants was seen. Participants analysed ranged in age from 18 (Rasmussen 2011), to 86 years old (Syndor 2017). The age and sex of study participants for all trials is given in Table 3.

Five studies compared endovenous laser ablation (EVLA) to radiofrequency ablation (RFA) (Nordon 2011; Rasmussen 2011; Recovery 2009; Shepherd 2010; Syndor 2017). Only LAST 2014 compared EVLA with endovenous steam ablation (EVSA). Three studies compared EVLA with ultrasound-guided foam sclerotherapy (UGFS) (Magna 2013; Rasmussen 2011; Vernermo 2016). Calik 2019 was the only study to compare EVLA to cyanoacrylate glue. Only one study compared endovenous laser ablation (EVLA) to mechanochemical ablation (MOCA) (Vähäaho 2019). Nine studies compared EVLA to SFJ ligation and stripping (HL/S; surgery) (Darwood 2008; Flessenkämper 2013; HELP-1 2011; Magna 2013; Pronk 2010; Rasmussen 2007; Rasmussen 2011; RELACS 2012; Vernermo 2016). The types of laser used in these trials can be found in Table 4. Rasmussen 2011 solely compared RFA with UGFS. Morrison 2015 was the only trial to compare RFA with cyanoacrylate glue. Three studies compared RFA with MOCA (Lane 2017; MARADONA 2019; Vähäaho 2019). Five studies compared RFA with SFJ ligation and stripping (EVOLVeS 2003; Helmy ElKaffas 2011; Rasmussen 2011; Rautio 2002; Subramonia 2010). Ultrasound-guided foam sclerotherapy was compared with SFJ ligation and stripping in four studies (FOAM 2010; Magna 2013; Rasmussen 2011; Vernermo 2016).

Four studies compared multiple interventions. Magna 2013 and Vernermo 2016 analysed endovenous laser ablation, ultrasound-guided foam sclerotherapy and SFJ ligation and stripping against each other. Rasmussen 2011 also analysed these, with the addition of radiofrequency ablation (RFA). Vähäaho 2019 compared EVLA, RFA and MOCA, but it was only powered to compare MOCA against thermal ablation. Hence, we have not included their outcomes for RFA or EVLA within our comparison of these two interventions. Flessenkämper 2013 included a comparison arm which was not included within the scope of this study (EVLA plus high ligation); therefore, we did not include these participants.

We identified no published RCTs which met the inclusion criteria for the following comparisons.

- Radiofrequency ablation versus endovenous steam ablation.
- Endovenous steam ablation versus ultrasound-guided foam sclerotherapy.
- Endovenous steam ablation versus cyanoacrylate glue.
- Endovenous steam ablation versus mechanochemical ablation.
- Endovenous steam ablation versus SFJ ligation and stripping.
- Ultrasound-guided foam sclerotherapy versus cyanoacrylate glue.
- Ultrasound-guided foam sclerotherapy versus mechanochemical ablation.
- Cyanoacrylate glue versus mechanochemical ablation.
- Cyanoacrylate glue versus SFJ ligation and stripping.
- Mechanochemical ablation versus SFJ ligation and stripping.

The duration of follow-up for included trials ranged from five weeks (Subramonia 2010), to eight years (FOAM 2010). The outcome measures for each of the included trials can be found in Table 5.

Excluded studies

We excluded 20 new studies for this update (Basela 2011; Campos 2015; CLASS 2014; De Oliveira 2018; Desai 2009; dos Santos 2020; Eroglu 2018; Honek 2019; Jindal 2018; Karathanos 2019; Kikuchi 2009; Leon 2018; Leung 2019; Mendes 2016; Mozafar 2014; Oster 2018; Ovali 2019; Shadid 2015; Sincos 2018; Tawfik 2020). Due to the wider scope of this update, we included two studies which were previously excluded (Recovery 2009; Shepherd 2010).

The total number of excluded studies is 33 (Basela 2011; Campos 2015; Chant 1972; Christenson 2010; CLASS 2014; Compagna 2010; De Medeiros 2006; De Oliveira 2018; Desai 2009; Disselhoff 2008; dos Santos 2020; Einarsson 1993; Eroglu 2018; Figueiredo 2009; Honek 2019; Jindal 2018; Kalodiki 2012; Karathanos 2019; Kikuchi 2009; Lattimer 2012; Leon 2018; Leung 2019; Lin 2007; Mendes 2016; Mozafar 2014; Oster 2018; Ouvry 2008; Ovali 2019; Shadid 2015; Sincos 2018; Stotter 2005; Tawfik 2020; Wright 2006). See Characteristics of excluded studies table.

A common reason for exclusion was the combination of GSV and small saphenous vein (SSV) participants within the context of a trial. This was the case for CLASS 2014, Eroglu 2018, Figueiredo 2009, Sincos 2018 and Wright 2006. We were unable to obtain GSV data to allow meta-analysis where applicable. Some studies included techniques not covered within the scope of this review as they are novel or hybrid techniques. These included cryostripping (Disselhoff 2008; Stotter 2005), ligation and axial ablation by foam or EVLA (Compagna 2010; De Medeiros 2006; Kalodiki 2012), RFA plus UGFS (Leon 2018), and ligation of the SFJ only (Mozafar 2014). dos Santos 2020 compared UGFS with UGFS plus tumescence. Honek 2019 compared different types of laser generator in EVLA. Tawfik 2020 performed additional UGFS to EVLA and/or ablated small or accessory veins and/or used foam injections for severely tortuous anterior saphenous vein and superficial varicosities. Lattimer 2012 combined EVLA with phlebectomies versus UGFS. Three studies were excluded as the techniques included liquid sclerotherapy (Chant 1972; Einarsson 1993; Ouvry 2008). Three studies were found not to be randomised controlled trials and therefore were not included (Basela 2011; Ovali 2019; Shadid 2015). Three studies were found to offer simultaneous treatment to both limbs and therefore were excluded (Christenson 2010; Jindal 2018; Mendes 2016). Campos 2015, De Oliveira 2018, and Leung 2019

were excluded due to the inclusion of participants with CEAP C5 or C6 disease, or both. Karathanos 2019 and Oster 2018 included participants with CEAP class C2 to C6. Two studies were conference abstracts only with no data available after contacting authors (Desai 2009; Kikuchi 2009). One study was found to be in a language besides English and despite translation, no meaningful data could be extracted (Lin 2007).

Ongoing studies

We identified four new ongoing studies for this update (Belramman 2018; Cho 2020; NCT04526626; NCT04534244). See Characteristics of ongoing studies.

Studies awaiting classification

We identified four studies from a top-up search and will incorporate these into the next version of this review (Belramman 2020; Morrison 2020; Rai 2019; Vähäaho 2021). See Characteristics of studies awaiting classification.

Risk of bias in included studies

Risk of bias within each of the included studies is discussed in the Characteristics of included studies section and illustrated by Figure 2 and Figure 3. In summary, there was a significant risk of bias in the majority of included studies that limited our certainty in the evidence. The greatest areas of weakness included the lack of both study personnel and participant blinding that may have introduced observer and performance bias. It is accepted, however, that a number of these interventions differ significantly in the way in which they are performed. It would be impossible to blind a participant to a general anaesthesia open surgical operation compared to a local anaesthesia endovenous procedure. However, some of these difficulties could be mitigated by study personnel blinding.

Figure 2. Methodological quality graph: review authors' judgements about each methodological quality item presented as percentages across all included studies

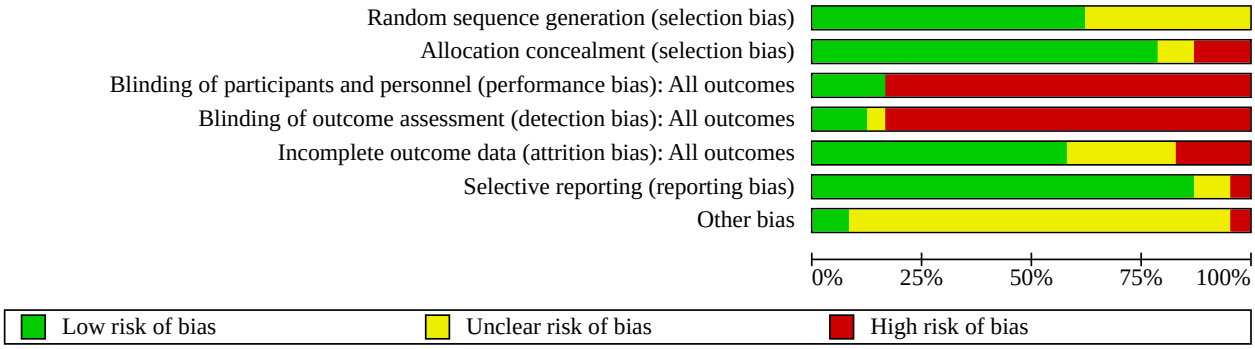


Figure 3. Methodological quality summary: review authors' judgements about methodological quality for each domain for each included study

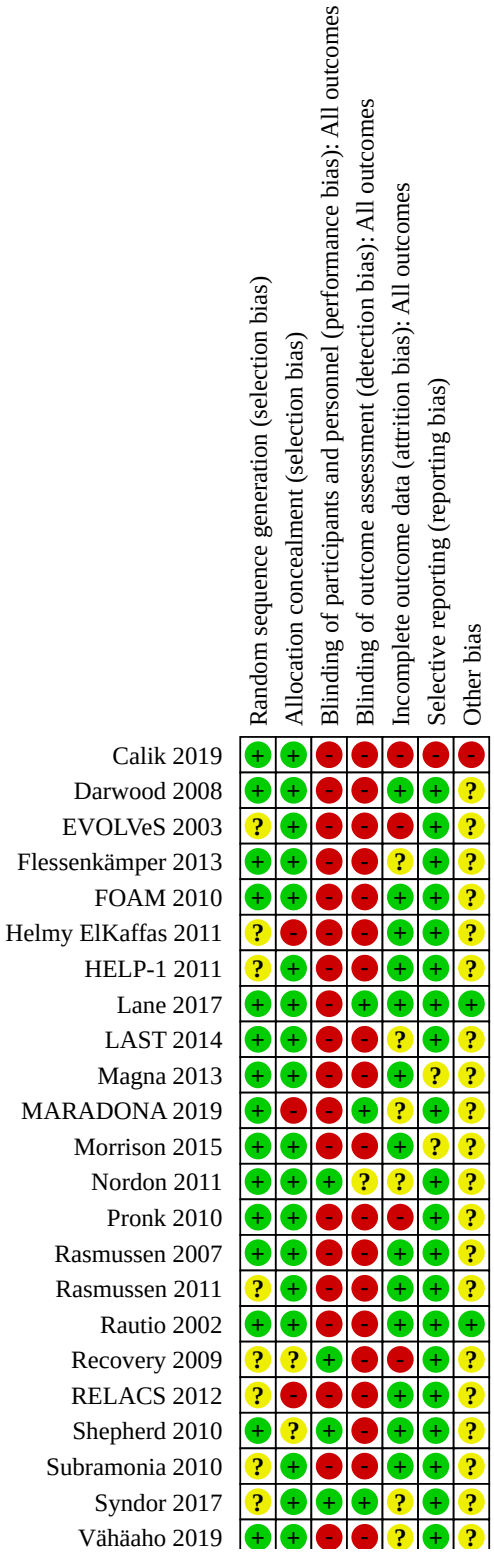
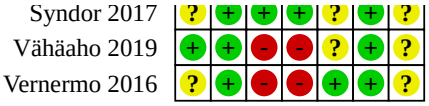


Figure 3. (Continued)



Allocation

Nine studies were at unclear risk of bias as it was unclear whether their methods were truly random or they gave insufficient descriptions of generation methods used (EVOLVeS 2003; Helmy ElKaffas 2011; HELP-1 2011; Rasmussen 2011; Recovery 2009; RELACS 2012; Subramonia 2010; Syndor 2017; Vernermo 2016). The remaining 15 studies thoroughly reported their random sequence methods so were at low risk (Calik 2019; Darwood 2008; Flessenkämper 2013; FOAM 2010; Lane 2017; LAST 2014; Magna 2013; MARADONA 2019; Morrison 2015; Nordon 2011; Pronk 2010; Rasmussen 2007; Rautio 2002; Shepherd 2010; Vähäaho 2019).

Risk of bias due to allocation concealment was deemed to be high within three studies, as methods of concealment were not described (Helmy ElKaffas 2011; MARADONA 2019; RELACS 2012). The single-blinded Recovery 2009 study was deemed to be at unclear risk, as they only stated that they did not discuss the allocated treatment with the participant. Shepherd 2010 was also deemed to be at unclear risk of allocation bias as they only stated they used Internet randomisation. The other 19 studies were judged to be at low risk of allocation concealment bias as methods of allocation concealment were adequately described (Calik 2019; Darwood 2008; EVOLVeS 2003; Flessenkämper 2013; FOAM 2010; HELP-1 2011; Lane 2017; LAST 2014; Magna 2013; Morrison 2015; Nordon 2011; Pronk 2010; Rasmussen 2007; Rasmussen 2011; Rautio 2002; Subramonia 2010; Syndor 2017; Vähäaho 2019; Vernermo 2016).

Blinding

Syndor 2017 was the only double-blinded RCT amongst the included studies and was therefore deemed to be at low risk of performance and detection bias. The Recovery 2009 and Shepherd 2010 studies were single-blinded trials (participants were blinded but the assessors were not blinded), thus conferring a low risk of bias in performance bias and high risk for detection. In Nordon 2011, the participants were blinded (low risk of performance bias) but assessor was blinded until the three-month follow-up scan, so this was judged to be at unclear risk of detection bias. Lane 2017 and MARADONA 2019 were deemed at high risk of performance bias as participants were not blinded but deemed at low risk of detection bias because of blinded duplex ultrasound scanning. The remaining 18 studies were all deemed to have a high risk of performance and detection bias, as none of the participants or assessors were blinded (Calik 2019; Darwood 2008; EVOLVeS 2003; Flessenkämper 2013; FOAM 2010; Helmy ElKaffas 2011; HELP-1 2011; LAST 2014; Magna 2013; Morrison 2015; Pronk 2010; Rasmussen 2007; Rasmussen 2011; Rautio 2002; RELACS 2012; Subramonia 2010; Vähäaho 2019; Vernermo 2016). It is appreciated that some interventions compared do not lend themselves to participant blinding.

Incomplete outcome data

Four studies were determined to be at high risk of attrition bias (Calik 2019; EVOLVeS 2003; Pronk 2010; Recovery 2009). Calik 2019 did not always state the number of participants analysed for outcomes at follow-up intervals, and they did not provide a cohort diagram. EVOLVeS 2003 provided details on all missing data. However, we noted an imbalance in the study treatment groups. There were also discrepancies between missing outcomes and explanations for these in the two-year follow-up paper. Pronk 2010 stated that two participants were lost at six weeks' follow-up, but gave no explanations. There was also an unexplained discrepancy between study groups and participant follow-up at one year. Recovery 2009 did not discuss their dropouts and the number of participants analysed for outcomes at follow-up was not given. Six studies were deemed to be at unclear risk of attrition bias as dropouts were reported but no explanation given (Flessenkämper 2013; LAST 2014; MARADONA 2019; Nordon 2011; Syndor 2017; Vähäaho 2019). The remaining 14 studies were deemed to be at low risk of attrition bias (Darwood 2008; FOAM 2010; Helmy ElKaffas 2011; HELP-1 2011; Lane 2017; Magna 2013; Morrison 2015; Rasmussen 2007; Rasmussen 2011; Rautio 2002; RELACS 2012; Shepherd 2010; Subramonia 2010; Vernermo 2016).

Selective reporting

The majority of studies had low risk of reporting bias as all predefined outcomes were reported. Magna 2013 did not report on several complications outlined in their methods, whilst Morrison 2015 did not report on analgesia use as planned, so we judged these studies to be at unclear risk of reporting bias. Calik 2019 did not explicitly state the outcome measures they intended to report.

Other potential sources of bias

The majority of studies (as shown in Table 6) used concomitant phlebectomies in their treatment groups, often at the discretion of the treating practitioner. This potentially introduces bias into outcomes such as life measures, pain and return to work. Some studies, including Calik 2019, Darwood 2008, LAST 2014 and Recovery 2009, tried to mitigate this potential source of bias by offering phlebectomies several weeks or months after the initial index procedure.

Only Rautio 2002 and Lane 2017 were found to be at low risk of other potential sources of bias. Calik 2019 was found to be at high risk of bias. The remaining 21 trials had potential sources of bias which were deemed to be of unclear risk.

In the Calik 2019 study, bilateral limbs were evaluated. The study authors made no attempt to account for the impact this may have had on outcomes such as pain and return to work. It was not explicitly stated whether each limb received the same treatment. Although the study population was 400 participants, study authors had performed no power analysis. Also, Calik 2019 did not specify

definitions for occlusion, partial and total recanalisation and used the Wong-Baker FACES pain scale, which is a paediatric pain assessment scale.

Darwood 2008 were unable to meet their necessary sample size. Therefore, the study authors declared that their sample size was insufficient to permit statistical testing for equivalence. The study also included participants who underwent bilateral treatment: these were allocated the same treatment on both limbs; however, they were not stratified within the results. Participants who underwent SFJ ligation and stripping also underwent concomitant phlebectomies. Those who were allocated to EVLA could request injection sclerotherapy for residual varicosities at six weeks. There was no stratification for these participants, and this could potentially add a risk of bias to participant satisfaction and QoL scores. We also noted that one participant randomised to SFJ ligation and stripping underwent EVLA, and was followed up in the EVLA cohort, showing no analysis with intention-to-treat.

The EVOLVeS 2003 study received financial support from VNUS Medical Technologies (manufacturers of RFA catheters). The trial centres were also proctored by the company, introducing a potential source of bias. The trial also included one participant who underwent treatment of both limbs. The participant was only randomised once and each limb was treated as a separate episode after a period of three months.

Flessenkämper 2013 calculated that 469 participants were required in the trial, but only 449 were randomised, meaning the study is potentially underpowered. A further source of bias is the admission of a number of participants undergoing concomitant phlebectomies within their respective treatments arms. This procedure could impact upon pain scores, QoL and return to work.

Mini-phlebectomies were also performed at the operating surgeon's discretion in the FOAM 2010 study in both the SFJ ligation and stripping and UGFS arms. Although the numbers of such participants were given, this procedure could alter the pain and other outcomes.

In Helmy ElKaffas 2011, it was unclear whether participants undergoing bilateral treatment were included or excluded. Concomitant phlebectomies were performed in both the RFA and SFJ ligation and stripping groups. Although the numbers of such procedures were given for both groups, there was no analysis of the impact that this could have had on outcomes such as complications, length of procedure and hospital stay, so this omission introduces a potential source of bias. In addition, some participants required UGFS for persistent varicosities following RFA. However, the timeframe for the additional procedure was not discussed and the only subanalysis of this group was a financial one.

As with other studies, the concomitant use of phlebectomies within HELP-1 2011 introduced a potential source of bias. The study was also possibly underpowered: a power calculation described a need for 120 participants in each group, but only 113 were available for follow-up in the surgery group.

LAST 2014 was also underpowered: power calculations required a total of 116 participants per study group, but there were only 92 and 107 participants in the EVLA and EVSA arms, respectively, due to dropouts. In addition, the protocol for the amount of energy required for EVSA was changed during the trial. In LAST 2014 the legs of participants with bilateral GSV incompetence were included separately, provided that there was at least 3 months between the two treatments.

The Magna 2013 trial also included simultaneously treated bilateral limbs. The study authors did not indicate how they analysed the impact of this on quality of life and other measures, conferring a potential risk of bias. The methods stated the intention of performing additional phlebectomies at the time of the initial procedure, but in several cases, the procedure was undertaken at three months. There was no subanalysis for this group of participants. The trial was also possibly underpowered: their power calculation stated that 240 participants would be required, but only 223 were analysed.

Trialists stopped enrolling participants in the MARADONA 2019 study earlier than planned. This was because reimbursement of MOCA treatment was suspended for treatments for class CEAP C3 disease and lower. The study was therefore only able to recruit 46% of the calculated required number of participants and was significantly underpowered for the anatomic success outcome measure. The trial also consequently included a higher proportion of participants with more severe chronic venous insufficiency compared to other such trials.

Additional sources of potential bias within the Morrison 2015 trial included the fact that the authors of the study were paid consultants of Sapheon, a company which manufactures cyanoacrylate glue. However, independent evaluation of ultrasound images was undertaken. The study stated that there were 31 missing or uninterruptible ultrasound scan (USS) reports. Attempts to account for this were made by the study authors by analysing the outcomes via various models for inputting missing data.

In order to blind their participants, Nordon 2011 performed RFA and EVLA under general anaesthesia, whilst all other studies performed these interventions under spinal or conscious sedation. The use of general anaesthesia could have an impact on pain scores, duration of hospital stay, QoL scores and expose participants to risk of anaesthetic-related complications avoided when the procedure is performed under block or local techniques. The use of general anaesthetic in these procedures is not standard practice, and thus potentially confers a risk of bias.

Pronk 2010 performed both EVLA and SFJ ligation and stripping under tumescent anaesthesia. Other studies evaluating SFJ ligation and stripping have not uniformly used this anaesthetic modality; therefore, it may confer an advantage in the Pronk 2010 trial and impact upon outcomes such as participant-reported post-operative pain, QoL, hospital stay and return to normal activities. The study was potentially underpowered: power calculations described a need for 120 participants in each treatment arm, yet only 113 participants were available for follow-up in the surgery group. The study is unclear about participants who underwent simultaneous bilateral intervention. The study authors claimed participants were only randomised to an intervention once, but the number randomised is reported as legs (130) and not participants (n = 122).

The inclusion of participants with simultaneous bilateral varicosities, with no subsequent stratification within the results, introduces a possible further source of bias in Rasmussen 2007.

However, all participants with bilateral disease received the same intervention.

Contrary to the inclusion criteria of this review, Rasmussen 2011 also included a small number of participants who had had previous SFJ ligation on the basis that they had recanalised their GSV and had a patent, refluxing SFJ and GSV. There was no stratification of these participants within the study's results or amongst the treatment arms, conferring a potential source of bias. The technique for EVLA was not uniform within Rasmussen 2011, with different methods, energies and diodes used amongst the trial centres. The trialists also analysed their results by limbs not participants.

We judged the Recovery 2009 study to have an unclear risk of further bias as it was sponsored by VNUS Medical Technologies, who manufacture radiofrequency ablation catheters.

In the RELACS 2012 study, there was no clear consensus on the number of additional phlebectomies, thereby impacting upon the outcomes of pain, QoL and return to normal activities. After three months, those with apparent residual varices and perforators could be treated with additional phlebectomies or sclerotherapy. This trial was also possibly underpowered: a total of 180 participants per treatment group was calculated, but after dropouts and losses to follow-up, the EVLA group had 173 and SFJ ligation and stripping group had 143.

Shepherd 2010 allowed for additional phlebectomies at the time of the procedure, as well as treatment for SSV and anterior thigh vein incompetence. The study authors stated that pain analysis was subsequently adjusted to make allowances for this. The study included participants undergoing concurrent treatment of bilateral disease. The most symptomatic limb (participant-reported) was randomised and both limbs received the same intervention. However, this approach impacts on pain and return to normal activities, suggesting a possible risk of bias.

The Subramonia 2010 trial included five participants with recurrent varicose veins, but there was no stratification of these individuals in the results. This could introduce potential bias into results such as pain, return to normal activities and QoL. The trial also Included 12 participants with bilateral varicose veins (randomised on one occasion to the same treatment, with a minimum of six weeks between treatment of the limbs, thus treating each limb as a separate case).

In Syndor 2017, it was noted that there was a vast range in the time frames at which participants were being followed up. For instance, the initial follow-up review ranged from one to 29 days, and participants who were followed up at one year were being included within the analysis of outcome measures at the six-week review. Therefore, potentially, participants who could have had complications at six weeks were being missed as they were only seen at one year, by which point, the complication may have resolved - this introduces a risk of bias. Participants underwent concomitant phlebectomies and UGFS, an approach not undertaken in other studies, thereby impacting on the risk of bias for outcomes such as pain, QoL and return to normal activities. No power calculations were performed.

Vähäaho 2019 did not manage to recruit the calculated required sample size (132 instead of 160 participants). Concomitant phlebectomies were also performed, which could impact upon pain and complications such as saphenous nerve injury.

The authors of Vernermo 2016 state that, "Owing to the operating surgeon's preference, five patients originally randomised to EVLA were treated with surgery but, because the analysis was made according to intention to treat, these patients were analysed in EVLA group". There was no further clarification why the surgeon preferred to undertake surgery in these individuals, and no subanalysis. The EVLA diode was also changed from a 980-nm diode to a 1470-nm diode during the course of the trial. In comparison to other trials, the sclerosant used in the UGFS arm was more concentrated (air to sclerosant ratio 2:1).

Effects of interventions

See: **Summary of findings 1** Endovenous laser ablation (EVLA) compared to radiofrequency ablation (RFA) for great saphenous vein (GSV) incompetence; **Summary of findings 2** Endovenous laser ablation (EVLA) compared to ultrasound-guided foam sclerotherapy (UGFS) for great saphenous vein (GSV) incompetence; **Summary of findings 3** Endovenous laser ablation (EVLA) compared to SFJ ligation and stripping (HL/S) for great saphenous vein (GSV) incompetence; **Summary of findings 4** Radiofrequency ablation (RFA) compared to mechanochemical ablation (MOCA) for great saphenous vein incompetence; **Summary of findings 5** Radiofrequency ablation (RFA) compared to SFJ ligation and stripping (HL/S) for great saphenous vein (GSV) incompetence; **Summary of findings 6** Ultrasound-guided foam sclerotherapy (UGFS) compared to SFJ ligation and stripping (HL/S) for great saphenous vein (GSV) incompetence

Study authors reported on outcomes using different definitions and at different time points, which impacted our ability to carry out analyses. We provide a brief description of how studies reported on outcomes below. We then present the results by comparison to allow consistent reporting between analyses and the summary of findings tables.

Technical success

We defined technical success as complete anatomical obliteration or absence of reflux within the GSV at six weeks on duplex ultrasound (DUS; standard criterion of 1 second (s) of reflux on DUS). This was evaluated in 18 studies at different time points (Calik 2019; Darwood 2008; FOAM 2010; HELP-1 2011; Lane 2017; LAST 2014; Magna 2013; MARADONA 2019; Morrison 2015; Nordon 2011; Rasmussen 2007; Rasmussen 2011; Rautio 2002; Recovery 2009; Shepherd 2010; Syndor 2017; Vähäaho 2019; Vernermo 2016). Three trials reported technical success at four weeks (Calik 2019; Recovery 2009; Morrison 2015). As Calik 2019 and Morrison 2015 were the sole studies for their comparison, their data were included. Vähäaho 2019 reported on technical success at 30 days. The results of these studies are shown in Table 7. Rasmussen 2011 reported on technical failure which they defined as "an open refluxing segment of 10cm or more at follow up". We were therefore able to extrapolate their technical success rate from the figures they presented. The primary outcome in Flessenkämper 2013 was inguinal reflux, which they defined as 'any reflux from the SFJ into the GSV lasting > 0.5 seconds'. Due to the manner in which they reported these data, we were unable to extrapolate this and include it within our technical success analysis. We defined long-

term technical success as complete anatomical obliteration, or absence of reflux, within the GSV on DUS at five years or greater. Five trials reported on this (HELP-1 2011; Magna 2013; Rasmussen 2007; Rasmussen 2011; Vernermo 2016).

Recurrence

We used the clinical definition reported by the clinician or the participant themselves. Definitions of recurrence used by the individual studies varied and are provided in the Characteristics of included studies tables. Fifteen studies reported recurrence (Calik 2019; EVOLVeS 2003; Flessenkämper 2013; FOAM 2010; Helmy ElKaffas 2011; HELP-1 2011; Lane 2017; MARADONA 2019; Magna 2013; Pronk 2010; Rasmussen 2007; Rasmussen 2011; Rautio 2002; RELACS 2012; Vähäaho 2019). See Table 8 for recurrence data.

Five year and longer-term follow-up data of Flessenkämper 2013, FOAM 2010, HELP-1 2011, Magna 2013, Pronk 2010, Rasmussen 2007, Rasmussen 2011 and RELACS 2012 were also available (see Table 9).

Rates of recurrence were not reported for the comparisons EVLA versus EVSA and RFA versus cyanoacrylate glue.

Post-operative complications

All 24 included studies reported rates of post-operative complications. Unfortunately, we could not perform meta-analysis due to the considerable array of different terms used within the studies to report adverse events (for instance, 'paraesthesia', 'numbness', 'regional neurological sensory deficit' and 'saphenous nerve injury' were reported separately amongst trials). There was a lack of uniformity in the time points at which these events were measured. Therefore, we divided post-operative adverse events into minor (i.e. not requiring intervention) and major (i.e. requiring intervention) within the first three months (early) and beyond three months (late) for this review. Within minor complications, we collated rates of haematoma, saphenous nerve injury, thermal injury or inflammation, wound problems (groin/stab), bruising and pigmentation and phlebitis from the included studies. Major complications included wound problems and 'other', further described in the footnotes to the tables. Complication rates are shown in Table 10 (early ≤ 3 months) and Table 11 (late > 3 months). Where complications were recorded at multiple time points during and after the first three months (e.g. in EVOLVeS 2003; Nesbitt 2014), we documented the highest rate of said event.

Quality of life (QoL)

Twenty-two studies reported on QoL (Calik 2019; Darwood 2008; EVOLVeS 2003; Flessenkämper 2013; FOAM 2010; HELP-1 2011; Lane 2017; LAST 2014; Magna 2013; MARADONA 2019; Morrison 2015; Nordon 2011; Pronk 2010; Rasmussen 2007; Rasmussen 2011; Rautio 2002; Recovery 2009; RELACS 2012; Shepherd 2010; Subramonia 2010; Vähäaho 2019; Vernermo 2016). Meta-analysis was not possible due to different questionnaires being used at different time points. See Table 12.

Venous Clinical Severity Score (VCSS)

Thirteen studies reported on VCSS (Calik 2019; EVOLVeS 2003; FOAM 2010; Lane 2017; LAST 2014; MARADONA 2019; Morrison 2015; Rasmussen 2007; Rasmussen 2011; Rautio 2002; Recovery 2009; Shepherd 2010; Syndor 2017). However, meaningful meta-analysis was prevented for each comparison by the limited studies available and by the different time points measured. Some studies presented the mean baseline and final score without calculating the mean difference. Other studies gave only the change in scores pre- and post-intervention. We have collated and presented the results of the included studies in Table 13.

Length of procedure

Eleven studies reported on length of procedure (Calik 2019; EVOLVeS 2003; Helmy ElKaffas 2011; HELP-1 2011; MARADONA 2019; Morrison 2015; Nordon 2011; Rasmussen 2011; Rautio 2002; Subramonia 2010; Syndor 2017). The results of the length of procedure for the reporting trials are shown in Table 14. What defines the start and end points of a 'procedure' is ambiguous, which is reflected in the various ways the included trials have reported length of procedure. Syndor 2017 presents the median ablation and procedure time with the range; Rasmussen 2011 reports on the mean 'surgeon's time' and range; Subramonia 2010 on theatre and procedure times with the median values and the interquartile range; whilst Rautio 2002 gives the mean operating time, room time and recovery time with standard deviation (SD).

Duration of hospital stay

The majority of the included studies reported that procedures were performed in day case surgical units or outpatient settings. Ten studies explicitly stated whether all participants were discharged home the same day or whether some required inpatient admission post-intervention (Darwood 2008; EVOLVeS 2003; Flessenkämper 2013; FOAM 2010; Helmy ElKaffas 2011; HELP-1 2011; Morrison 2015; Pronk 2010; Rasmussen 2007; Shepherd 2010). See Table 15 for details. For the most part, these procedures were performed as day cases.

Return to normal activities (days)

Table 16 illustrates the time taken by participants to return to work or normal activities following the intervention within their respective trials. Studies have presented this outcome as either parametric or non-parametric data (mean, median, range, interquartile range (IQR)), or in the case of Shepherd 2010, the percentage of participants to return to work within a certain time frame. We were not able to perform meta-analysis.

Endovenous laser ablation (EVLA) versus radiofrequency ablation (RFA)

See Summary of findings 1.

Five studies compared EVLA to RFA (Nordon 2011; Rasmussen 2011; Recovery 2009; Shepherd 2010; Syndor 2017).

Technical success

These studies reported technical success at one month, three months, six weeks and six months, respectively. Pooling the data from these studies showed little or no differences to success rates within five years (OR 0.98, 95% CI 0.41 to 2.38; I^2 = 0%; 5 studies, 780 participants; moderate-certainty evidence; Analysis 1.1).

Only Rasmussen 2011 provided data for five years or beyond, and no evidence of a difference in success rates was seen (OR 0.85, 95% CI 0.30 to 2.41; I^2 = 0%; 1 study, 291 participants; low-certainty evidence; Analysis 1.2).

We downgraded the certainty of the evidence from high to moderate due to risk of bias concerns.

Recurrence

Only Rasmussen 2011 reported on recurrence in the comparison EVLA versus RFA. At three years, there was no clear difference in recurrence between the groups (OR 1.53; 95% CI 0.78 to 2.99; 291 participants; low-certainty evidence; Analysis 1.3).

Rasmussen 2011 also reported five-year recurrence rates, which favoured RFA (OR 2.77; 95% CI 1.52 to 5.06; 291 participants; low-certainty evidence; Analysis 1.4). We downgraded the certainty of the evidence from high to low due to risk of bias concerns and possible imprecision as a result of wide CIs.

Post-operative complications

We were not able to undertake meta-analysis for post-operative complications due to different definitions and time points used. Nordon 2011 evaluated complications at one week and reported a 2.6% rate of skin burns, a 1.3% rate of paraesthesia and a 2.6% rate of thrombophlebitis with EVLA, compared to rates of 1.3%, 2.6% and 1.3%, respectively, with RFA. Rasmussen 2011 reported phlebitis in 12 of their RFA participants compared to four in EVLA participants at one month. There were six cases of paraesthesia and eight cases of hyperpigmentation, with three of each seen with EVLA. Recovery 2009 reported complications at 48 hours, one week, two weeks and one month: 22% of EVLA participants had a complication compared with 4% of RFA participants at one of these time points. Six participants (14.6%) had phlebitis with EVLA compared with zero with RFA. Two participants (4.9%) reported paraesthesia following EVLA (2.2% with RFA), and there was one case of deep vein thrombosis (DVT) following EVLA. In Shepherd 2010, there was a higher rate of complications within the RFA group. Eight participants (12%) developed paraesthesia after RFA compared to five (8%) in EVLA; six participants (9%) had skin staining after RFA compared to two (3%) in EVLA; and one participant developed pulmonary embolism (PE) two weeks after RFA. Syndor 2017 showed comparable rates of phlebitis in EVLA and RFA (1.04% and 1.03%) and hyperpigmentation (3.16% and 3.13%). More paraesthesia was seen following RFA (13.68%) compared to EVLA (9.38%). Results of individual studies were inconsistent with each other, so we are not able to draw any conclusions (very low-certainty evidence). See Table 10 and Table 11.

Quality of life (QoL)

Due to the variety of different QoL questionnaires used and scores recorded at different time points amongst the included trials, we decided it was inappropriate to combine these for meta-analysis (see Table 12). The majority of studies for this comparison showed no clear difference in QoL scores between the two treatments compared. Nordon 2011 found no difference in improvement in QoL using the Aberdeen Varicose Vein Questionnaire (AVVQ) and EuroQol-5D (EQ-5D) at three months between EVLA and RFA. The mean (SD) AVVQ reduction in the EVLA group was 5.9 (6.1) and 6.2 (5.9) in the RFA group (P = 0.12). The mean improvement in EQ-5D was 0.22 (0.3) in EVLA and 0.16 (0.3) with RFA (P = 0.66). Shepherd 2010 showed comparable improvements in QoL between treatment groups at six months: mean (SD) AVVQ improved in EVLA from 18.9 (9.8) to 10.9 (8.7) at six months; and from 20.6 (9.4) to 10.2 (9.4) in RFA. The mean (SD) SF-12 physical component score (PCS) improved from 48.1 (10.1) in EVLA to 51.4 (9.6) and from 48.9 (9.5) to 51.7 (9.3) in RFA at six months. Rasmussen 2011 found that the Aberdeen Varicose Vein Symptom Severity Score (AVVSS) improved in all groups from three days onwards (P < 0.001) with no difference between the groups at any time point. Mean (SD) AVVSS at baseline was 17.94 (9) in EVLA and 18.74 in RFA, improving to 4.61 (5.8) and 4.43 (6.58), respectively, at three years. Rasmussen 2011 reported no difference in Medical Outcomes Study Short Form 36 (SF-36) at one month. Recovery 2009 reported changes in mean (SD) global QoL scores were better in RFA at 7 and 14 days post operation; (RFA 27.7 (11.5) and 23 (6.1) compared to EVLA 33.7 (13.7) and 29.5 (8.5), respectively). By one month, they were comparable (RFA 22.7 (5) versus EVLA 22.2 (3.3)). Syndor 2017 did not evaluate QoL measures in their study. We assessed the certainty of the evidence for this outcome as moderate, downgrading for concerns regarding risk of bias.

Pain

All studies reported reduced pain in the RFA groups compared to EVLA. Nordon 2011 showed RFA participants took less analgesia during the week after the procedure (median 0 mg ibuprofen; range 0 to 600 mg, compared to median of 200 mg; range 0 to 1050 mg in EVLA group). Median post-procedural pain scores were higher in EVLA than in RFA: reporting at day one (28 versus 9.5 (P = 0.001)); day three (23.5 versus 6 (P = 0.001)); and day seven (13.5 versus 0 (P = 0.001)), respectively. Recovery 2009 reported significantly lower mean pain levels (SD) on visual analogue system (VAS) at 48 hours in participants who had RFA (0.7 (0.9) versus 1.9 (1.6); P < 0.001); one week (0.2 (0.6) versus 1.8 (1.8) P < 0.001), and two weeks (0.1 (0.4) versus 1.2 (1.7) P < 0.001). In Rasmussen 2011, mean pain scores on VAS at 10 days in EVLA and RFA were 2.58 (2.4) and 1.21 (1.72), respectively. Shepherd 2010 reported that participants who had RFA reported less pain over the first 10 days with mean (SD) VAS score of 22 (19.8) compared to 34.3 (21.1) in EVLA. Also, participants who underwent RFA took fewer analgesic tablets with a mean (SD) consumption of 8.8 (9.5) tablets over three days compared to 14.2 (10.7) in the EVLA group. In Syndor 2017, the median post-procedure pain score (on a scale of one to ten) was five in the EVLA group compared to two in RFA on initial evaluation (median day of evaluation was five in EVLA (range 1 to 29 days) and six in RFA (range 1 to 9 days).

Venous Clinical Severity Score (VCSS)

Four trials reported on change in VCSS, showing comparable rates between groups at final follow-up (Rasmussen 2011; Recovery 2009; Shepherd 2010; Syndor 2017). Rasmussen 2011 reported that the VCSS improved significantly in all groups (P < 0.001) with no difference between groups at any evaluated time point through three years. Mean (SD) VCSS at baseline was 2.68 (2.25) in EVLA and 2.95 (2.06) in RFA; at three years, this was 0.34 (1.3) and 0.44 (1.82), respectively. Recovery 2009 reported no difference between treatment groups at baseline. In the RFA group, mean VCSS scores were reduced compared with EVLA at 48 hours (4.7 versus 5.3, P < 0.001), one week (4.2 versus 5.9, P < 0.001); and two weeks (4 vs 5.3; P = 0.0035); there was no difference by one month (2.7 versus 3.2; P = 0.28). In Shepherd 2010, VCSS was comparable between the two groups at six months, with mean improvement of 3.3 in EVLA (initial 4.7 and 1.4 at six months) and 3.7 in RFA (initial 5.1 and 1.4 at six months). Syndor 2017 found participants in both groups demonstrated a reduction in VCSS at six months from baseline. Median (range) VCSS improved from 5 (2 to 26) at baseline to 1 (0

to 18) at six months in EVLA and from 5 (1 to 20) to 1 (0 to 6) with RFA. See Table 13.

Length of procedure

The duration of the procedure was similar between treatment groups. However, the reporting trials used different time points, metrics and terminology, thus impeding analysis. Nordon 2011 reported the median procedural time (range) was 30 minutes (10 to 60 minutes) with EVLA and 30 minutes (15 to 60 minutes) with RFA. In Rasmussen 2011, mean (range) surgeon's time was 26 minutes (12 to 80 minutes) for EVLA and 27 minutes (12 to 80 minutes) with RFA. In Syndor 2017, median (range) total procedure time was 23.5 minutes (8 to 95 minutes) with EVLA and 21 minutes (6 to 64 minutes) with RFA. See Table 14.

Duration of hospital stay

Shepherd 2010 explicitly stated all procedures were day case procedures. Despite their intention to perform all procedures as day case procedures, four participants (3.1%) required overnight admission: three participants in the RFA groups for nausea, hypotension secondary to general anaesthesia or pain requiring opoid analgesia, and one participant in the EVLA group for post-operative nausea. See Table 15.

Return to normal activities

Three trials reported on return to work and normal activities (Nordon 2011; Rasmussen 2011; Shepherd 2010). Results were comparable but studies evaluated this outcome by different means. Nordon 2011 reported median (range) return to work was seven days (1 to 60 days) after EVLA compared with nine days after RFA (1 to 28 days). In Rasmussen 2011, median (range) return to normal activities was 2 days (0 to 25 days) and to work was 3.6 days (0 to 46 days) compared with 1 day (0 to 30 days) and 2.9 days (0 to 14 days) with RFA. Shepherd 2010 reported 74% of participants had returned to normal activities and 71% had returned to work at seven days following EVLA. This was comparable with RFA, with 77% of participants at normal levels of activity and 71% back at work by seven days. See Table 16.

Endovenous laser ablation (EVLA) versus endovenous steam ablation (EVSA)

Only LAST 2014 compared EVLA with EVSA.

Technical success

In LAST 2014, no clear difference in success was seen between the groups (OR 1.94, 95% CI 0.53 to 7.15; 1 study, 166 participants; Analysis 2.1). There were no reports of data for five years or beyond.

Recurrence

LAST 2014 did not report this outcome.

Post-operative complications

Complication profiles were similar between the two groups. Participants had similar rates of thrombophlebitis following treatment (10 participants in each group at two weeks) and one participant in the EVLA group developed a DVT. Two participants within the EVSA group had nerve injury reported at two weeks. See Table 10 and Table 11.

Quality of life

LAST 2014 reported that the EQ-5D and EQ visual analogue scale scores were comparable for EVSA and EVLA at 12 weeks.

Pain

LAST 2014 reported that the EVSA group had less post-procedural pain (mean VAS score in EVLA of 5.6 and 2.6 in EVSA; $P < 0.001$); and a shorter duration of analgesic use (mean 0.9 days compared with 3.3 days in EVLA; $P < 0.001$).

Venous Clinical Severity Score (VCSS)

Changes in VCSS between baseline and 12 weeks were similar between the two treatment arms: -2.69 (95% CI -2.34 to -3.04) in ESVS and -2.51 (95% CI -2.10 to -2.93) in the EVLA group. See Table 13.

Length of procedure

LAST 2014 did not report this outcome.

Duration of hospital stay

LAST 2014 did not report this outcome.

Return to normal activities

Convalescence was measured as the number of days lost from work or normal activities. Participants undergoing EVSA had a mean return to normal activity of 1.6 days (95% CI 1 to 2.1), compared to 4.2 days (95% CI 3.4 to 5) with EVLA. See Table 16.

Endovenous laser ablation (EVLA) versus ultrasound-guided foam sclerotherapy (UGFS)

See Summary of findings 2.

Three studies compared EVLA with UGFS (Magna 2013; Rasmussen 2011; Vernermo 2016).

Technical success

Three studies evaluated EVLA compared to UGFS for technical success up to five years (Magna 2013; Rasmussen 2011; Vernermo 2016). Two of these also reported data for greater than five-year follow-up (Magna 2013; Vernermo 2016). Meta-analysis showed technical success may be improved in those undergoing EVLA up to five years (OR 6.13, 95% CI 0.98 to 38.27; 3 studies, 588 participants; low-certainty evidence; Analysis 3.1); and over five years follow-up (OR 6.47, 95% CI 2.60 to 16.10; 3 studies, 534 participants; low-certainty evidence; Analysis 3.2) noting the wide CIs. Heterogeneity was detected at up to and over five years so a random-effects method was used (I^2 = 78% and I^2 = 68%, respectively). We downgraded the certainty of the evidence from high to low due to risk of bias concerns and inconsistency.

Recurrence

Two studies compared recurrence in EVLA and UGFS at one and three years, respectively (Magna 2013; Rasmussen 2011), and showed no clear difference between the groups (OR 0.68, 95% CI 0.20 to 2.36; 2 studies, 443 participants; very low-certainty evidence; Analysis 3.3). Five-year recurrence rates were also available for both studies and again no clear differences were seen (OR 1.08, 95% CI 0.40 to 2.87; 2 studies, 418 participants; very low-certainty evidence; Analysis 3.4). Heterogeneity was detected so a

random-effects model was used (I^2 = 82% and 76%, respectively). We downgraded the certainty of the evidence due to risk of bias concerns, inconsistency and imprecision.

Post-operative complications

All three studies reported on post-operative complications. However, meta-analysis was impeded by the different definitions of complications used amongst trials and the varying time points at which complications were assessed. At one month, Rasmussen 2011 reported an iliac vein thrombosis with subsequent pulmonary embolism in one participant who had undergone UGFS one week prior. Phlebitis rates were higher amongst the UGFS group and were seen in 17 participants compared to 4 in the EVLA group. UGFS also had higher rates of hyperpigmentation at one month with eight cases compared to three within the EVLA arm. In Vernermo 2016, skin pigmentation was common in the UGFS arm at one month - seen in 67% of participants compared to 4% in the EVLA group. Vernermo 2016 found haematomas in 42% of participants undergoing EVLA compared to 20% of UGFS participants at one month. Magna 2013 reported two cases of hyperpigmentation in EVLA participants compared to one case in UGFS at three months. We downgraded to very-low certainty evidence due to risk of bias concerns, inconsistency, imprecision and possible publication bias. See Table 10 and Table 11.

Quality of life

All three studies reported on this outcome but evaluated QoL using different questionnaires at different time points. Magna 2013 reported no significant differences between EVLA and UGFS at three months and one year in Chronic Venous Insufficiency Quality of Life Questionnaire (CIVIQ2) and EQ-5D scores. While in Rasmussen 2011, UGFS was deemed to be better with regard to bodily pain and physical functioning in the SF-36 score initially, but showed no difference between comparisons at one month. Vernermo 2016 found no significant difference in median AVVSS between the treatment groups at one year. We assessed the overall certainty of evidence for QoL as moderate, downgrading by one step due to risk of bias concerns.

Pain

Two studies evaluated pain scores, with both reporting lower post-procedural pain with UGFS compared to EVLA treatment, but we were not able to undertake meta-analysis as data were not reported for both studies (Rasmussen 2011; Vernermo 2016). Vernermo 2016 reported pain after treatment was significantly reduced (lower VAS score) both at the time of discharge, and one week following UGFS treatment compared with EVLA. In Rasmussen 2011, less pain was reported during the first ten days after UGFS treatment (mean (SD) VAS score was 1.6 (2.04) in the UGFS group and 2.58 (2.4) in the EVLA group).

Venous Clinical Severity Score (VCSS)

VCSS was only analysed by Rasmussen 2011, who found that VCSS improved in all groups from baseline, with no difference between treatment arms at any evaluated time point. Initial mean (SD) VCSS improved from 2.68 (2.25) to 0.34 (1.3) in EVLA compared to 2.66 (1.45) to 0.15 (0.4) in UGFS. See Table 13.

Length of procedure

Rasmussen 2011 was the only study which evaluated length of procedure as surgeon's time. Mean surgeon's time was 26 minutes in the EVLA group (range 12 to 80 minutes) and 19 minutes in the UGFS group (range 5 to 145 minutes).

Duration of hospital stay

No studies reported on duration of hospital stay.

Return to normal activities

Vernermo 2016 reported the mean duration of sick leave, and this was eight days in the EVLA group (range 0 to 29 days) and one day in the UGFS (range 0 to 21 days).

Endovenous laser ablation (EVLA) versus cyanoacrylate glue

Calik 2019 was the sole trial to evaluate this comparison. We assessed it as having a high risk of bias in five bias categories, but we included it as it was the sole RCT found for this comparison.

Technical success

Calik 2019 evaluated technical success at 1-, 3-, 6- and 12-month follow-up. As the one-month data is the closest to our definition of technical success (complete anatomical obliteration, or absence of reflux, within the GSV around six weeks on DUS) we have used this time point in our analysis. Occlusion rates showed no evidence of a difference between the treatment groups (OR 0.33, 95% CI 0.01 to 8.03; 1 study, 412 participants; Analysis 4.1). At 12 months, there was no clear difference in recurrence between groups (OR 2.59, 95% CI 0.50 to 13.49; 1 study, 412 participants). These participants had no clinically significant symptoms. There were no long-term data available.

Recurrence

There were two recanalisations in the cyanoacrylate glue group and five within the EVLA group, and results showed no evidence of a difference in recanalisation rates at one year (OR 2.59, 95% CI 0.50 to 13.49; 1 study, 412 participants; Analysis 4.2). There were no long-term data available.

Post-operative complications

Higher rates of post-procedural induration, bruising and paraesthesia were reported following EVLA at one week, but there was no difference by the three-month time point except for paraesthesia, which was reported in 13 EVLA participants and 2 cyanoacrylate glue participants (P < 0.001). Two DVTs were found within the EVLA group. See Table 10 and Table 11.

Quality of life

Quality of life was evaluated via the CIVIQ2 score. The mean CIVIQ2 scores demonstrated meaningful improvement in all groups at follow-up (P < 0.001) with no clear difference between cyanoacrylate glue and EVLA groups reported. The mean pre-procedural score was 41.4 in the EVLA group, improving to 12.8 at one year. In the cyanoacrylate glue group, the mean pre-procedural score was 40.6 and 12.3 at one year.

Pain

Calik 2019 evaluated participant-reported pain using the Wong-Baker FACES pain rating scale. At one week, participants who had

undergone EVLA had a higher mean pain score (5.4 (SD 3.7)) than participants who underwent cyanoacrylate glue (2.8 (SD 3.1); P < 0.001). However, at three months, there was no evidence of a difference between the mean pain scores 0.7 (SD 0.5) and 0.6 (SD 0.4), respectively (P < 0.46).

Venous Clinical Severity Score (VCSS)

At one year, VCSS (SD) had declined from 5.8 (1.9) to 1.3 (0.9) (P < 0.001) for the EVLA group, and from 5.7 (1.9) to 1.3 (0.9) (P < 0.001) for the cyanoacrylate glue group, with no evidence of difference between groups. See Table 13.

Length of procedure

The mean operative time (SD) was longer for the EVLA group (31.7 (8.8) minutes) than for cyanoacrylate glue group (13 (3.4) minutes) (P < 0.001). See Table 14.

Duration of hospital stay

Calik 2019 did not evaluate this outcome.

Return to normal activities

Amongst the cyanoacrylate glue group, there was a faster return to daily activities (1.5 days) compared to participants who underwent EVLA (2.9 days; P < 0.001). Results are summarised below under 'Narrative summaries' and detailed within Table 16.

Endovenous laser ablation (EVLA) versus mechanochemical ablation (MOCA)

One study compared EVLA with MOCA (Vähäaho 2019).

Technical success

At one month, all treated great saphenous veins were occluded, regardless of treatment modality (Analysis 5.1). There were no long-term data available.

Recurrence

Ten participants within the MOCA treatment group had ultrasound-proven recanalisation at one year compared to none in the EVLA group (OR 0.06, 95% CI 0.00 to 1.14; 1 study, 88 participants; Analysis 5.2). There were no long-term data available.

Post-operative complications

Three participants in the EVLA group reported sensory disturbance at one year; no nerve injuries were seen in the MOCA group. There was one superficial infection seen in the MOCA treatment group. See Table 10 and Table 11.

Quality of life

Mean AVVQ at baseline was 16.1 in EVLA group and 15.8 in the MOCA group. By year one, all had improved and there was no evidence of a difference between the treatment groups reported by the study authors (mean AVVQ in EVLA was 5.3, and in MOCA 6.2 (P = 0.9).

Pain

Vähäaho 2019 evaluated pain using the visual analogue system (VAS) and recorded scores as zero to ten. During the procedure, the mean VAS pain score was 3.9 for EVLA and 4.6 for MOCA (P = 0.12). The study authors reported that use of extra periprocedural sedative (propofol) was less in participants undergoing MOCA than in participants undergoing thermal ablation (P < 0.001). The use of fentanyl and diazepam periprocedurally did not differ between treatment groups (P = 0.12 and P = 0.41, respectively). Prior to discharge, pain scores were found to be similar between interventions (P = 0.18), as well as at one week (P = 0.92). The amount of post-operative analgesia consumed by participants did not differ (P = 0.12).

Venous Clinical Severity Score (VCSS)

Vähäaho 2019 did not report on this outcome.

Length of procedure

Vähäaho 2019 did not report on this outcome.

Duration of hospital stay

Vähäaho 2019 did not explicitly mention whether all procedures were performed as day case surgery.

Return to normal activities

Participants undergoing EVLA took a mean of 5.3 days sick leave compared to 4.3 days in those undergoing MOCA. See Table 16.

Endovenous laser ablation (EVLA) versus SFJ ligation and stripping (HL/S, surgery)

See Summary of findings 3.

Nine studies compared EVLA with SFJ ligation and stripping (Darwood 2008; Flessenkämper 2013; HELP-1 2011; Magna 2013; Pronk 2010; Rasmussen 2007; Rasmussen 2011; RELACS 2012; Vernermo 2016).

Technical success

A total of six studies compared technical success in EVLA and SFJ ligation and stripping (Darwood 2008; HELP-1 2011; Magna 2013; Rasmussen 2007: Rasmussen 2011; Vernermo 2016); with five studies also reporting five-year data (HELP-1 2011; Magna 2013; Rasmussen 2007: Rasmussen 2011; Vernermo 2016).

There was a possible benefit in technical success at less than five years in the EVLA group (OR 2.31, 95% CI 1.27 to 4.23; 6 studies, 1051 participants; low-certainty evidence; Analysis 6.1). There was no clear difference seen at five years and beyond (OR 0.93, 95% CI 0.57 to 1.50; 5 studies, 874 participants; low-certainty evidence; Analysis 6.2). We downgraded the certainty of the evidence from high to low due to risk of bias concerns and imprecision. See Summary of findings 3.

Recurrence

Seven studies reported on recurrence (one to three years) between EVLA and SFJ ligation and stripping (Flessenkämper 2013; HELP-1 2011; Magna 2013; Pronk 2010; Rasmussen 2007; Rasmussen 2011; RELACS 2012). We were able to pool these data. Meta-analysis showed no clear difference in recurrence rate between the EVLA or surgery group up to 5 years (OR 0.78, 95% CI 0.47 to 1.29; 7 studies, 1459 participants; moderate-certainty evidence; Analysis 6.3).

Five-year data was available also from seven studies (Flessenkämper 2013; HELP-1 2011; Magna 2013; Pronk 2010; Rasmussen 2007; Rasmussen 2011; RELACS 2012). Pooling showed no clear difference in recurrence rates (OR 1.09, 95% CI 0.68 to 1.76;

7 studies, 1267 participants; moderate-certainty evidence; Analysis 6.4). Heterogeneity was detected so a random-effects model was used (I^2 = 62% and I^2 = 70%, respectively). We downgraded from high to moderate certainty due to the lack of blinding inherent within these studies.

Post-operative complications

We were not able to undertake meta-analysis for post-operative complications because the included trials used different definitions and time points. Darwood 2008 reported higher rates of phlebitis amongst EVLA participants (11%) compared to SFJ ligation and stripping (0%). Neurosensory loss was reported in 13% of SFJ ligation and stripping participants compared to 1% in EVLA. One participant undergoing SFJ ligation and stripping developed acute respiratory distress syndrome after aspirating on extubation and required intensive care unit (ICU) care for seven days. Flessenkämper 2013 reported similar rates of saphenous nerve injury between groups at two months (15% and 17%, respectively); early bruising and pigmentation was higher in the SFJ ligation and stripping group (68%) compared to the EVLA group (47.9%). HELP-1 2011 reported higher rates of sensory disturbance (9.8%), haematoma (8.3%) and infection (8%) following SFJ ligation and stripping compared to EVLA (4%, 1% and 1.5%, respectively). Magna 2013 reported low rates of complications at three months' follow-up. Paraesthesia was reported in 5.9% of SFJ ligation and stripping participants compared to 2.6% with EVLA; 2.6% of EVLA participants had hyperpigmentation, none was seen with SFJ ligation and stripping. Pronk 2010 reported low levels of complications in their trial: paraesthesia was seen in 3% of their EVLA participants and 1% of SFJ ligation and stripping participants. Rasmussen 2007 reported higher rates of bruising at 12 days following SFJ ligation and stripping (25%) compared to EVLA (11%) (P > 0.05). Paraesthesia was slightly higher following SFJ ligation and stripping (4.2%) than EVLA (2.4%) as was hyperpigmentation (5% compared to 2.45) in Rasmussen 2011. High levels of bruising were reported with each treatment group (90.1% in both) in RELACS 2012. Phlebitis was more pronounced in the EVLA group (10.8% versus 2.5%) as was pigmentation (32% versus 12%). At one month, higher rates of haematoma were seen with SFJ ligation and stripping (62%) compared with EVLA (42%). We downgraded to very low-certainty evidence due to risk of bias concerns, inconsistency, imprecision and possible publication bias. See Table 10 and Table 11.

Quality of life

Darwood 2008 reported that the AVVSS improved at three months and was similar between groups (P = 0.694). At baseline, AVVSS (SD) was 11.76 (9.81 - 19.44), improving to 5.6 (1.45 - 8.2) at three months in the EVLA group, while in the SFJ ligation and stripping group, baseline AVVSS was 14.02 (9.49 - 19.16), improving to 5.32 (1.03 - 7.66) at three months. HELP-1 2011 found that AVVSS, EQ-5D and several domains of the SF-36 showed deterioration within the first post-operative week for both treatment groups (P < 0.001). However, these scores improved for the rest of the duration of the follow-up period (P < 0.001), with no statistical difference seen between either groups at any time point for AVVSS and EQ-5D, and none after four weeks in the SF-36. For the SF-6D (a variation of SF-36), the EVLA group was seen to have significantly better scores than the surgical group (P = 0.003). Magna 2013 showed improvement in both CIVIQ2 and EQ-5D scores at three months but no significant difference in score was seen between either groups. Within the EVLA group in Pronk 2010, the EQ-5D scores for daily activity were better than for those in the surgery group on day one (P = 0.01). However, the EVLA group had lower mobility scores on days seven and ten (P < 0.01, P = 0.01, respectively) than the surgery group. At six months and five years, there was no change in EQ-5D in either EVLA or surgery groups. Rasmussen 2007 showed significant improvements at five years in the AVVSS and SF-36 scores with no significant differences in outcomes between the groups. Rasmussen 2011 showed the AVVSS improved from baseline from day three onwards (P > 0.001) with no difference at any evaluated time point. SF-36 scores showed improvement in all domains at some time point with no difference between groups. The RELACS 2012 study demonstrated that CIVIQ scores remained stable up to five years after treatment, without significant differences between the two groups. Vernermo 2016 reported that the AVVSS was improved from baseline with no difference between EVLA and SFJ ligation and stripping. We downgraded the certainty of the evidence from high to moderate due to risk of bias concerns.

Pain

We were not able to undertake meta-analysis for pain because the included trials used different definitions, methods of measuring the outcome and evaluation times. Darwood 2008 evaluated daily pain scores through use of an ungraded visual analogue pain score over the first week, and found no difference between interventions at any time point. Median (IQR) duration of analgesic use was six days (3 to 7) with EVLA, and four days (1 to 7) with SFJ ligation and stripping. Flessenkämper 2013 reported no difference in pain during the first five days following intervention (P = 0.12). The HELP-1 2011 study reported that the EVLA group reported less pain from day one compared with the SFJ ligation and stripping group (P = 0.004 to P < 0.001), with a resultant increase in the latter group's analgesic consumption over the same period (P = 0.012 to P = 0.001). Pronk 2010 demonstrated higher mean pain scores (SD) following EVLA compared with SFJ ligation and stripping at day 7 (3.74 (2.72) versus 1.78 (1.94), P < 0.01), day 10 (2.65 (2.21) versus 1.18 (1.49), P < 0.01), and day 14 (1.66 (2.04) versus 0.77 (1.46), P = 0.01). However, periprocedural pain scores were higher with SFJ ligation and stripping, with a mean (SD) periprocedural pain score of 3.39 (2.57) versus EVLA pain score of 2.21 (2.4); P = 0.02. The higher pain in EVLA could possibly be attributed to the use of tumescent analgesia with SFJ ligation and stripping. Within the Rasmussen 2007 trial, VAS pain scores were not significantly statistically different between groups (P < 0.01). No difference in the mean use of analgesia was found, with 12 tablets consumed in the EVLA group and 12.9 in the SFJ ligation and stripping group. Rasmussen 2011 reported no difference in mean pain score (SD) within ten days, with a score of 2.58 (2.41) in EVLA and 2.25 (2.23) with SFJ ligation and stripping. RELACS 2012 reported similar mean (SD) VAS pain scores during the first post-operative week between EVLA (1.6 (0.8)) and SFJ ligation and stripping (1.3 (0.6)) (P = 0.005). Duration of pain (SD) was 8 (6) days in EVLA and 17 (20) days in SFJ ligation and stripping.

Venous Clinical Severity Score (VCSS)

Four studies reported on VCSS with comparable improvements in scores between interventions. Darwood 2008 reported that, following treatment, VCSS improved from a median (IQR) of 4 (1 - 3) to 0 (0 - 1) (P < 0.001). HELP-1 2011 reported that both groups showed a similar improvement in VCSS from a median of 4 (3 - 5) to 1 (0 - 3) by three months (P < 0.001). This was maintained up to a year

with no difference between interventions at any evaluation point. Rasmussen 2007 found mean VCSS (SD) improved from baseline from 2.8 (1.7) to 0.4 (0.9) at five years in EVLA and from 2.4 (1.4) to 2.4 (1.4) with SFJ ligation and stripping. Scores were not seen to differ between interventions at any time point. Rasmussen 2011 reported improvement in both groups (P > 0.001), with no difference at any time point over three years. The mean (SD) VCSS at baseline was 2.68 (2.25) for EVLA and 2.75 (1.62) for SFJ ligation and stripping. This had improved to 0.34 (1.3) and 0.3 (0.5) by three years. See Table 13.

Length of procedure

Three studies reported on length of procedure. HELP-1 2011 reported that EVLA took longer, with a mean time (SD) of 67 minutes (16) compared to 61 minutes (14) with SFJ ligation and stripping. Rasmussen 2011 reported a mean surgeon's time (range) of 26 minutes (12 to 80) with EVLA and 32 minutes (15 to 80) with SFJ ligation and stripping. Vernermo 2016 reported a mean (SD) duration of treatment of 83 (17) minutes (range 50 to 139 minutes) in EVLA compared to 95 (19) minutes (range 62 to 155 minutes) with SFJ ligation and stripping. See Table 14.

Duration of hospital stay

Darwood 2008, Flessenkämper 2013, Pronk 2010 and Rasmussen 2007 stated that all their procedures were undertaken in an outpatient setting. HELP-1 2011 reported that 21.2% of their participants undergoing SFJ ligation and stripping required inpatient admission due to their unsuitability for day case general anaesthesia. See Table 15.

Return to normal activities

Seven studies evaluated return to normal activities and work. The majority of studies demonstrated that participants undergoing EVLA returned to work faster. Darwood 2008 found that participants undergoing EVLA returned to work faster than with SFJ ligation and stripping, with a median time to return to work (IQR) of four days (2.5 to 7) in the EVLA group compared to 17 days (7.25 to 33.25) with SFJ ligation and stripping. Median (IQR) return to normal activities was two days (0 to 7) and seven days (2 to 26), respectively. HELP-1 2011 reported a median (range) return to work of four days (2 to 14 days) and a median (range) return to normal activities of three days (1 to 10 days) with EVLA, compared to 14 days (13 to 28) and 14 days (7 to 25), respectively with SFJ ligation and stripping. Mean return to work was comparable between interventions in Pronk 2010, with a mean return (SD) of 4.38 (5.43) in EVLA and 4.15 (3.72) SFJ ligation and stripping. Mean (SD) return to normal activities was 3.16 days (4.34) in EVLA and 3.20 days (4.01) with SFJ ligation and stripping. In Rasmussen 2007, mean (SD) return to normal activities (6.9 days (7) versus 7.7 days (6.1)), and mean (SD) time to resume work (7 days (6) versus 7.6 days (4.9)) was comparable between EVLA and SFJ ligation and stripping. Rasmussen 2011 reported no difference between EVLA and SFJ ligation and stripping concerning return to normal activities and work (P = 0.18 and P = 0.26, respectively). The median time to return to work (range) was 3.6 days (0 to 46 days) in EVLA and 4.3 days (0 to 42 days) with SFJ ligation and stripping. Median time to return to normal activities was 2 days (0 to 25 days) and 4 days (0 to 30 days). RELACS 2012 reported a mean return to basic activity of 4 days with EVLA and 4.8 days with SFJ ligation and stripping; the ability to work or perform comparable tasks was achieved after 10.4 days and 11.8 days, respectively, for the two groups. Vernermo 2016 reported a mean (range) length of sick leave of 8 days (0 to 29 days) after EVLA and 12 days (0 to 33 days) following SFJ ligation and stripping. See Table 16.

Radiofrequency ablation (RFA) versus ultrasound-guided foam sclerotherapy (UGFS)

Only Rasmussen 2011 compared RFA with UGFS.

Technical success

There was no clear benefit to either treatment in technical success up to 5 years (OR 5.21, 95% CI 0.25 to 109.48; 1 study, 292 participants; Analysis 7.1) with a notably wide CI.

Rasmussen 2011 also reported on long-term technical success with a possible benefit to RFA treatment detected (OR 3.23, 95% CI 1.32 to 7.89; 1 study, 291 participants; Analysis 7.2).

Recurrence

Rasmussen 2011 evaluated recurrence in RFA against UGFS at three years, and results show no clear difference (OR 0.81, 95% CI 0.41 to 1.62; 1 study, 291 participants; Analysis 7.3).

Five-year comparison data was also available and again showed no clear difference (OR 0.61, 95% CI 0.33 to 1.16; 1 study, 291 participants; Analysis 7.4).

Post-operative complications

One participant developed an iliac vein thrombosis and subsequent pulmonary embolus one week post-UGFS. Equal levels of hyperpigmentation were seen between groups. More episodes of phlebitis were recorded in the UGFS group than in RFA (12 versus 17). See Table 10 and Table 11.

Quality of life

Rasmussen 2011 did not present data but reported that "for all groups in all domains there was statistically significant improvement in most scores from pre-treatment to one year. At three days participants treated with UGFS and RFA had significantly better scores for bodily pain, physical functioning and role-physical, this difference went by one month".

Pain

In Rasmussen 2011, the mean (SD) pain score (VAS) for the first 10 days post-procedure was 1.21 (1.72) and 1.6 (2.04) in RFA and UGFS, respectively.

Venous Clinical Severity Score (VCSS)

Mean (SD) VCSS at baseline was 2.95 (2.06) in RFA and 2.06 (1.45) in UGFS, reducing to 0.44 (1.82) and 0.15 (0.4), respectively, at three years. See Table 13.

Length of procedure

The length of procedure was recorded as 'surgeon's time' within the trial. The median surgeon's time for RFA was 27 minutes (range of 12 to 80 minutes) compared to 19 minutes (range of 5 to 145 minutes) with UGFS. See Table 14.

Duration of hospital stay

Rasmussen 2011 did not report upon duration of hospital stay.

Return to normal activities

The median time to return to normal activities was one day in both groups, with a range of 0 to 30 days. The median time to return to work was 2.9 days in both groups, with a range of 0 to 14 days in the RFA group and 0 to 33 days in the UGFS group. See Table 16.

Radiofrequency ablation (RFA) versus cyanoacrylate glue

Morrison 2015 was the only trial to compare RFA with cyanoacrylate glue.

Technical success

Morrison 2015 reported technical success at one and three months. We report the one-month results in this review as these are closest to the primary outcome of six-week technical success. There were increased occlusions in the cyanoacrylate glue group compared to RFA (OR 0.03, 95% CI 0.00 to 0.54; 1 study, 215 participants; Analysis 8.1). The two-year follow-up results (n = 171) found there to be equivalent technical success for cyanoacrylate glue: 82/86 (95.3%) and RFA: (94.0% (79/84). Follow-up data were also available for 36 months, and the study authors reported that at this time point, occlusion was comparable between cyanoacrylate glue (94.4%, 68/72) and RFA (91.9%, 68/74) (P = 0.75).

Recurrence

The two-year follow-up identified 12/86 recanalisations in the cyanoacrylate glue group and only 1/84 in the RFA group. This was non-inferior.

Post-operative complications

Within the first three months, three participants in each treatment group were reported to have paraesthesia. There were 16/84 episodes of phlebitis with RFA and 22/86 with cyanoacrylate glue. Between three and twelve months, there was one DVT within the RFA arm, one case of endovenous heat-induced thrombosis with RFA, and one participant with chronic phlebitis who had undergone cyanoacrylate glue. See Table 10 and Table 11.

Quality of life

Morrison 2015 demonstrated that at one year, QoL, as measured by the EQ-5D, increased by small and similar amounts in both RFA and cyanoacrylate glue groups (P = 0.12). At 36 months, there was no statistical difference between cyanoacrylate glue and RFA in both AVVQ (P = 0.45) and EQ-5D (P = 0.4). See Table 12.

Pain

Morrison 2015 found there was no difference in the pain experienced between the two treatment arms during the 24 hours before the day three visit (P = 0.36).

Venous Clinical Severity Score (VCSS)

VCSS was evaluated at baseline and was to found to have improved by approximately 3.5 points at three months (P > 0.01). Initial VCSS was 5.6 in RFA and 5.5 in cyanoacrylate glue, improving to 2 and 1.9, respectively. There was no difference between treatment groups. See Table 13.

Length of procedure

Mean procedural time was five minutes longer for cyanoacrylate glue (24 minutes) than RFA (19 minutes) (P < 0.01). See Table 14.

Duration of hospital stay

All interventions were undertaken as day case procedures.

Return to normal activities

Morrison 2015 did not evaluate post-operative return to activity.

Radiofrequency ablation (RFA) versus mechanochemical ablation (MOCA)

See Summary of findings 4.

Three studies compared RFA with MOCA (Lane 2017; MARADONA 2019; Vähäaho 2019).

Technical success

All three studies compared technical success rates in RFA and MOCA (Lane 2017; MARADONA 2019; Vähäaho 2019). Both Vähäaho 2019 and MARADONA 2019 reported on technical success at 30 days, while Lane 2017 reported technical success rates at 6 months. Following discussion between all review authors it was felt inclusion in meta-analysis was warranted. Meta-analysis showed no clear evidence of a benefit for RFA over MOCA (OR 1.76, 95% CI 0.06 to 54.15; 3 studies, 435 participants; low-certainty evidence; Analysis 9.1), noting the wide CI. We downgraded by two levels due to risk of bias concerns and inconsistency. A random-effects model was used as heterogeneity was detected (I^2 = 60%).

No long-term data were available.

Recurrence

All three studies compared recurrence rates for RFA versus MOCA (Lane 2017; MARADONA 2019; Vähäaho 2019). Meta-analysis did not show a clear benefit for one intervention over the other (OR 1.00, 95% CI 0.21 to 4.81; 3 studies, 389 participants; low-certainty evidence; Analysis 9.2). We downgraded by two levels due to risk of bias concerns and inconsistency. A random-effects model was used as heterogeneity was detected (I^2 = 67%).

No long-term data were available.

Post-operative complications

All three studies reported on complication rates, which were similar between treatment arms. In the MARADONA 2019 trial, there was one DVT at one year in the RFA group. Lane 2017 showed equal rates of DVTs between groups. In Vähäaho 2019, two participants who had undergone RFA were found to have sensory disturbance; none was seen in the MOCA group. We were unable to perform meta-analysis because the trials used different definitions and evaluated complications at different time points. We downgraded to very-low certainty evidence due to risk of bias concerns, inconsistency and possible publication bias. See Table 10 and Table 11.

Quality of life

All studies evaluated quality of life scores. For disease-specific quality of life (AVVQ), the Lane 2017 study authors report that there was no difference at any time point during the study. At one month, mean AVVQ was 12.1 (7.3 to 21.2) for MOCA versus 12.9 (6.6 to 20.4) for RFA (P = 0.80); and 11.8 (7.2 to 20.5) for MOCA versus 9.4 (3.6 to 21.4) for RFA at six months (P = 0.51). Between groups, there was no significant difference in EQ-5D QoL at one month (MOCA 0.76 (0.659

to 1.00) versus RFA −0.76 (0.69 to 1) (P = 0.94)); or at six months (MOCA 0.76 (0.69 to 1.00) versus RFA 0.76 (0.49 to 1.00) (P = 0.13)).

The MARADONA 2019 trial reported "no difference were observed between groups in drawn blocks and total AVVQ scores at 1- and 2-year follow-up". AVVQ improvement at one year was 90% in MOCA and 78% RFA (P = 0.19). At two years, this was 88% and 89%, respectively (P = 0.90). Participants who underwent RFA demonstrated an improvement in physical functioning at one year on the SF-36, whilst in MOCA, there were significant improvements in physical and social functioning, both physical and emotional role functioning, mental health and pain. In Vähäaho 2019, the mean AVVQ at baseline was 16.1 in EVLA participants and 15.8 in MOCA. By year one, all had improved and there was no statistically difference (mean AVVQ 5.3 in EVLA and 6.2 in MOCA; P = 0.90).

We downgraded the certainty of evidence by one level due to risk of bias concerns.

Pain

This was the primary outcome for Lane 2017. The study authors reported that the maximum periprocedural pain score, measured on a visual analogue scale, was significantly lower following MOCA (median 15 mm (IQR 7 mm to 36 mm)) compared with the score following RFA (34 mm (IQR 16 mm to 34 mm)) (P = 0.003). In the MARADONA 2019 trial, lower pain scores were seen in the first two weeks after MOCA. Median pain score in this group was 0.2 with a range of 0 to 0.8; and in participants undergoing RFA, the median pain score was 0.5 with a range of 0.2 to 1.3 (P = 0.01). However, the analgesic requirement was similar. Pain was evaluated using a visual analogue system (VAS) in Vähäaho 2019 and ranked from 0 to 10. During the procedure, the mean VAS pain score was 3.5 for RFA and 4.6 for MOCA (P = 0.12). The use of extra periprocedural sedative (propofol) was found to be significantly less in participants undergoing MOCA (P < 0.001) than in participants undergoing RFA. The use of fentanyl and diazepam periprocedurally did not differ between treatment groups (P = 0.11 and P = 0.41, respectively). Prior to discharge, pain scores were found to be similar between interventions (P = 0.18) as well as at one week (P = 0.92). The amount of post-operative analgesia consumed by participants did not differ (P = 0.12).

Venous Clinical Severity Score (VCSS)

Both Lane 2017 and MARADONA 2019 reported on VCSS. The Lane 2017 study authors reported that, between groups, there was no significant difference for VCSS at either one month (MOCA 2 (1 to 4) versus RFA 3 (1 to 5), P = 0.1); or six months (MOCA 2 (1 to 4) versus RFA 2 (1 to 5), P = 0.54)). MARADONA 2019 reported on the components of VCSS individually, precluding meta-analysis. They found no difference in VCSS between groups at baseline. Absolute VCSSs were similar in both arms at one and two years with a comparable improvement compared to baseline (P = 0.05). See Table 13.

Length of procedure

Only the MARADONA 2019 trial reported on this outcome, and showed that times were similar, with RFA taking an average of 13 minutes (range 4 to 85 minutes) and MOCA taking 12 minutes (range 5 to 45 minutes). See Table 14.

Duration of hospital stay

No study explicitly stated their rates of day case or inpatient procedures. See Table 15.

Return to normal activities

All studies reported on return to daily activities or work, with no difference found between participants within the RFA or MOCA arms. See Table 16.

Radiofrequency ablation (RFA) versus SFJ ligation and stripping (HL/S, surgery)

See Summary of findings 5.

Five studies compared RFA with SFJ ligation and stripping (EVOLVeS 2003; Helmy ElKaffas 2011; Rasmussen 2011; Rautio 2002; Subramonia 2010).

Technical success

Three studies comparing RFA with SFJ ligation and stripping reported on this outcome (EVOLVeS 2003; Rasmussen 2011; Rautio 2002). The EVOLVeS 2003 trial reported that in "many cases the GSV was completely obliterated by the intervention"; however, authors did not give actual figures to allow inclusion into the meta-analysis. Combining the under five year data from Rasmussen 2011 and Rautio 2002 showed no clear difference in the technical success of the two procedures (OR 5.71, 95% CI 0.64 to 50.81; 2 studies, 318 participants; low-certainty evidence; Analysis 10.1). We downgraded the certainty of the evidence from high to low due to risk of bias concerns and inconsistency, reflected in the wide CI.

Rasmussen 2011 reported data for over five years and no evidence of a difference was demonstrated (OR 0.88, 95% CI 0.29 to 2.69; 1 study, 289 participants; low-certainty evidence; Analysis 10.2).

Recurrence

Four studies assessed recurrence at two and three years for RFA versus SFJ ligation and stripping (EVOLVeS 2003; Helmy ElKaffas 2011; Rasmussen 2011; Rautio 2002). No clear difference was detected between the groups (OR 0.93, 95% CI 0.58 to 1.51; 4 studies, 546 participants; moderate-certainty evidence; Analysis 10.3). We downgraded the certainty of the evidence from high to moderate due to risk of bias concerns.

Rasmussen 2011 also reported long-term data, and a possible benefit to RFA treatment was seen (OR 0.41, 95% CI 0.22 to 0.75; 1 study, 289 participants; low-certainty evidence; Analysis 10.4).

Post-operative complications

All five studies reported complications. We were not able to undertake meta-analysis for complications because the trials used different definitions and time points. While the number of complications was low in the studies, surgery was associated with higher rates of wound problems, haematomas and saphenous nerve injuries within both the early and late comparisons. More phlebitis was seen with RFA. EVOLVeS 2003 reported more paraesthesia in participants undergoing RFA at one week (23.3%) compared to SFJ ligation and stripping (13.9%). In the SFJ ligation and stripping group, two participants developed wound infections; one settled with antibiotics while the other required surgical debridement and admission for intravenous

antibiotic therapy. Helmy ElKaffas 2011 found more cases of paraesthesia with RFA (10%) compared with SFJ ligation and stripping (3%), and more episodes of thrombophlebitis (six cases compared to none with SFJ ligation and stripping). There was one iliofemoral DVT with SFJ ligation and stripping and higher rates of haematoma (seen in 30 participants compared to one with RFA). Three participants developed groin infections requiring parenteral antibiotics. Rasmussen 2011 reported one case of popliteal vein thrombosis with SFJ ligation and stripping at one month. There were more cases of phlebitis following RFA (12) compared to SFJ ligation and stripping (five). Rautio 2002 reported more saphenous nerve injuries (23%) with SFJ ligation and stripping than RFA (13%), higher rates of haematomas were also seen (31% compared to 7% with RFA). Among the RFA group, 20% developed clinical thrombophlebitis and 7% had thermal skin injuries; no cases of either these complications were seen with SFJ ligation and stripping. Subramonia 2010 reported numbness in 49% of participants undergoing SFJ ligation and stripping at one week compared to 19% of those undergoing RFA. Groin wound problems were present in 17% of SFJ ligation and stripping participants while 11% of RFA participants had hyperpigmentation at initial follow-up. We downgraded the certainty of the evidence to very low due to risk of bias concerns, inconsistency, imprecision and possible publication bias. See Table 10 and Table 11.

Quality of life

Four studies evaluated QoL scores (EVOLVeS Study; Rasmussen 2011; Rautio 2002; Subramonia 2010). Rautio 2002 demonstrated improved QoL scores within all subgroups of RAND-36 (a validation version of the SF-36 for Finland), and reported that physical functioning was restored faster in the RFA group. Median difference from baseline for physical functioning/role functioning was 0 in RFA and five with SFJ ligation and stripping at four weeks. Subramonia 2010 showed significant improvement in AVVSS QoL scores following treatment, with no difference between the groups (mean improvement in QoL score was -9.12 in RFA compared to -8.24 with SFJ ligation and stripping). Using the Venous Insufficiency Epidemiological and Economics Study (VEINES)-QoL/Sym questionnaire (V-Q/SymQ) at five weeks, improvement was reported with RFA compared with SFJ ligation and stripping (mean improvement 12.62 versus 9.94; 95% CI -1.65 to 7.01; P = 0.22). The EVOLVeS Study reported significant improvement via the CIVIQ2 QoL tool (global score and bodily pain) in participants undergoing RFA at 72 hours and one week, with the mean difference in global score -3 and -9.2 in RFA compared with 13.3 and 3.7 with SFJ ligation and stripping. However, the magnitude of the difference was negligible by four months. The EVOLVeS Study adjusted their figures for the number of adjunctive procedures undertaken. Rasmussen 2011 found improved AVVQ from day three onwards, with no difference between groups at any time point (mean (SD) AVVSS at baseline was 18.74 (8.63) for RFA and 19.3 (8.46) for SFJ ligation and stripping, reduced to 4.43 (6.58) and 4.0 (4.87), respectively, at three years). Their SF-36 results demonstrated comparable short- and medium-term benefits overall. However, participants who underwent SFJ ligation and stripping had poorer bodily pain and physical function domains compared to participants in the RFA group in the three-day follow-up. This difference was not seen at one month. We downgraded the certainty of the evidence from high to moderate due to risk of bias concerns.

Pain

Four studies comparing RFA with SFJ ligation and stripping reported less post-operative pain and analgesic consumption within the RFA arm (EVOLVeS 2003; Rasmussen 2011; Rautio 2002; Subramonia 2010). The EVOLVeS 2003 study reported statistically significant differences in the pain scores recorded at 72 hours and one week post-intervention (P < 0.001, for both time points). Rautio 2002 found less ibuprofen consumption in RFA participants compared to surgical participants (average daily number of 600 mg ibuprofen tablets (SD) 0.4 (0.49) versus 1.3 (1.09); P = 0.004). Mean pain scores at rest, standing and walking in RFA participants were reported as lower than surgical participants. This was especially so between the fifth to fourteenth post-operative day. The average VAS (SD) score at rest was 0.7 (0.5) for RFA and 1.7 (1.3) for SFJ ligation and stripping; on standing, 1.3 (0.7) versus 2.6 (1.9), respectively; and on walking, 1.8 (0.8) versus 3 (1.8), respectively (Rautio 2002). In Rasmussen 2011, the mean pain (SD) score for the first ten days was 1.21 (1.72) in RFA and 2.25 (2.23) in surgery. The number of phlebectomies did not affect pain scores. In Subramonia 2010, the median pain score during the first week post-intervention was higher in surgical participants (P = 0.001), whilst the duration of analgesic consumption was lower for RFA participants (P = 0.001).

Venous Clinical Severity Score (VCSS)

Three studies reported on change in VCSS and demonstrated comparable rates of improvement between RFA and surgery (EVOLVeS 2003; Rasmussen 2011; Rautio 2002). We were not able to undertake meta-analysis for VCSS because the trials used different time points. EVOLVeS 2003 found improved changes in VCSS for RFA over SFJ ligation and stripping at 72 hours (P > 0.05) and one week (P > 0.5). This difference disappeared at subsequent follow-ups. In Rautio 2002, the average decrease (SD) in VCSS at three years was 4.3 (2.3) in RFA and 4 (1.2) after surgery (P = 0.7). Rasmussen 2011 reported that VCSS improved in all groups with no difference between groups at any time point. See Table 13.

Length of procedure

Five studies reported on the length of procedure but we were not able to undertake meta-analysis for length of procedure because the studies defined the procedure differently (EVOLVeS 2003; Helmy ElKaffas 2011; Rasmussen 2011; Rautio 2002; Subramonia 2010). EVOLVeS 2003 reported mean treatment time (SD) as 74 minutes (10) and 89 minutes (12) for RFA and SFJ ligation and stripping, respectively. In Helmy ElKaffas 2011, the mean (SD) procedure time was 40 (10) minutes for RFA and 45 (13) minutes for SFJ ligation and stripping. Rasmussen 2011 recorded the mean surgeon's time (range) as 27 (12 to 80) minutes for RFA and 32 (15 to 80) minutes for SFJ ligation and stripping. In Subramonia 2010, median theatre time (IQR) was 82 (73 to 91) minutes for RFA and 55 (48 to 63) minutes for SFJ ligation and stripping; procedural time was 76 (67 to 84) minutes for RFA and 48 (39 to 54) minutes for SFJ ligation and stripping. Mean operating time (SD) in Rautio 2002 was 75 (16.6) minutes in RFA and 57 (11) minutes for SFJ ligation and stripping. See Table 14.

Duration of hospital stay

Three studies reported on duration of hospital stay (EVOLVeS 2003; Helmy ElKaffas 2011; Rautio 2002). EVOLVeS 2003 reported that 95% of their RFA procedures were day case compared to 86% with SFJ ligation and stripping. In Rautio 2002, one participant in

each treatment group stayed overnight for social reasons; 93.3% of RFA procedures were undertaken as day case and 92.3% with SFJ ligation and stripping. Helmy ElKaffas 2011 reported that RFA participants stayed in hospital for 14 hours (SD 3.6 hours (range 12 to 18 hours)), as compared to 30 hours (SD 11.5 hours (range 18 to 48 hours)) with SFJ ligation and stripping. See Table 15.

Return to normal activities

Five studies reported on return to normal activities, but we were not able to undertake meta-analysis due to differing measurements used (EVOLVeS 2003; Helmy ElKaffas 2011; Rasmussen 2011; Rautio 2002; Subramonia 2010). In EVOLVeS 2003, mean return to normal activities was adjusted for the type of anaesthetic and number of adjunctive procedures. The study reported that participants who were given general anaesthesia took longer to return to work. Mean return to normal activities was 1.15 days with RFA and 3.89 days with SFJ ligation and stripping; return to work was 4.74 and 12.4 days, respectively. In Helmy ElKaffas 2011, time to return to normal physical activity was three (SD 3) days for RFA and seven (SD 2.6) days for SFJ ligation and stripping. Median time to resume work in Rasmussen 2011 was 2.9 days (range 0 to 14 days) for RFA compared to 4.3 days (range 0 to 42 days) in SFJ ligation and stripping; return to normal activities was one day (range 0 to 30 days) in RFA and four days (0 to 30 days) with SFJ ligation and stripping. Rautio 2002 found mean sick leave was shorter with RFA, with a mean of 6.5 (SD 3.3) days taken compared with 15.6 (SD 6) days with SFJ ligation and stripping. In Subramonia 2010, mean return to work and normal activities was 10 days (IQR 4 to 13 days) and three days (IQR 0 to 7) with RFA compared to 18.5 days (IQR 11 to 28) and 12.5 days with SFJ ligation and stripping of GSV respectively. See Table 16.

Ultrasound-guided foam sclerotherapy (UGFS) versus SFJ ligation and stripping (HL/S, surgery)

See Summary of findings 6.

Four studies compared ultrasound-guided foam sclerotherapy to SFJ ligation and stripping (FOAM 2010; Magna 2013; Rasmussen 2011; Vernermo 2016).

Technical success

All four studies assessed technical success between UGFS and SFJ ligation and stripping (FOAM 2010 (two years); Magna 2013 (one year and five years); Rasmussen 2011 (one month and five years); and Vernermo 2016 (one year and five years). Pooling the early data shows a possible benefit for SFJ ligation and stripping compared to UGFS (OR 0.32, 95% CI 0.11 to 0.94; 4 studies, 954 participants; low-certainty evidence; Analysis 11.1). This indicates UGFS may be inferior to surgery. Heterogeneity was detected so a random-effects model was used (I^2 = 78%). We downgraded the certainty of the evidence from high to low due to risk of bias concerns and inconsistency.

Three studies reported data for over five years (Magna 2013; Rasmussen 2011; Vernermo 2016). In the more than five-year follow-up, the probability of technical success was lower in the UGFS than the SFJ ligation and stripping group (OR 0.09, 95% CI 0.03 to 0.30; 3 studies, 525 participants; moderate-certainty evidence; Analysis 11.2). Heterogeneity was detected so a random-effects model was used (I^2 = 73%). We downgraded the certainty of the evidence due to risk of bias concerns.

Recurrence

Three trials compared recurrence in UGFS and SFJ ligation and stripping between one and three years (FOAM 2010; Magna 2013; Rasmussen 2011). Pooling the data did not show a clear difference (OR 1.81, 95% CI 0.87 to 3.77; 3 studies, 822 participants; low-certainty evidence; Analysis 11.3).

Five-year data were also available from these studies and, again, no clear difference was detected (OR 1.24, 95% CI 0.57 to 2.71; 3 studies, 639 participants; low-certainty evidence; Analysis 11.4).

Heterogeneity was detected so a random-effects model was used (I^2 = 72% and I^2 = 76%, respectively). We downgraded the certainty of the evidence from high to low due to risk of bias concerns and inconsistency.

Post-operative complications

All four studies reported on complication rates (FOAM 2010; Magna 2013; Rasmussen 2011; Vernermo 2016). FOAM 2010 reported a higher rate of phlebitis with UGFS (17 participants out of 230) compared to none with SFJ ligation and stripping. Six of 200 participants who underwent SFJ ligation and stripping developed paraesthesia compared to none with UGFS. There was one DVT and one PE in the UGFS group one week post-procedure. At two years, hyperpigmentation was seen in 12 of the 213 UGFS participants and in two of 200 in the SFJ ligation and stripping group. In Magna 2013, the frequency of reported complications was low, with one reported case of paraesthesia following UGFS and four with SFJ ligation and stripping at three months; and one reported case in each group at one year. Magna 2013 reported three cases of wound infection in the SFJ ligation and stripping arm and none in the UGFS arm. Rasmussen 2011 reported one DVT in each group at one month. Rates of phlebitis were higher with UGFS (17 cases compared to 12 in SFJ ligation and stripping), whilst more participants who underwent SFJ ligation and stripping had paraesthesia at one month (six participants versus two with UGFS). Vernermo 2016 reported at one month that skin pigmentation was more common after UGFS (67%) compared to SFJ ligation and stripping (5%); rates of paraesthesia were comparable (2% vs 3%); and 91% of participants who underwent UGFS had palpable lumps compared to 54% with SFJ ligation and stripping. We downgraded the certainty of the evidence from high to very low due to risk of bias concerns, inconsistency and possible publication bias. See Table 10 and Table 11.

Quality of life

None of the four included studies showed any difference in QoL scores between the two treatment groups. The FOAM 2010 study found no difference in improvement between EQ-5D scores at two years. The change from baseline to two years was 0.064 and 0.061 in UGFS and SFJ ligation and stripping, respectively (P = 0.89). Magna 2013 excluded participants who had undergone bilateral interventions from their analysis, and reported that CIVIQ and EQ-5D improved in all groups with no difference seen at two years. Rasmussen 2011 reported no significant difference between groups in the improvement of the SF-36 score at one month. Vernermo 2016 reported no difference between treatment groups in AVVSS at one year, and similarly at five years, the mean AVVSS was 11.2 (95% CI 8.5 to 14) in the UGFS group and 8.7 (95% CI 6.7 to 10.7) in the SFJ ligation and stripping (P = 0.64). We downgraded the certainty of the evidence from high to moderate due to risk of bias concerns.

Pain

Three studies evaluated pain between UGFS and SFJ ligation and stripping treatment groups (FOAM 2010; Rasmussen 2011; Vernermo 2016). Rasmussen 2011 reported that participants who underwent UGFS had less post-operative pain than those who had surgery: mean (SD) score during the first ten days was 1.6 (2.04) in UGFS, and 2.25 (2.23) for surgery (P < 0.001). The number of phlebectomies was not found to alter pain scores. Vernermo 2016 also showed participants had a lower VAS pain score after UGFS, both at discharge and one week post-procedure. FOAM 2010 found that the intervention did not greatly influence pain, with similar scores for 'more', 'stable' or 'less' pain at 3, 12 and 24 months, for both surgery and UGFS.

Venous Clinical Severity Score (VCSS)

Two studies reported on change in VCSS (FOAM 2010; Rasmussen 2011). In FOAM 2010, no difference was detected at different time points. At baseline, the mean (SD) VCSS was 3.2 (1.9) in UGFS and 3.5 (2.2) in SFJ ligation and stripping. This score had improved in both groups to 1.7 (1.2) and 1.9 (1.4), respectively, at two years. By eight years, VCSS had deteriorated to 5.4 (3.3) and 4.6 (2.9) in each group, showing regression to worse scores when compared to baseline. Rasmussen 2011 reported that the VCSS score improved in both groups, with no difference between groups at any time point over three years. See Table 13.

Length of procedure

Rasmussen 2011 was the sole study to evaluate length of procedure as surgeon's time. Mean surgeon's time (range) in the UGFS group was 19 (5 to 145) minutes compared to 32 (15 to 80) minutes in SFJ ligation and stripping. See Table 14.

Duration of hospital stay

Only FOAM 2010 reported duration of hospital stay, with 100% of cases undertaken as day cases. See Table 15.

Return to normal activities

Two trials reported on return to normal activities, with participants undergoing UGFS possibly returning to normal activities faster. Rasmussen 2011 reported a median (range) return to work of one (0 to 21) day with UGFS, and 12 (0 to 33) days with SFJ ligation and stripping. Vernermo 2016 reported median (range) sick leave of 2.9 (0 to 33) days with UGFS and 4.3 (0 to 42) days with SFJ ligation and stripping. See Table 16.

Reporting bias and subgroup analysis

As none of the analyses included more than the ten studies required to create meaningful funnel plots, we could not evaluate reporting bias. None of the studies presented outcome data by the predefined variables of interest, so we did not perform subgroup analysis.

Sensitivity analysis

We planned to carry out sensitivity analyses by excluding studies that had a high risk of bias in four or more bias domains. Only one study, Calik 2019, had four or more bias domains at high risk. As this study was the only study in the comparison 'EVLA versus cyanoacrylate glue', we were unable to carry out this analysis.

DISCUSSION

Summary of main results

This Cochrane Review included 24 studies with a total of 5135 randomised participants. Some studies involved multiple comparisons of interventions (Magna 2013; Rasmussen 2011; Vähäaho 2019; Vernermo 2016), or a comparison group not included in our analysis (Flessenkämper 2013). The duration of follow-up ranged from five weeks (Subramonia 2010), to eight years (FOAM 2010). We did not find studies to provide results for all possible comparisons, especially newer treatments (see Types of interventions). Single studies provided evidence for five comparisons. When more than one study reported on a particular comparison, we were only able to pool the outcomes of technical success and recurrence due to heterogeneity in how the studies defined outcomes and reported time points. All studies had some risk of bias concerns. This has limited our ability to draw firm conclusions. Below, we report on the clinically most relevant comparisons. Details for all comparison and outcomes can be found in the Effects of interventions section.

EVLA versus RFA

See Summary of findings 1.

Five studies reported on technical success (Nordon 2011; Rasmussen 2011; Recovery 2009; Shepherd 2010; Syndor 2017). Their data demonstrated that the rate of technical success was comparable between RFA and EVLA to five years (OR 0.98, 95% CI 0.41 to 2.38; 5 studies, 780 participants; moderate-certainty evidence; Analysis 1.1).

Only Rasmussen 2011 provided data for long-term technical success, and no evidence of a difference in success rates was seen (OR 0.85, 95% CI 0.30 to 2.41; 291 participants; low-certainty evidence; Analysis 1.2).

Only Rasmussen 2011 reported on recurrence and there was no clear difference between the groups at three years (OR 1.53, 95% CI 0.78 to 2.99; 291 participants; low-certainty evidence; Analysis 1.3). Five-year recurrence rates were also reported and favoured RFA (OR 2.77, 95% CI 1.52 to 5.06; 291 participants; low-certainty evidence; Analysis 1.4).

Complication rates were recorded by all five studies using different definitions and time points, which prevented meta-analysis. Results of individual studies were inconsistent with each other, so we are not able to draw any conclusions (very low-certainty evidence).

The included trials used different QoL questionnaires at different time points, so we decided it was inappropriate to combine these for meta-analysis. Improvement in QoL scores over follow-up were similar between the two procedures in Nordon 2011, Rasmussen 2007 and Shepherd 2010. Recovery 2009 reported improved global QoL scores in the RFA group at 7 and 14 days post-operation compared to EVLA, but by one month they were comparable. Syndor 2017 did not evaluate QoL measures in their study. We assessed the certainty of the evidence for this outcome as low.

All studies reported reduced pain in the RFA groups compared to EVLA. Nordon 2011 showed RFA participants took less analgesia during the week post-procedure and post-procedural pain scores

were less following RFA at days one, three and seven. In Rasmussen 2011, mean pain scores on VAS at ten days were less in the RFA group compared to EVLA. Recovery 2009 reported significantly lower pain levels on VAS in participants who had RFA, at 48 hours, one week and two weeks. Shepherd 2010 reported lower mean (SD) VAS in RFA over the first ten days compared to EVLA, and a lower consumption of analgesic tablets over three days. In Syndor 2017, the median post-procedural pain scores on a scale of one to ten were worse in the EVLA group compared to RFA, on initial evaluation.

Four trials reported on change in VCSS, showing comparable rates between both groups at final follow-up (Rasmussen 2011; Recovery 2009; Shepherd 2010; Syndor 2017). Rasmussen 2011 reported that the VCSS improved significantly in all groups ($P < 0.001$), with no difference between groups at any evaluated time point through three years. Recovery 2009 reported no difference between treatment groups at baseline, and reduced VCSS scores in the RFA group compared with EVLA at 48 hours, one week and two weeks, but no difference was detected by one month. In Shepherd 2010, VCSS was comparable between the two groups at six months. Syndor 2017 found participants in both groups demonstrated a reduction in VCSS at six months from baseline. See Table 13 .

The duration of the procedure was similar in the three reporting studies. However, the reporting trials used different time points, metrics and terminology, impeding analysis (Nordon 2011; Rasmussen 2011; Syndor 2017). See Table 14 .

Shepherd 2010 was the sole trial to explicitly state that all procedures were intended to be day cases. However, 3.1% of participants required inpatient admission. See Table 15.

Three trials reported on return to work and normal activities (Nordon 2011; Rasmussen 2011; Shepherd 2010). Results were comparable between treatment groups but studies evaluated this outcome by different means, making it difficult to draw conclusions. See Table 16.

It is worth noting that we compared studies on a statistical front only. There are a number of radiofrequency devices historically available, and the same is true for laser devices. We did not sub-define these modalities.

EVLA versus EVSA

Only one study compared EVLA and EVSA (LAST 2014). At one year, rates of technical success were comparable between high dose EVSA and EVLA (OR 1.94, 95% CI 0.53 to 7.15; 166 participants; Analysis 2.1). No long-term data were available.

Complication profiles were similar between both treatment groups, as were reports of QoL. For QoL, LAST 2014 evaluated AVVQ, EQ-5D and EQ VAS at baseline and after 12 weeks; improvement in scores were found to be comparable between EVLA and EVSA groups.

Participants who underwent EVSA reported less post-procedural pain and had a shorter duration of analgesic consumption than participants who had EVLA. Convalescence was measured as the number of days lost from work or normal activities, with participants in the EVSA group returning to normal activity faster than those in the EVLA group. Rates of recurrence, length of procedure and duration of hospital stay were not reported.

EVLA versus UGFS

See Summary of findings 2.

Three studies compared EVLA with UGFS (Magna 2013; Rasmussen 2011; Vernermo 2016). Technical success may be improved in participants undergoing EVLA, both up to five years (OR 6.13, 95% CI 0.98 to 38.27; 3 studies, 588 participants; low-certainty evidence; Analysis 3.1), and over five years' follow-up (OR 6.47, 95% CI 2.60 to 16.10; 3 studies, 534 participants; low-certainty evidence; Analysis 3.2).

Two studies evaluated recurrence (Magna 2013; Rasmussen 2011), and showed no clear difference between the groups (OR 0.68, 95% CI 0.20 to 2.36; 2 studies, 443 participants; very low-certainty evidence; Analysis 3.3). Five-year recurrence rates were also available for both studies, and again no clear differences were seen (OR 1.08, 95% CI 0.40 to 2.87; 2 studies, 418 participants; very low-certainty evidence).

All three studies reported on post-operative complications. However, meta-analysis was impeded because the studies used different definitions of complications and assessed complications at varying time points. Rasmussen 2011 reported more phlebitis and hyperpigmentation rates amongst the UGFS group compared to the EVLA group. In Vernermo 2016, skin pigmentation was more common in the UGFS arm compared to EVLA, but haematomas were seen more often after EVLA compared to UGFS at one month. Magna 2013 reported two cases of hyperpigmentation in EVLA participants compared to one case in UGFS at three months (very low-certainty evidence).

Each of the three studies evaluated QoL using different questionnaires at different time frames. No differences were detected beyond one month by any measurement (Magna 2013; Rasmussen 2011; Vernermo 2016). We assessed the certainty of the evidence for this outcome as moderate.

Two studies evaluated pain scores, with both reporting lower post-procedural pain with UGFS compared to EVLA treatment (Rasmussen 2011; Vernermo 2016).

Only Rasmussen 2011 analysed VCSS, finding no difference between treatment arms at any evaluated time point.

Again, Rasmussen 2011 was the sole study which evaluated length of procedure as surgeon's time. Mean surgeon's time was 26 minutes in EVLA (range 12 to 80 minutes) and 19 minutes in UGFS (range 5 to 145 minutes).

Participants undergoing UGFS returned to work faster in the two studies which reported this outcome. Rasmussen 2011 reported the median time to return to work (range) as 3.6 days (0 to 46 days) in the EVLA group and 2.9 days (0 to 42 days) in the UGFS group. The mean duration of sick leave in Vernermo 2016 was eight days in EVLA (range 0 to 29 days) and one day in UGFS (range 0 to 21 days). No studies reported on duration of hospital stay.

EVLA versus cyanoacrylate glue

Calik 2019 was the sole trial to evaluate EVLA against cyanoacrylate glue. The trial analysed occlusion rates at one, three, six and twelve months. There was no evidence of a difference in occlusion rates at one month (OR 0.33, 95% CI 0.01 to 8.03; 412 participants; Analysis 4.1). Similarly, results showed no evidence of difference in

recanalisation rates at one year (OR 2.59, 95% CI 0.50 to 13.49; 412 participants; Analysis 4.2).

Higher rates of post-procedural induration, bruising and paraesthesia were seen following EVLA at one week compared to cyanoacrylate glue, but there was no difference by the three-month time point, except for paraesthesia which was more common after EVLA. Two DVTs were found within the EVLA group. Both groups demonstrated improved QoL at follow-up, but there was no clear difference between the groups.

Calik 2019 evaluated periprocedural pain levels using the Wong-Baker FACES pain score. Pain scores were lower in the cyanoacrylate glue group at one week, but by three months they were comparable. There were improvements in VCSS in both groups post-operatively, although there was no evidence of a difference between groups.

The operative time was longer for EVLA than for cyanoacrylate glue, and there was a faster return to daily activities in the cyanoacrylate glue group. Calik 2019 did not evaluate duration of hospital stay.

EVLA versus MOCA

Vähäaho 2019 was the only trial which compared EVLA to MOCA. At one month, they found 100% occlusion rates of the GSV via DUS amongst both treatment groups. There were no long-term data available.

At one year, 100% of the participants who underwent EVLA treatment still had GSV occlusion, while ten participants in the MOCA treatment group showed recanalisation of the GSV (OR 0.06, 95% CI 0.00 to 1.14; 88 participants; Analysis 5.2).

Three participants in the EVLA group reported sensory disturbance at one year; no nerve injuries were seen in the MOCA group. There was one superficial infection seen in the MOCA treatment group. There was no evidence of a difference between the treatment groups in QoL at one year. The VAS pain score prior to discharge and at one week post-procedure was similar between treatment modalities, and there was no difference between the amount of painkillers required. Participants undergoing EVLA took a mean of 5.3 days sick leave compared to 4.3 days in those undergoing MOCA. Vähäaho 2019 did not report change in VCSS, duration of procedure and duration of hospital stay.

EVLA versus SFJ ligation and stripping (HL/S, surgery)

See Summary of findings 3.

Nine trials compared EVLA with SFJ ligation and stripping. There was a possible benefit to technical success at less than five years in the EVLA group (OR 2.31, 95% CI 1.27 to 4.23; 6 studies, 1051 participants; low-certainty evidence; Analysis 6.1). No clear difference in results were seen at five years and beyond (OR 0.93, 95% CI 0.57 to 1.50; 5 studies, 874 participants; low-certainty evidence; Analysis 6.2). We downgraded the certainty of the evidence from high to low due to risk of bias concerns and imprecision. See Summary of findings 3.

Seven studies analysed recurrence, showing it to be comparable between groups within three years post-intervention (OR 0.78, 95% CI 0.47 to 1.29; 7 studies, 1459 participants; moderate-certainty evidence; Analysis 6.3). Similar results were seen with five year data (OR 1.09, 95% CI 0.68 to 1.76; 7 studies, 1267 participants; moderate-certainty evidence; Analysis 6.4).

All studies reported on complications. However, the reporting studies used different definitions and evaluation time points, impeding accurate comparison of post-operative complications. Slightly higher rates of early haematomas and wound problems may be seen with SFJ ligation and stripping. EVLA may be associated with slightly higher rates of phlebitis. We assessed the certainty of the evidence for this outcome as very low.

All studies evaluated QoL scores using a variety of different questionnaires at variable time points, impeding accurate comparison. Rates of improvement were comparable between interventions in all studies (moderate-certainty evidence).

The studies analysed pain in a wide variety of ways, precluding accurate meta-analysis. The majority of studies reported comparable post-operative pain scores between interventions (Darwood 2008; Flessenkämper 2013; Rasmussen 2007; Rasmussen 2011; RELACS 2012). HELP-1 2011 reported higher pain scores and analgesic consumption with SFJ ligation and stripping. Pronk 2010 reported higher mean post-operative pain scores with EVLA.

Four trials reported change in VCSS, with comparable improvements in scores between interventions (Darwood 2008; HELP-1 2011; Rasmussen 2007; Rasmussen 2011).

Three studies measured length of procedure (non-comparably), using various different definitions and metrics, with no clear difference seen in the times taken (HELP-1 2011; Rasmussen 2011; Vernermo 2016).

Four trials conducted all their procedures as day case (Darwood 2008; Flessenkämper 2013; Pronk 2010; Rasmussen 2007). One study reported that 21% of participants required admission following SFJ ligation and stripping (HELP-1 2011).

Seven studies reported on time to return to work or normal activity. EVLA was associated with a quicker return to work and normal activity in three of the trials (Darwood 2008; HELP-1 2011; Vernermo 2016). Four studies reported comparable rates of return to work and normal activity (Pronk 2010; Rasmussen 2007; Rasmussen 2011; RELACS 2012). The disparity in methodology, definitions and metrics within the studies should be borne in mind before drawing conclusions.

RFA versus UGFS

Rasmussen 2011 was the sole study comparing these interventions. Technical success rates did not clearly favour one treatment compared to another, at up to 5 years (OR 5.21, 95% CI 0.25 to 109.48; 1 study, 292 participants; Analysis 7.1). There may be a benefit for RFA at five years (OR 3.23, 95% CI 1.32 to 7.89; 1 study, 291 participants; Analysis 7.2). Three- and five-year recurrence rates showed no clear difference between the treatment groups (OR 0.81, 95% CI 0.41 to 1.62; 1 study, 291 participants; Analysis 7.3; and OR 0.61, 95% CI 0.33 to 1.16; 1 study, 291 participants; Analysis 7.4, respectively).

One participant developed an iliac vein thrombosis and subsequent pulmonary embolus one week post-UGFS. Equal levels of hyperpigmentation were seen between groups. More episodes of phlebitis were recorded in the UGFS group than in RFA (12

versus 17). Rasmussen 2011 evaluated quality of life using the SF-36. There was no evidence of a difference in the mean (SD) pain score (VAS) between the RFA and UGFS groups during the first ten days post-procedure. It was noted that the number of concomitant phlebectomies did not alter the pain scores. The VCSS score improved in both groups, with no difference between groups at any time point over three years. No clear differences were detected in pain between groups. The VCSS reduced from baseline in both groups, with no clear difference between groups by three years. Rasmussen 2011 recorded the length of procedure as 'surgeon's time' within the trial, and there was no clear difference in procedure time between treatment groups. The return to normal activities and return to work time was comparable between groups. Rasmussen 2011 did not report upon duration of hospital stay.

RFA versus cyanoacrylate glue

Morrison 2015 was the only included trial comparing these interventions. There were increased occlusions in the cyanoacrylate glue group compared to the RFA group after one month (OR 0.03, 95% CI 0.00 to 0.54; 1 study, 215 participants; Analysis 8.1). The study reported a final time point of 36 months, showing comparable occlusions in cyanoacrylate glue (94.4%, 68/72) compared to RFA (91.9%, 68/74) (P = 0.75).

The two-year follow-up identified 12 recanalisations in the cyanoacrylate glue group and only one in the RFA group. Within the first three months, there were similar reports of paraesthesia and phlebitis between RFA and cyanoacrylate glue groups. QoL scores were seen to improve throughout the trial duration, and by three years, there was no clear difference between RFA and cyanoacrylate glue in both AVVQ (P = 0.45) and EQ-5D (P = 0.4). There was no difference in the pain experienced between the two treatment arms, or in VCSS between treatment groups. Mean procedural time was five minutes longer for cyanoacrylate glue (24 minutes) than for RFA (19 minutes) (P < 0.01). All interventions were undertaken as day case procedures. Morrison 2015 did not evaluate post-operative return to activity.

RFA versus MOCA

See Summary of findings 4.

Three trials compared RFA to MOCA (Lane 2017; MARADONA 2019; Vähäaho 2019). All three trials reported on technical success. Pooling the data showed no clear evidence of a benefit for RFA over MOCA (OR 1.76, 95% CI 0.06 to 54.15; 3 studies, 435 participants; low-certainty evidence; Analysis 9.1). No long-term data were available.

The evaluation of recurrence rates amongst the trials did not show a clear benefit for one intervention over the other (OR 1.00, 95% CI 0.21 to 4.81; 3 studies, 389 participants; low-certainty evidence; Analysis 9.2). No long-term data were available.

All three studies reported on complication rates, which were similar between treatment arms (very low-certainty evidence). All three studies reported on QoL and found no significant difference between treatment arms (moderate-certainty evidence).

All three studies evaluated rates of post-procedural pain, but the differing time points and assessment modalities prevented formal meta-analysis. Lane 2017 reported on maximum pain experienced (measured by VAS) and reported that it was significantly less in the MOCA group. MARADONA 2019 and Vähäaho 2019 showed similar rates of analgesic consumption post-operatively. The MARADONA 2019 study demonstrated lower median pain scores for MOCA during the first two post-operative weeks, while Vähäaho 2019 reported similar scores between the groups, using VAS, in the first post-operative week. Lane 2017 evaluated VCSS at one and six months, and MARADONA 2019 at one and two years. Both trials showed comparable improvement in VCSS between modalities. Only MARADONA 2019 reported on the duration of procedures, which showed they were similar. No study explicitly stated their rates of day case or inpatient procedures. All studies reported on return to daily activities or work, with no difference found between participants within the RFA or MOCA arms.

RFA versus SFJ ligation and stripping (HL/S, surgery)

See Summary of findings 5.

Five studies compared RFA with surgery (EVOLVeS 2003; Helmy ElKaffas 2011; Rasmussen 2011; Rautio 2002; Subramonia 2010).

Two studies reported data for technical success up to five years (Rasmussen 2011; Rautio 2002). No clear difference in technical success was detected between groups (OR 5.71, 95% CI 0.64 to 50.81; 2 studies, 318 participants; low-certainty evidence; Analysis 10.1). Rasmussen 2011 reported data for over five years, and no evidence of a difference was demonstrated (OR 0.88, 95% CI 0.29 to 2.69; 1 study, 289 participants; low-certainty evidence; Analysis 10.2).

Four studies compared recurrence rates between RFA and surgery (EVOLVeS 2003; Helmy ElKaffas 2011; Rasmussen 2011; Rautio 2002). No clear difference was detected between the groups at two and three years (OR 0.93, 95% CI 0.58 to 1.51; 4 studies, 546 participants; moderate-certainty evidence; Analysis 10.3). Long-term data were also reported by Rasmussen 2011, and a possible benefit to RFA treatment was seen (OR 0.41, 95% CI 0.22 to 0.75; 1 study, 289 participants; low-certainty evidence; Analysis 10.4).

All five studies reported complications, but meta-analysis was impeded because the studies used different definitions and evaluated complications at different time points. While the number of complications was low for all studies, surgery may be associated with slightly higher rates of wound problems, haematomas and saphenous nerve injuries within both the early and late comparisons. More phlebitis was seen after RFA (very low-certainty evidence). See Table 10 and Table 11.

Four studies evaluated QoL scores. The EVOLVeS Study reported improvement via the CIVIQ2 QoL tool (global score and bodily pain) in RFA over SFJ ligation and stripping at 72 hours and one week, but this difference was negligible by four months. Rautio 2002 demonstrated improved QoL scores within all subgroups of RAND-36 (a validation version of the SF-36 for Finland), and reported that physical functioning was restored faster in the RFA group. Subramonia 2010 did not demonstrate a clear difference in groups using V-Q/SymQ or AVVSS. Rasmussen 2011 found no difference in improvement between groups using the AVVQ and SF-36 by one month, but reported poorer bodily pain and physical function domains with SFJ ligation and stripping initially. Overall, we assessed QoL evidence as moderate-certainty.

Four studies reported on post-operative pain, with higher pain scores and analgesic consumption with SFJ ligation and stripping

compared to RFA (EVOLVeS 2003; Rasmussen 2011; Rautio 2002; Subramonia 2010).

Three studies reported on change in VCSS, and demonstrated comparable rates of improvement between RFA and surgery (EVOLVeS 2003; Rasmussen 2011; Rautio 2002).

Three studies indicated that RFA may be faster to perform, while two studies found surgery was faster. The discrepancy between the five trials reporting length of procedure may be due to the discrepancy in the definitions used (EVOLVeS 2003; Helmy ElKaffas 2011; Rasmussen 2011; Rautio 2002; Subramonia 2010). We cannot draw any conclusions.

Three studies reported on duration of hospital stay, and all five reported more hospital admissions for SFJ ligation and stripping (EVOLVeS 2003; Helmy ElKaffas 2011; Rautio 2002).

All five studies indicated that time to return to work and normal activities was shorter amongst participants who underwent RFA (EVOLVeS 2003; Helmy ElKaffas 2011; Rasmussen 2011; Rautio 2002; Subramonia 2010). However, this conclusion is tentative due to the lack of standardisation in the measurement of this outcome by reporting studies.

UGFS versus SFJ ligation and stripping (HL/S, surgery)

See Summary of findings 6.

Four studies compared ultrasound-guided foam sclerotherapy to SFJ ligation and stripping (FOAM 2010; Magna 2013; Rasmussen 2011; Vernermo 2016).

Pooling the early data shows a possible benefit for SFJ ligation and stripping compared to UGFS in technical success (OR 0.32, 95% CI 0.11 to 0.94; 4 studies, 954 participants; low-certainty evidence; Analysis 11.1). Similarly, in the more than five years follow-up, the probability of technical success is lower in the UGFS than the surgery group (OR 0.09, 95% CI 0.03 to 0.30; 3 studies, 525 participants; moderate-certainty evidence; Analysis 11.2).

Three trials compared recurrence in UGFS and SFJ ligation and stripping (FOAM 2010; Magna 2013; Rasmussen 2011). No clear difference was detected between the procedures at one and three years (OR 1.81, 95% CI 0.87 to 3.77; 3 studies, 822 participants; low-certainty evidence; Analysis 11.3), or after five years (OR 1.24, 95% CI 0.57 to 2.71; 3 studies, 639 participants; low-certainty evidence; Analysis 11.4).

All four studies reported on complication rates. We were not able to pool the data and cannot draw any conclusions because the trials reported different complications and time points (very low-certainty evidence).

The studies used a variety of QoL scores and time points to evaluate the interventions, preventing meta-analysis. No difference in QoL was detected between treatment groups in any of the studies during follow-up (moderate-certainty evidence).

Of the three studies evaluating pain between UGFS and SFJ ligation and stripping, two studies reported lower post-operative pain after UGFS (Rasmussen 2011; Vernermo 2016), and the other found pain was comparable between UGFS and SFJ ligation and stripping groups (FOAM 2010).

Two studies reported on change in VCSS, with no differences detected between groups at any time points in either study (FOAM 2010; Rasmussen 2011).

Rasmussen 2011 was the sole study which evaluated length of procedure as 'surgeon's time', with no clear difference detected between groups.

FOAM 2010 was the only study to report duration of hospital stay, with 100% of cases undertaken as day case.

Two trials reported on return to normal activities, with participants undergoing UGFS possibly returning to normal activities sooner (Rasmussen 2011; Vernermo 2016).

Overall completeness and applicability of evidence

We identified no RCTs for ten of the comparisons we hoped to review. We found only one RCT for the following comparisons: EVLA versus EVSA, EVLA versus cyanoacrylate glue, EVLA versus MOCA, RFA versus UGFS and RFA versus cyanoacrylate glue. The trial for EVSA did not report on recurrence rates. We identified no new trials for the comparison of RFA and SFJ ligation and stripping of GSV. This update included long-term follow-up data (greater than five years) on recurrence and technical success, which was not available in earlier versions of this Cochrane Review. The validity of this review has been hampered by lack of standardisation in the reporting of outcomes methods with regard to follow-up time points, metrics and terminology used by the included trials. This has significantly impeded our ability to perform accurate meta-analysis for the majority of outcomes, echoing the sentiments of the previous version of the review in 2014 (Nesbitt 2014). This review focused on the management of C2 to C4 grade varicose veins. We excluded varicose veins with healed ulcers (C5) or active ulcers (C6) from this Cochrane Review.

A number of studies included interventions for bilateral GSV incompetence, and this fact also hampered meta-analysis (Calik 2019; Darwood 2008; EVOLVeS 2003; LAST 2014; Magna 2013; Pronk 2010; Rasmussen 2007; Rasmussen 2011; Recovery 2009; Shepherd 2010; Subramonia 2010). In Darwood 2008, Pronk 2010, Rasmussen 2007, Rasmussen 2011 and Shepherd 2010, participants were randomised and received the same treatment on the same day, but trialists made no separate stratification of bilateral and unilateral participants. EVOLVeS 2003, LAST 2014 and Subramonia 2010 waited over six weeks (three months in LAST 2014) from the initial procedure to randomise the other limb. This reality brings into question the reliability of the results for these participants, as ongoing disease in the second untreated limb may have impacted on the QoL outcomes, and results cannot accurately represent the outcome of the intervention.

Studies reported different complications, used different definitions to describe complications (such as symptomatic DVT) and measured complications at different time points. In addition, the complications reported can vary by the extent of venous treatment or stripping. This Cochrane Review did not assess this variation, but it should be noted as an impact on the strength of the complication results.

Quality of life and patient-reported outcome measures are valuable metrics for assessing interventional success. Unfortunately, the studies included in this review employed a variety of quality of life tools, and reported them in different ways, meaning we could

not pool the results. This represents a significant limitation to the patient-level power of this review. Technical outcomes can be useful in guiding practitioners and patients alike, but more consistent and rigorous quality of life assessment would be of value in future venous literature.

Three studies allowed the inclusion of participants who had residual ultrasound-proven SFJ reflux despite previous surgery (Rasmussen 2007; Rasmussen 2011; Subramonia 2010). In Rasmussen 2011 and Rasmussen 2007, 5.6% and 16% of randomised limbs had recurrence, respectively. Subramonia 2010 gave no breakdown of participants. None of the studies provided stratification of these participants.

Some varicosities are not amenable to endovenous treatments (i.e. they are too tortuous or are greater than 1.2 cm in diameter with extensive superficial varicosities). These can only be treated with open surgical methods. Conversely, not all participants are able to undergo general anaesthesia and open surgery. Tumescent and non-tumescent techniques are now a feasible option in the treatment of venous insufficiency within this participant group.

Quality of the evidence

See Summary of findings 1; Summary of findings 2; Summary of findings 3; Summary of findings 4; Summary of findings 5; Summary of findings 6.

Overall, the lack of standardisation amongst trials for reporting their findings led to a lack of comparable data. This prevented meta-analysis for many outcomes. We downgraded the certainty of the evidence for all outcomes as a result of concerns about detection and performance bias arising from a lack of blinding in the majority of the included studies. Other risk of bias concerns arose from attrition bias (missing data not explained by the study authors) or other potential risk of bias concerns (reasons included evaluation of bilateral limbs, underpowered studies, participants also underwent phlebectomies, etc.; see Risk of bias in included studies). We downgraded some outcomes further for imprecision as they involved limited numbers of participants from a small number of studies. Where studies reported conflicting or heterogenous results for an outcome, we downgraded for inconsistency. For the outcome of complications, studies reported different complications, used different definitions to describe complications (such as symptomatic DVT) and measured these at different time points. It was not unusual for different studies to have effects in opposite directions for the same complication, or have wide confidence intervals. Therefore, for each comparison, we downgraded the certainty of the evidence for outcome complications by three levels (risk of bias concerns, inconsistency, imprecision and possible publication bias).

Potential biases in the review process

We excluded several trials as they treated both GSV and SSV but provided no subgroup analysis (See Excluded studies for further details).

Within this review, we used the number of participants analysed for meta-analysis as opposed to the number of participants randomised (as in the intention-to-treat method). This was due to discrepancies between the two numbers. Trials often noted that participants would drop out following randomisation as they were unhappy with the treatment arm to which they had been allocated (predominantly surgery).

As none of the studies which included bilateral treatment of varicose veins provided any stratification, we were unable to exclude them from this review. This has introduced a potential bias as simultaneous bilateral treatment of varicose veins impacts on outcome measures, such as procedural time, quality of life scores, pain and duration of hospital stay.

Agreements and disagreements with other studies or reviews

National Institute for Health and Care Excellence (NICE) guidelines recommend an hierarchical approach, with endothermal ablation preferred. According to the guidelines, if endothermal ablation is unsuitable, “offer ultrasound-guided foam sclerotherapy", and if "ultrasound-guided foam sclerotherapy is unsuitable, offer surgery” (NICE 2013a). These recommendations are based on cost-effectiveness analysis. The Gloviczki 2012 review of guidelines, recommended by the Society for Vascular Surgery (SVS) and the American Venous Forum (AVF) Venous Guideline Committee, reported that endovenous thermal ablation (EVLA or RFA) is preferential to SFJ ligation and stripping for the treatment of GSV incompetence (recommendation: GRADE 1 (strong), level of evidence: B (medium quality)). They did not support the use of one endothermal technique over another. UGFS was also suggested as an option to treat the incompetent saphenous vein; however, the recommendation for this was weak and based on low- to very low-quality evidence.

A meta-analysis by Kheirelseid 2018 compared long-term recurrence rates after conventional surgery versus endovenous treatments. This analysis included nine RCTs, including three trials rejected for this Cochrane Review because their comparisons did not meet the inclusion criteria of this Cochrane review (Disselhoff 2008; Disselhoff 2011; Kalteis 2015). In keeping with this Cochrane Review, Kheirelseid 2018 found no statistical difference between EVLA and surgery for recurrence (36.6% versus 33.3%, respectively; pooled RR 1.35, 95% CI 0.76 to 2.37; P = 0.3). UGFS had a higher recurrence rate than EVLA (68.6% versus 24.4%; RR 6.08, 95% CI 1.62 to 22.82; P = 0.007). Recurrence was lower in surgery participants compared to UGFS (68.6% versus 18.1%; RR 8.88, 95% CI 1.67 to 47.14; P < 0.01). UGFS was also found to be inferior to RFA. They, too, were unable to comment on QoL measures due to the heterogeneity of how this outcome was reported.

A meta-analysis by Hamann 2017 compared the five-year efficacy of surgery, endovenous laser therapy (EVLT, equivalent to EVLA) and UGFS. Their primary outcome was anatomical success, and secondary outcomes were recurrent reflux rate and changes in disease-specific QoL (AVVQ, CIVIQ). They included three RCTs and ten follow-ups of RCTs. Of these, seven are included within this review. In an attempt to overcome the wide variation of definitions of anatomical success and recurrent reflux, Hamann 2017 standardised the definitions to be able to pool the data together, which could significantly impact on the results. As reported in this review, UGFS was found to be inferior at five years compared to EVLA and HL/S with regard to anatomical success. Hamann 2017 demonstrated high rates of recurrent reflux. VCSS scores were comparable between EVLA and SFJ ligation and stripping.

AUTHORS' CONCLUSIONS

Implications for practice

Our conclusions are limited due to the small numbers of studies available for each comparison, especially newer treatments, and by differences in definitions used and time points reported. Technical success was broadly comparable between most modalities. EVLA may offer improved technical success compared to UGFS (low-certainty), or surgery (low-certainty); and surgery may have improved success compared to UGFS both under (low-certainty) and over five years (moderate-certainty evidence). Similarly, no evidence of a difference in recurrence rates was detected, except for a possible long-term benefit for RFA compared to EVLA (low-certainty), or compared to surgery (low-certainty evidence).

In the absence of better evidence, it is not currently possible to reach firm conclusions as to which of the methods reviewed are to be preferred in treating GSV varicosities. As well as variation in individual venous anatomy and vein size, there will also be significant variation in individual and surgeon preferences as to which procedure is preferred. More evidence is required before treatment modality recommendations for individuals with GSV varicosities can be made.

Implications for research

We identified no RCTs that met the inclusion criteria for 10 of our comparisons. This was particularly so for the newer therapies, with only one RCT for EVSA (which lacked data on recurrence rates) and a paucity of long-term data for MOCA and cyanoacrylate glue. Further research comparing these novel treatments with more conventional tumescent techniques, with longer-term follow-up and the inclusion of recurrence rates, is required.

The high recurrence rate after foam sclerotherapy seems to have been confirmed. Further research should be conducted on the requirement for re-treatment after foam sclerotherapy within the follow-up periods, and the subsequent cost implications of this, as this recurrence rate may reflect initial under-treatment. Some trials have reported on re-intervention rates for their comparisons, which could be included within subsequent updates of this review.

The vast majority of studies either performed phlebectomies or foam sclerotherapy to visible varicosities in addition to the intervention, either concomitantly or at a later date. This obviously impacted on the outcomes from the included trials. Further research is required on the optimum time to perform these procedures, and which groups need phlebectomies, if not all do.

Future trials should seek to standardise the clinical terminology of their outcome measures and the time points at which they are measured. Although we included 24 trials in this review, the ability to perform accurate meta-analysis of the majority of outcome measure (namely, complications, pain, VCSS, quality of life scores, return to normal function, duration of procedure and inpatient stay) was impeded due to lack of consistency in how they were reported. Only one trial was double-blinded. To improve the quality of the outcome measures, future trials should seek to blind the post-operative assessors to which intervention the participant has undergone, and to include the participant and not 'legs' with varicose veins, for clarity.

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* Indicates the major publication for the study

CHARACTERISTICS OF STUDIES

Characteristics of included studies *[ordered by study ID]*

Calik 2019

Study characteristics	
Methods	***Study design:*** single centre, prospective comparative (but used randomisation) ***Country:*** Turkey ***Setting/Location:*** Erzurum Regional Training and Research Hospital ***Source of funding:*** not stated ***Intention-to-treat analysis:*** not stated
Participants	***No of participants randomised:*** n = 400 participants, 412 procedures (EVLA = 200 (204 procedures) CA = 200 (208 procedures)) ***No of participants analysed:*** no cohort diagram EVLA = 200 (204 procedures) CA = 200 (208 procedures) ***Exclusions post-randomisation:*** not stated ***Losses to follow-up:*** "The 1, 3, 6 and 12 month follow-up visits and CDUS examinations were done in 181 (90.5%) patients in the CAA group and 174 (87%) in the EVLA group" ***Age - mean years (SD):*** EVLA 38.4 (11.9) CA 38.6 (11.6) ***Sex - F/M:*** EVLA 114/86 CA 109/91

Calik 2019 *(Continued)*

	No. bilateral limbs randomised: EVLA 4 CA 8 ***Inclusion criteria:*** aged 18-75 years with symptomatic varicose veins; CEAP C2-C5; GSV insufficiency 0.5 sec determined by CDUS; could come to follow-up examinations and mentally healthy to approve ***Exclusion criteria:*** saphenous vein duplication or accessory saphenous vein with venous insufficiency; advanced tortuous GSV; saphenous vein under 3 mm and over 15 mm diameter, history of DVT; active thrombophlebitis in deep or superficial veins; arterial insufficiency history or ABPI < 0.9; significant femoral or popliteal vein insufficiency; history of saphenous vein intervention (surgical, thermal or chemical ablation)
Interventions	***Treatment(s):*** EVLA - performed under mild sedation. 1470 nm radial tip laser inserted 2 cm below SFJ. TA administrated. EVLA catheter withdrawn at 2.08 cm ± 0.6 cm/sec, 15 W power applied with external pressure from the ultrasound probe. Elastic bandage applied for 1 to 4 days. Then compression stockings (20 - 30 mmHg) for one month. ***Control:*** CA - performed under mild sedation. GSV punctured, 0.035' guidewire placed, delivery catheter (CA delivery system (CADS)) inserted and placed 3 cm distal to SFJ, CA injected, delivery catheter pulled back at 2 cm/sec whilst compression with ultrasound probe applied. Injection/retraction process repeated until whole segment sealed. Elastic bandage (20-30 mmHg) applied for one day following. ***Duration:*** follow-up was at 1 day, week 1 and at 1, 3, 6, and 12 months
Outcomes	***Primary outcomes:*** it is not clear from the paper what the specific primary or secondary outcomes were. Calik states the aims of the study were to assess the safety and efficacy of the CA in GSV in comparison to EVLA, and to present both anatomic and clinical results of 12 months follow-up. They have reported on occlusion rates, recanalisation rates, post-procedural complications, pain scores procedural time, VCSS, quality of life measures via the CIVIQ and time to return to daily activity. ***Recurrence definition:*** reported on recanalisation but definition not given
Notes	Additional phlebectomies and treatment with UGFS allowed after 3 months Use of bilateral procedures which could impact upon outcome measures such as pain, quality of life and return to work

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Consecutive treatment methods were blindly assigned by using block randomisation.
Allocation concealment (selection bias)	Low risk	Sealed envelopes
Blinding of participants and personnel (performance bias) All outcomes	High risk	No blinding of participants or personnel
Blinding of outcome assessment (detection bias) All outcomes	High risk	No blinding of assessors
Incomplete outcome data (attrition bias) All outcomes	High risk	No consort diagram, losses to follow-up not discussed, difficult to decipher how many participants were analysed at each of the time frames.

Calik 2019 *(Continued)*

Selective reporting (reporting bias)	High risk	The specific outcomes of the study were not explicitly stated.
Other bias	High risk	No power calculation performed Use of bilateral procedures which could impact upon outcome measures such as pain, quality of life and return to work. No subanalysis of these participants performed. Definitions for occlusion, partial and total recanalisation never specified Use of the Wong-Baker FACES pain scale, which is a paediatric pain assessment scale.

Darwood 2008

Study characteristics	
Methods	***Study design:*** prospective, RCT ***Country:*** UK ***Setting/Location:*** hospital ***Source of funding:*** Promed (Bluntisham, UK) - sponsor had no input in study design, data collection, data analysis/interpretation or preparation of the manuscript ***Intention-to-treat analysis:*** no (one surgery participant had EVLT1 and was followed up in the laser cohort)
Participants	***No of participants randomised:*** total n = 118 participants (136 legs) (EVLT1 49 legs; EVLT2 42 legs; HL/S 45 legs) ***No of participants analysed:*** total n = 95 participants (114 legs) (EVLT1 42 legs; EVLT2 29 legs; HL/S 32 legs) ***Exclusions post-randomisation:*** seven participants (11 legs) withdrew from the study as not happy with their treatment allocation. Six participants were treated outside the study interval and were also excluded. ***Losses to follow-up:*** total n = 11 participants (EVLT1 5 legs; EVLT2 4 legs; HL/S 2 legs) ***Age* - median years (IQR):** EVLT1: 42 (30.5 - 54.5); EVLT2: 52 (35 - 59); HL/S: 49 (38.5 - 57.5) ***Sex - F/M*** : EVLT1: 22/16; EVLT2: 16/11; HL/S: 16/14 ***No bilateral limbs randomised:*** EVLT1 9, EVLT2 6, HL/S 4 ***Inclusion criteria:*** > 18 years of age; symptomatic varicose veins and primary SFJ incompetence (confirmed on DUS) ***Exclusion criteria:*** on warfarin; unsuitable for EVLT (tortuous GSV, large incompetent anterior accessory saphenous vein)
Interventions	***Treatment(s):*** 2 EVLT techniques: EVLT1: 12 W power with 1s laser pulses and 1s intervals between pulses; laser fibre withdrawn 2 - 3 mm during intervals EVLT2: 14 W continuous power and continuous laser withdrawal

Darwood 2008 *(Continued)*

	Both procedures performed with EVLT; Diomed, Andover, Massachusetts, USA ***Control:*** HL/S - open surgery; SFJ ligation, GSV stripping to knee level and multiple phlebectomies of varicosities ***Duration:*** follow-up at 1, 6, 12 weeks and 1 yr after treatment
Outcomes	***Primary outcomes:*** abolition of reflux in the treated segment of GSV and improvement in disease-specific QoL 3 months after treatment ***Secondary outcomes:*** post-procedure pain, time to return to normal activity and work, cosmesis, overall satisfaction at 3 months ***Recurrence definition:*** study authors state "This short-term study was not designed to assess recurrence rates"
Notes	Participants with bilateral veins were randomised once and received the same treatment simultaneously on each leg. Study authors reported difficulty recruiting participants to the study. They did not meet the sample sizes for their study groups to make their desired power calculations. Statistical tests for equivalence were therefore not performed.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Block randomisation using sealed envelopes. Randomisation was stratified by consultant 'to allow for any minor variations in technique'. No clear details on how this stratification was achieved
Allocation concealment (selection bias)	Low risk	Used sealed envelopes
Blinding of participants and personnel (performance bias) All outcomes	High risk	Not possible to blind investigators or participants. No blinding of participants
Blinding of outcome assessment (detection bias) All outcomes	High risk	No blinding of assessors
Incomplete outcome data (attrition bias) All outcomes	Low risk	Missing data are balanced across the groups, with similar reasons given for the missing data
Selective reporting (reporting bias)	Low risk	The pre-specified outcomes in the study protocol were reported in the pre-specified way
Other bias	Unclear risk	Study authors reported difficulty recruiting participants to the study. They declared that their sample sizes were insufficient to permit statistical testing for equivalence One participant randomised to surgery underwent laser, and was followed up in the laser cohort showing no analysis of intention to treat

Darwood 2008 *(Continued)*

	Some participants received bilateral treatment. Study authors stated these participant would receive the same treatment on both limbs. These participants who received bilateral treatment were not stratified in the results Some outcome measures can be affected by bilateral treatment e.g. QoL, pain, time to return to work etc. therefore introducing a bias Participants who underwent laser did not have concomitant mini-phlebectomies. This adds a potential confounding bias when analysing results of post-operative pain, time to return to work etc.

EVOLVeS 2003

Study characteristics	
Methods	***Study design:*** multicentre, prospective, RCT ***Country:*** France, Austria and USA ***Setting/Location:*** hospitals ***Source of funding:*** VNUS medical technologies provided financial support for data collection, clinical monitors and disposable catheters (RFA) free of charge ***Intention-to-treat analysis:*** no
Participants	***No of participants randomised:*** total n = 85 participants (86 limbs); RFA n = 45 (46 limbs); HL/S n = 40 (40 limbs) ***No of participants analysed:*** at 72 hs, total 80 legs (RFA 44 legs; HL/S 36 legs) at 4 months, total n = 79 (77 legs) (RFA 43 legs; HL/S 34 legs) at 2 ys, total n = 65 (65 legs) (RFA 36 legs; HL/S 29 legs) ***Exclusions post-randomisation:*** 3 participants refused surgery, 1 participant repeatedly DNA, 2 participants excluded from RFA due to inclusion criteria violation ***Losses to follow-up:*** yes: (a) clinical examination: 2 surgery and 1 RFA no follow-up at 4 months; (b) QoL questionnaires: surgery: 1 at 72 hrs, 4 at 4 months not completed. RFA: 1 at 72 hrs, 1 week, 3 weeks and 4 months not completed; at 1 yr 19 limbs in RFA and 16 limbs in HL/S were lost but at 2 yrs it improved with only 8 RFA and 7 HL/S losses ***Age - mean years (SD):*** RFA 49 (4); HL/S 47 (4) ***Sex - F/M:*** RFA 32/12; HL/S 26/10 ***No bilateral limbs randomised:*** RFA 1, HL/S 0 ***Inclusion criteria:*** reverse flow in GSV lasting > 0.5 s in standing position; age 21 - 80; CEAP classification C2, C3, C4; ambulatory status; segmental deep reflux allowable; saphenous vein diameter ≤ 1.2 cm in supine position; availability for follow-up visits (72 hrs, 1 week, 3 weeks, 4 months) ***Exclusion criteria:*** saphenous vein diameter > 1.2 cm or < 0.2 cm; duplication of saphenous trunk or incompetent accessory branch; SSV reflux; varices of the thigh; previous DVT; ABI < 0.9; axial deep venous reflux from groin through popliteal vein; tortuosity of GSV segment to be treated on basis of appearance and USS as unsuitable for catheterisation

EVOLVeS 2003 *(Continued)*

Interventions	***Treatment(s):*** GSV obliteration with RFA without high ligation of SFJ: used the Closure catheter and system (VNUS Medical Technologies) ***Control:*** HL/S: vein stripping (from knee or upper calf to the SFJ) with high ligation of SFJ ***Duration:*** follow-up was at 72 hrs, 1 week, 3 weeks, 4 months, 1 yr and 2 yrs
Outcomes	***Primary outcomes:*** it is not clear from the paper what the specific primary or secondary outcomes were. EVOLVeS was designed to compare procedure-related complications, participant recuperation and QoL outcomes ***Secondary outcomes:*** although it was not initially declared, the EVOLVeS trials later presented rates of neovascularisation in the groin and recurrence at 2 yrs ***Recurrence definition:*** new varicose veins below the knee
Notes	Two investigators audited the study's raw data handling and storage methods, data processing accuracy, and presentation of specific results. They reported all was in order and that the raw data reflected the results accurately. This was done at 4 months and 2 yrs post-data collection

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	'Randomisation was allocated via Internet' - no further details were given
Allocation concealment (selection bias)	Low risk	Allocation performed via the Internet
Blinding of participants and personnel (performance bias) All outcomes	High risk	Not possible to blind participants or operators. No blinding of participants
Blinding of outcome assessment (detection bias) All outcomes	High risk	No blinding of assessors
Incomplete outcome data (attrition bias) All outcomes	High risk	Details were provided on all missing outcome data; however, it led to an imbalance in the study treatment group There is also discrepancy with the missing outcome data and explanations of these missing data compared to the published two-year follow-up
Selective reporting (reporting bias)	Low risk	The pre-specified outcomes in the study protocol were reported in the pre-specified way
Other bias	Unclear risk	The RFA treatment cohort included one participant who underwent treatment of both limbs with a 3-month gap between treatments. The participant was only randomised once and each limb treated as a separate episode. All centres were established centres in the use of RFA and the company funded the research. No subjective data were reported. However, as in all of these studies, surgical technique and ultrasonographic results are operator-dependent.

Flessenkämper 2013

Study characteristics	
Methods	***Study design:*** multicentre, prospective, RCT ***Country:*** Germany ***Setting/Location:*** 1) Centre for Vascular Medicine, Helios Klinikum Emil von Behring, Berlin 2) Centre for Venous Diseases, Frieburg 3) Centre for Venous Diseases, Saarlois ***Source of funding:*** sponsored by Deutschen Gessellschaft für Phlebologie (DGP) ***Intention-to-treat analysis:*** not indicated
Participants	***No of participants randomised:*** total n = 449 (EVLT n = 142; EVLT+HL n = 148; HL/S n = 159). Details of the EVLT+HL group are reported here but were not used in this review. ***No of participants analysed:*** 100% at 2 months; 86% at 6 months; total n = 385 (EVLT n = 127; EVLT+HL n = 133; HL/S n = 128) ***Exclusions post-randomisation:*** not indicated ***Losses to follow-up:*** at 6 months EVLT n = 15; EVLT+HL n = 15; HL/S n = 39 ***Age - mean years (SD):*** EVLT 47.4 (12.9); EVLT+HL 48.7 (12.0); HL/S 47.7 (11.5) ***Sex - M/F:*** EVLT 45/97; EVLT+HL 37/111; HL/S 47/112 ***Inclusion criteria:*** people between 18 and 72 years old with clinical signs or symptoms of superficial venous insufficiency with proven reflux into GSV, with a life expectancy of more than 5 years; all people suitable for open and endoluminal therapy with diameter of GSV not exceeding 16 mm at a point 5 cm distal to the SFJ ***Exclusion criteria:*** previous surgery of the GSV was the only reported exclusion criteria
Interventions	***Treatment(s):*** EVLT: laser therapy with a 980 nm diode laser, used local tumescent and general anaesthesia EVLT with high ligation (EVLT+HL): EVLT performed combined with HL, under general anaesthesia. Both EVLT procedures performed with instruments from Biolitec Jena, Germany (30 W) ***Control:*** HL/S: resection of all branches down to the dorsal level of the femoral vein; under general anaesthesia ***Duration:*** follow-up at 2, 6, 12 and 24 months for re-examination, then followed participants as long as possible
Outcomes	***Primary outcomes:*** inguinal venous reflux after 2 yrs ***Secondary outcomes:*** peri-operative technical success rate, rate of hyperpigmentation and matting, neurological compilations, duration of compression therapy and lymphoedema, complications, post-operative ecchymosis, pain (visual analogue scale 1 -10) or discomfort, duration of disability, participant satisfaction, clinical severity (CEAP, VCSS, Hach classification, VDS) ***Recurrence definition:*** any reflux more than 0.5 s from the SFJ into the GSV, which was assessed by physicians by DUS ultrasound at 2-yr follow-up
Notes	May 2005 to July 2009 Reflux was defined as retrograde flow of > 0.5 s duration after Valsalva manoeuvre or manual compression and decompression of distal vein Nearly all participants were treated as inpatients

Flessenkämper 2013 *(Continued)*

All 3 groups had simultaneous mini-phlebectomies, as required

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Used lottery ticket box at central office and telephone randomisation
Allocation concealment (selection bias)	Low risk	Used central office and telephone randomisation
Blinding of participants and personnel (performance bias) All outcomes	High risk	No blinding of participants and personnel
Blinding of outcome assessment (detection bias) All outcomes	High risk	No blinding of assessor. "Because of the scars, blinding for the follow-up was not possible"
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Dropouts reported but no reasons given
Selective reporting (reporting bias)	Low risk	All outcomes reported on
Other bias	Unclear risk	Possibly underpowered; power calculation described a need for 469 participants, but only 449 were randomised Number of participants needing additional phlebectomies was not recorded, which could affect post-operative pain, QoL, etc.

FOAM 2010

Study characteristics

Methods	***Study design:*** multicentre, prospective RCT ***Country:*** the Netherlands ***Setting/Location:*** hospital outpatient dermatology and surgery departments (n = 3) ***Source of funding:*** the Netherlands Organization for Health Research and Development (ZonMw); sponsor had no input in study design, data collection, data analysis/interpretation or preparation of the manuscript ***Intention-to-treat analysis:*** no: "Only patients who underwent the allocated intervention were included in the analysis"
Participants	***No of participants randomised:*** total n = 460 (UGFS n = 233; HL/S n = 227) ***No of participants analysed:*** total n = 390 (UGFS n = 213; HL/S n = 177) ***Exclusions post-randomisation:*** UGFS n = 3; HL/S n = 27 ***Losses to follow-up:*** UGFS n = 17; HL/S n = 23

FOAM 2010 *(Continued)*

	Age - mean years (SD): UGFS 55.8 (13.4); HL/S 54.6 (13.4)
	Sex (F/M): UGFS 175/58; HL/S 162/65
	Inclusion criteria: people with primary GSV incompetence, presence of one or more venous symptoms in combination with incompetence of the SFJ and GSV; reflux time of more than 0.5 s; normal deep venous system on DUS imaging
	Exclusion criteria: people with an incompetent deep venous system; sign of a previous DVT on DUS imaging; an active ulcer; contraindication to the use of polidocanol
Interventions	***Treatment(s):*** UGFS: sclerosing foam was prepared with the double-syringe technique, applying a 1:4 ratio of sclerosant:air; the treatment was considered successful when the proximal GSV was completely filled with foam and maximal venospasm was achieved
	Control: HL/S: performed as day-case procedure under general or spinal anaesthesia; SFJ was ligated and the GSV divided and stripped to just below the knee
	Duration: follow-up at 3 months, 1 and 2 yrs. An eight year follow-up was performed but this was not in the original study protocol
Outcomes	***Primary outcomes:*** recurrence
	Secondary outcomes: recurrent reflux (irrespective of symptoms), reduction of symptoms, QoL (EQ-5D), adverse events, direct hospital costs, participant satisfaction
	Recurrence definition: defined as reflux longer than 0.5 s by DUS, combined with the presence of one or more venous symptoms
Notes	October 2005 to December 2007
	Phlebectomies: UGFS - as needed; HL/S - at discretion of the surgeon (UGFS n = 26; HL/S n = 87)

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	"… assigned randomly to UGFS or surgery using a computer-generated randomisation scheme with random permuted blocks of eight"
Allocation concealment (selection bias)	Low risk	Used computer-generated randomisation
Blinding of participants and personnel (performance bias) All outcomes	High risk	No blinding of participants and personnel
Blinding of outcome assessment (detection bias) All outcomes	High risk	In initial study (two-year follow-up), there was no blinding of the outcome assessors. At the subsequent eight-year follow-up, the vascular technicians performing the DUS examinations were blinded to previous treatments.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Dropouts and reasons were thoroughly reported
Selective reporting (reporting bias)	Low risk	All outcomes reported on

FOAM 2010 *(Continued)*

Other bias	Unclear risk	Mini-phlebectomies were performed at the operating surgeon's discretion and 26 people in the UGFS group received phlebectomies compared to 7 in the surgery treatment group; this could alter the pain and other outcomes. As seen in the commentary letter from MJ Gough at the end of the British Journal of Surgery publication (Gough 2012), there are concerns with the high incidence of recurrence in the surgery treatment group and the definition of recurrence solely as reflux; caution should be taken when interpreting data from this study.

Helmy ElKaffas 2011

Study characteristics	
Methods	***Study design:*** prospective, RCT ***Country:*** Egypt ***Setting/Location:*** not indicated ***Source of funding:*** not indicated ***Intention-to-treat analysis:*** not indicated
Participants	***No of participants randomised:*** total n = 180 (RFA n = 90; HL/S n = 90) ***No of participants analysed:*** at 24 months: total n = 162 (RFA n = 81; HL/S n = 81) ***Exclusions post-randomisation:*** it appears 2 were excluded from the RFA group, but no explanation; none excluded from HL/S ***Losses to follow-up:*** RFA n = 7; HL/S n = 9 ***Age - mean years (SD):*** RFA 33.1 (2.6); HL/S 34.9 (3.7) ***Sex - M/F:*** RFA 42/48; HL/S 45/45 ***Inclusion criteria:*** people with SFJ and great saphenous reflux on DUS, either in response to Valsalva manoeuvre or with standing manual compression and release ***Exclusion criteria:*** people with DVT or superficial venous thrombosis; people on anticoagulants; those with concomitant PAD, pacemakers or serious systemic disease; pregnant women; people with GSV lumen more than 18 mm in the thigh or extremely tortuous veins
Interventions	***Treatment(s):*** UGFS: RFA Closure system, using local (tumescent) anaesthesia, managed as day patients; ClosureSystem VNUS Medical Technologies Inc ***Control:*** standard surgical treatment (HL/S): saphenofemoral high ligation and great saphenous stripping at ankle (in 40 participants) and at knee level (in 50 participants), using general anaesthesia, managed as inpatients ***Duration:*** followed up after 1 week, 1 month, 6-month intervals for 24 months
Outcomes	***Primary outcomes:*** operative time, hospital stay, costs, short-term and mid-term complications, recurrence ***Recurrence definition:*** not provided
Notes	Conducted between May 2006 and January 2009

Helmy ElKaffas 2011 *(Continued)*

	No information was given on the inclusion or exclusion of participants with bilateral treatment; study authors have been contacted, but no response received Adjuvant stab phlebectomies were performed in n = 15 participants in RFA and n = 39 in the surgical group; all phlebectomies took place at the primary intervention. In addition, n = 24 participants required foam sclerotherapy for persistent veins following RFA; n = 0 required foam following HL/S.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	No description of sequence generation methods
Allocation concealment (selection bias)	High risk	Allocation concealment not described
Blinding of participants and personnel (performance bias) All outcomes	High risk	No blinding or participants or personnel
Blinding of outcome assessment (detection bias) All outcomes	High risk	No blinding of assessor
Incomplete outcome data (attrition bias) All outcomes	Low risk	Dropouts were reported and similar between groups, although reasons were not given
Selective reporting (reporting bias)	Low risk	All outcomes were reported on
Other bias	Unclear risk	Two operators performed RFA and just one performed HL/S; this could have led to enhanced outcomes; no indication was given about whether bilaterally treated participants were included or excluded, and how many between groups (study authors were contacted).

HELP-1 2011

Study characteristics

Methods	***Study design:*** single centre, prospective, RCT ***Country:*** UK ***Setting/Location:*** tertiary referral vascular surgical department ***Source of funding:*** internal university funding; Diomed/Angiodynamics provided 50% of a research nurse's salary over 12 months; sponsor had no input in study design, data collection, data analysis/interpretation or preparation of the manuscript ***Intention-to-treat analysis:*** yes
Participants	***No of participants randomised:*** total n = 280 (EVLT n = 140; HL/S n = 140) ***No of participants analysed:*** total n = 237 (EVLT n = 124; HL/S n = 113)

HELP-1 2011 *(Continued)*

	Exclusions post-randomisation: EVLT n = 1; HL/S n = 3 ***Losses to follow-up:*** EVLT n = 15; HL/S n = 24 ***Age - mean years (SD):*** EVLT 49 (14); HL/S 49 (13) ***Sex - F/M:*** EVLT 85/54; HL/S 90/47 ***Inclusion criteria:*** primary, symptomatic unilateral varicose veins with isolated SFJ incompetence, leading to reflux into the GSV; incompetence was defined as reflux of at least 1 s on spectral Doppler analysis; both surgeon and participant had to occupy position of equipoise for either procedure ***Exclusion criteria:*** previous treatment for ipsilateral varicose veins; deep venous incompetence or obstruction; age less than 18 years; pregnancy; impalpable foot pulses; inability to give informed consent
Interventions	***Treatment(s):*** EVLT (810 nm, bare-tipped): performed under local tumescent anaesthesia within an outpatient department; GSV was cannulated percutaneously; cannulation was performed laterally at the lowest point of demonstrable reflux; catheter positioned at the SFJ, aiming for a flush occlusion; bar-tipped 600 nm laser fibre was introduced and delivered energy using an 810 nm diode laser generator set to 14 W; Diomed/Angiodynamics, Cambridge UK ***Control:*** HL/S: all participants received general anaesthesia; flush SFJ ligation followed by ligation of all tributaries to second branch; inversion stripping of the GSV to the knee ***Duration:*** assessed at 1 week, 6 weeks, 3 months, 1 yr and 5 yrs. Have ethical approval up to 10-year time point
Outcomes	***Primary outcomes:*** QoL (UK SF-36 V1); recurrence ***Secondary outcomes:*** QoL (EQ-5D), AVVQ, severity of venous disease by CEAP and VCSS, post-operative pain scores (0 - 10 VAS scale), time to return to normal activity and work, participant satisfaction (0 - 10 scale) ***Recurrence definition:*** clinically evident varicose veins at least 3 mm in diameter and not present at 1 week or 6 weeks
Notes	September 2004 to March 2009 Concomitant phlebectomies were performed via stab incisions (EVLT n = 7; HL/S n = 10)

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	"Patients were randomised equally into two groups by means of sealed opaque envelopes, receiving either surgery or EVLA. Patients selected their own envelope in the clinic under the supervision of a research nurse". Does not adequately describe sequence generation
Allocation concealment (selection bias)	Low risk	Used sealed opaque envelopes
Blinding of participants and personnel (performance bias) All outcomes	High risk	No blinding of participants and personnel
Blinding of outcome assessment (detection bias) All outcomes	High risk	No blinding of assessor

HELP-1 2011 *(Continued)*

Incomplete outcome data (attrition bias) All outcomes	Low risk	Dropouts and reasons were thoroughly reported
Selective reporting (reporting bias)	Low risk	All outcomes reported on
Other bias	Unclear risk	Possibly underpowered; power calculation described a need for 120 participants in each group, but only 113 were available for follow-up in the surgery group

Lane 2017

Study characteristics	
Methods	***Study design:*** multicentre, randomised control trial ***Country:*** UK ***Setting/Location:*** Charing Cross Hospital (Imperial College Healthcare NHS Trust) and Northwick Park Hospital (London North West Healthcare NHS Trust) in London, UK ***Source of funding:*** the study author(s) disclosed receipt of the following financial support for the research, authorship, and/or publication of this article: "This study was supported by a research grant from the Clarivein device manufacturer, Vascular Insights and an educational research grant from the Graham-Dixon Charitable Trust. Vascular Insights provided funding for Clarivein devices, patient follow-up and DUS. Case funding was not used in this study. All trial particulars (design, data collection, analysis, discussion and data access) were performed independently of the funding bodies and the trial's research sponsor was Imperial College London." ***Intention-to-treat analysis:*** yes
Participants	***No of participants randomised:*** 170 ***No of participants analysed (n, %):*** 1 month follow-up 69 MOCA and 60 RFA (129, 79%), 6 months 121, 71% ***Exclusions post-randomisation:*** 0 ***Losses to follow-up (n, %):*** 1 month follow-up 69 MOCA and 60 RFA (129, 79%), 6 months 62 MOCA and 59 RFA (121, 71%) ***Age - median:*** 50 overall; MOCA 54.5, RFA 58 ***Sex - percent female:*** MOCA 57.5%, RFA 60.2% ***Inclusion criteria:*** people with symptomatic primary varicose veins with either great saphenous vein (GSV) incompetence (> 0.5 s reflux on colour DUS) ***Exclusion criteria:*** people with recurrent varicose veins, current deep vein thrombosis, arterial disease (ankle brachial pressure index < 0.8), veins < 3 mm in diameter or hypercoagulability were excluded from participation. Additionally, people unable or unwilling to complete questionnaires or to participate were also excluded.
Interventions	***Treatment(s):*** MOCA (Clarivein, Vascular Insights, USA), DUS guided cannulation. MOCA chemical-ablative catheter. ***Control:*** RFA Closure system, using local (tumescent) anaesthesia, managed as day patients; ClosureSystem VNUS Medical Technologies Inc

Lane 2017 *(Continued)*

	Duration: assessed at 1 month and 6 months.
Outcomes	***Primary outcomes:*** degree of pain experience during endovenous ablation using a validated patient-reported VAS and 0–10 number scale, prior to completion of any phlebectomies ***Secondary outcomes:*** improvement in patient-reported quality of life, both disease specific (Aberdeen Varicose Vein Questionnaire – AVVQ) and generic (EuroQol 5 Domain 3 Level – EQ-5D-3L and EuroQol VAS), clinical scores (Venous Clinical Severity Score – VCSS, Venous Disability Score – VDS and Clinical Etiology Anatomy Pathology score) and time taken to return to normal activities and work ***Recurrence definition:*** clinically-evident varicose veins at least 3 mm in diameter and not present at 1 month.
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	"Consenting participants were then randomised on the day of treatment to either MOCA (group one) or RFA (group two), using an online computerised randomisation software (SealedEnvelope, London, UK)"
Allocation concealment (selection bias)	Low risk	Methods of allocation concealment adequately described
Blinding of participants and personnel (performance bias) All outcomes	High risk	Given the nature of the interventions, blinding of the participant to the intervention allocated would be impossible.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	"blinded venous duplex ultrasound scanning"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Dropouts were reported and similar between groups, although reasons were not given
Selective reporting (reporting bias)	Low risk	All outcomes reported on
Other bias	Low risk	No other potential risk detected

LAST 2014

Study characteristics	
Methods	***Study design:*** prospective, multicentre, RCT ***Country:*** the Netherlands ***Setting/Location:*** Department of Dermatology, Erasmus MC University Medical Centre ***Source of funding:*** Erasmus Medical Centre ***Intention-to-treat analysis:*** no, per-protocol analysis

LAST 2014 *(Continued)*

Participants	***No of participants randomised:*** 237 legs (in 217 participants); EVLA n = 119/EVSA n = 118 ***No of participants analysed:*** EVLA = 110/EVSA = 117 ***Exclusions post-randomisation:*** 5 technical failures: 4 EVLA 1 EVSA, 5 EVLA withdrew after allocation ***Losses to follow-up:*** EVLA: 2 weeks = 1 (n = 109); 12 weeks = 6 (n = 104); 1 year = 18 (n = 92) EVSA: 2 weeks = 0 (n = 117); 12 weeks = 3 (n = 114); 1 year = 10 (n = 107) ***Age - mean years (SD):*** EVLA 55 (12); EVSA 56 (13) ***Sex (legs) - F/M:*** EVLA 62/48; EVSA 76/41 ***Inclusion criteria:*** > 18 years, informed consent and symptomatic primary incompetence of the GSV with reflux time exceeding 0.5 s and diameter 5 mm or more (at mid-thigh level) according to DUS examination ***Exclusion criteria:*** acute DVT or superficial vein thrombosis, agenesis of the deep venous system, vascular malformation or syndrome, PTS of the obstruction type, pregnancy, immobility, allergy to lidocaine and arterial insufficiency (ABI < 0.9)
Interventions	***Treatment(s):*** EVLA: tumescent anaesthesia, 940 nm diode laser using a bare fibre, a power setting of 12 W, delivering approximately 60 J/cm; medical elastic compression stockings for 1 week and to mobilise immediately ***Control:*** EVSA: tumescent anaesthesia, Steam Vein Sclerosis (SVS) system (cermaVEIN, Archamps, France). "For the first 36 procedures the treatment protocol was to apply 1 pulse/cm in veins smaller than 7 mm, 2 pulses/cm in veins of 7–10 mm, and 3 pulses/cm in veins larger than 10 mm. With insight and after temperature experiments, this was increased to 2, 3 and 4 pulses/cm respectively during the study." ***Duration:*** 2, 12 and 52 weeks post-intervention
Outcomes	***Primary outcomes:*** treatment success "Obliteration of the GSV and/or absence of reflux (more than 0.5 s of retrograde flow) along the treated segment of the GSV, according to DUS", VCSS ***Secondary outcomes:*** pain (VAS and 0 - 10 duration of painkiller use (ds)), satisfaction, convalescence, complications, changes in Health-related QoL (AVVQ), EQ-5D
Notes	November 2009 to 2011 Limbs not participants. "The legs of patients with bilateral GSV incompetence were included separately, provided that there was at least 3 months between the two treatments" "When needed, tributaries were treated with phlebectomies at least 3 months after EVLA or EVSA"

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	"Consenting patients were randomised to either EVLA or EVSA, using a computerized randomisation list"
Allocation concealment (selection bias)	Low risk	Used a computerised randomisation list
Blinding of participants and personnel (performance bias)	High risk	No blinding of participants and personnel

LAST 2014 *(Continued)*

All outcomes		
Blinding of outcome assessment (detection bias) All outcomes	High risk	No blinding of assessors
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Dropouts reported, no reasons given
Selective reporting (reporting bias)	Low risk	All outcomes reported
Other bias	Unclear risk	Possibly underpowered; needs 116 per study group – with dropouts had 92 and 107 in EVLA and EVSA, respectively Changed protocol for EVSA during study – increased amount of energy

Magna 2013

Study characteristics	
Methods	***Study design:*** sIngle-centre*, prospective, RCT (* second centre was added in May 2009 due to slow inclusion rate) ***Country:*** the Netherlands ***Setting/Location:*** Departments of Dermatology and Vascular Surgery in two hospitals ***Source of funding:*** Erasmus Medical Centre listed under Sponsors and Collaborators ***Intention-to-treat analysis:*** yes
Participants	***No of participants randomised:*** total n = 240 legs (EVLT n = 80 legs; UGFS n = 80 legs; HL/S n = 80 legs) ***No of participants analysed:*** total n = 223 legs (EVLT n = 78 legs; UGFS n = 77 legs; HL/S n = 68 legs) ***Exclusions post-randomisation:*** not indicated ***Losses to follow-up:*** total n = 1 (EVLT n = 0; UGFS n = 1; HL/S n = 0) ***Age - mean years (SD):*** EVLT 49 (15.03); UGFS 56 (13.30); HL/S 52 (15.59) ***Sex - M/F:*** EVLT 24/54; UGFS 25/52; HL/S 22/46 ***No bilateral limbs randomised:*** EVLT 16, UGFS 19, HL/S 17 ***Inclusion criteria:*** adults with symptomatic primary incompetent GSV at least above the knee with a diameter ≥ 0.5 cm; with an incompetent SFJ (incompetence defined as reflux ≥ 0.5 s at colour DUS ***Exclusion criteria:*** previous treatment of the ipsilateral GSV; deep venous incompetence or obstruction; agenesis of the deep system; vascular malformations; use of anticoagulant; pregnancy; heart failure; contraindication for one of the treatments; immobility; arterial insufficiency; age under 18 yrs; inability to provide written informed consent
Interventions	***Treatment(s):*** EVLT (940 nm diode laser): performed under UG tumescent anaesthetic UGFS: prepared foam made with 1 cc aethoxysclerol 3%, 3 cc air; if considered necessary procedure could be repeated after 3 months; no manufacturer information given

Magna 2013 *(Continued)*

	Control: HL/S: high ligation with short (above knee) stripping; performed under spinal or general anaesthesia ***Duration:*** evaluated at 3 months, 12 months and 5 yrs
Outcomes	***Primary outcomes:*** anatomic success according to DUS, neovascularisation ***Secondary outcomes:*** C of the CEAP classification; type and frequency of complications; QoL (CIVIQ and EuroQol-5D) ***Recurrence definition:*** for the UGFS and EVLT groups - flow or reflux of the GSV at midthigh; for surgery - presence of the GSV in the saphenous compartment at thigh level (both groups evaluated by clinical examination and DUS)
Notes	January 2007 to May 2010 Intention for additional phlebectomies was to perform during initial treatment, but in several cases were performed after 3 months (during initial treatment: EVLT n = 15; UGFS n = 0; HL/S n = 18; after 3 months: EVLT n = 12; UGFS n = 15; HL/S n = 11)

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	"...randomised using a computerized list by an independent research nurse."
Allocation concealment (selection bias)	Low risk	"...randomised using a computerized list by an independent research nurse."
Blinding of participants and personnel (performance bias) All outcomes	High risk	No indication of blinding of participants and personnel
Blinding of outcome assessment (detection bias) All outcomes	High risk	No indication of blinding of assessors
Incomplete outcome data (attrition bias) All outcomes	Low risk	Dropouts and reasons were thoroughly reported
Selective reporting (reporting bias)	Unclear risk	For complications, study authors stated they would report on migraine, skin burns, skin necrosis, and anaphylactic shock. No data were presented for these outcomes.
Other bias	Unclear risk	Possibly underpowered; power calculation described a need for 240 participants, but only 223 were analysed. Also unclear how QoL was evaluated for bilaterally treated participants - study authors do not clarify

MARADONA 2019

Study characteristics

Methods	***Study design:*** multicentre randomised control trial (single-blinded) ***Country:*** the Netherlands

MARADONA 2019 *(Continued)*

	Setting/Location: Department of surgery, Rijinstate Arnhem; Department of surgery, OLVG; Department of surgery, BovenIJ Hospital Amsterdam; Department of vascular surgery, St Antonius Hospital Nieuwegein; and the division of vascular surgery, UMCG, Groningen ***Source of funding:*** 'investigator-initiated study supported by Vascular Insights Ltd' ***Intention-to-treat analysis:*** yes
Participants	***No of participants randomised:*** n = 213 (using an online randomisation module with block randomisation per site); MOCA n = 107; RFA n =106 ***No of participants analysed:*** MOCA 1 yr analysed ITT n = 101 PP n = 99, 2 yr ITT n = 95, PP n = 93 RFA = 1 yr analysed ITT n = 99, PP n = 99, 2 yr ITT n = 97, PP n = 97 ***Exclusions post-randomisation:*** MOCA n = 5, RFA n = 3 ***Losses to follow-up:*** MOCA 1 yr n = 20, 2 yr n = 19; RFA 1 yr n = 32. 2 yr n = 16 ***Age - median years (IQR):*** MOCA 54.9 (16.3 - 81.2); RFA 53.4 (22.6 – 77.9) ***Sex percent female:*** MOCA 62.4; RFA 59.3 ***Inclusion criteria:*** GSV incompetence (> 3 mm and < 12 mm) with CEAP C2 to C5 ***Exclusion criteria:*** active ulcer, previous surgery or treatment of ipsilateral GSV, use of oral anticoagulants, pregnancy or lactation, previous DVT, immobilisation, contraindication or known allergy to sclerosant, coagulation disorders or increased risk of thromboembolism, severe renal or liver insufficiency and severe peripheral artery disease.
Interventions	***Treatment(s):*** MOCA USS guidance, Clarivein tip placed 5 mm below orifice of superficial epigastric vein or 2 cm below the SFJ. Wire activated for 10 sec, device withdrawn at speed of 7 s/cm while liquid sclerosant continuously injected using 2 mL of 3% polidocanol for first 10 cm - 15 cm and 1.5% for remainder. ***Control:*** RFA, Closure fast device positioned as above, TA (500 mL of NaCl including 20 mL of 8.4% sodium bicarbonate and 50 mL of lidocaine 1% with epinephrine 1:200,000 injected along entire segment) every 20 sec 7 cm segment of GSV treated after pullback. Most proximal segment treated twice. Both groups had compression stockings continuously for first 24 hr then daily for first 2 weeks ***Duration:*** 30 days (± 7 days), 1 yr (± 1 month), 2 yrs (± 2 months)
Outcomes	***Primary outcomes:*** post-procedural pain evaluated using 100-point visual analogue scale two weeks post procedure. Anatomic success at one year. ***Secondary outcomes:*** anatomic success, clinical success using VCSS, 30-day morbidity, disease-specific quality of life (AVVQ), general health-related (HR) QoL (SF-36), time to return to daily activities/work, re-intervention rate and additional varicose vein treatment during 2-year follow-up. ***Recurrence definition:*** recanalisation (failure of treatment) which could be complete or partial (> 10 cm) ***Success definitions:*** initial success of the procedure (i.e. catheter placed at defined location and GSV treated without technical problems). Anatomic success was occlusion of the treated GSV segment, objective by DUS. Failure of treatment is recanalisation which could be complete or partial (> 10 cm). Clinical success was defined as improvement in the VCSS of > 1 point. ***Duration:*** two years
Notes	***Phlebectomies:*** 'No concomitant phlebectomy or sclerotherapy was scheduled to be performed unless indicated by the treating physician'. In the MOCA group. 1 participant had phlebectomies, none did in the RFA arm

MARADONA 2019 *(Continued)*

Notes *:* Only managed to randomise 46.3% of intended. Reimbursement of MOCA was suspended and enrolment was stopped at the end of 2014; this was not reinstated for over a year. Trial was therefore advised by the ethics committee to terminate the study.

In both groups, 6 participants had adjunctive therapies; however, these were reported and sub-analysis done (median pain score similar).

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Randomisation performed using online randomisation module with block randomisation per site
Allocation concealment (selection bias)	High risk	Not stated
Blinding of participants and personnel (performance bias) All outcomes	High risk	No blinding
Blinding of outcome assessment (detection bias) All outcomes	Low risk	DUS was performed by vascular technicians who were blinded for treatment
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Dropouts recorded, no reasons provided; reported as 'unknown why'
Selective reporting (reporting bias)	Low risk	All outcomes reported
Other bias	Unclear risk	Sample size calculation to assess anatomical and clinical success rate at one year showed the need for 230 participants in each arm (accounting for a 10% dropout rate). Study only managed to recruit 46% of this number.

Morrison 2015

Study characteristics

Methods	***Study design:*** prospective, multicentre RCT for incompetent GSV (Veclose) ***Country:*** USA ***Setting/Location:*** 10 vein, dermatology and vascular clinics ***Source of funding:*** sponsored by Sapheon. Multiple authors work as consultants for Sapheon ***Intention-to-treat analysis:*** yes
Participants	***No of participants randomised total:*** n = 122; CA = 108; RFA = 114 ***No of participants analysed:*** CA = 108; RFA = 114 ***Exclusions post-randomisation:*** CA: 2 withdrawn; RFA: 4 withdrawn ***Losses to follow-up:*** CA = 2; RFA = 6 ***Intention-to-treat analysis:*** yes ***Age years (range):*** CA 49.0 (26.6 - 70.6); RFA 50.5 (25.6 - 70.1) ***Sex F/M:*** CA 83/25; RFA 93/21 ***No bilateral limbs randomised:*** 0

Morrison 2015 *(Continued)*

	Inclusion criteria: adults 21 - 70, symptomatic moderate to severe varicosities (CEAP C2 to C4B), incompetent GSV (reflux at least 0.5 s), ability to walk unassisted, able to attend follow-up, provide informed consent ***Exclusion criteria:*** haemodynamically significant reflux of SSV or anterior accessory vein, prior treatment of GSV, prior treatment of target GSV, symptomatic PAD (ABI < 0.89), history of DVT, PE, aneurysm of target GSV > 12 mm, life expectancy 1 yr, malignant disease, anticoagulation, known hypercoagulable states, pregnancy, peoples who require bilateral treatment within 3 months, people who require further ipsilateral treatment within 3 months
Interventions	***Treatment description:*** "Catheter inserted under high resolution US guidance to 5 cm below SFJ. Proximal GSV ultrasound compression applied. 2 injections of 0.10 mL CA given 1 cm apart, with 3 min compression. This is repeated along length of the vein with 30 s of compression in between. Patients wore compression stockings for 3 ds following. Performed in an outpatient clinic". ***Control description:*** "Closure fast system used. Perivenous tumescent anaesthesia used double cycles of RF. Performed in outpatient clinics and compression stockings worn for 3 days following." ***Duration:*** day 3, 1 month, 3 months, 12 months, 24 months and 36 months
Outcomes	***Primary outcomes:*** complete closure at target GSV on DUS at 3 months (closure of entire length with no discrete segments of patency > 5 cm) (day 3 and 1 month also performed) ***Secondary outcomes:*** pain during procedure rated 0 - 10 on numerical scale, number of analgesia taken in the 24 hrs prior to day 3 review, investigator-rated ecchymosis at day 3, changes in VCSS, AVVQ, EQ-5D - baseline, day 3, 1 month and 3 months
Notes	No additional phlebectomies

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Randomised 1:1 to CA or RFA. Stratified by study site. Random block 4 or 6. Assignments were given by an interactive voice response system linked to web bound database
Allocation concealment (selection bias)	Low risk	Randomised 1:1 to CA or RFA. Stratified by study site. Random block 4 or 6. Assignments were given by an interactive voice response system linked to web bound database
Blinding of participants and personnel (performance bias) All outcomes	High risk	No blinding of participants and personnel
Blinding of outcome assessment (detection bias) All outcomes	High risk	No blinding of assessors: "could not blind assessors due to characteristic appearances of CA, to reduce bias both groups wore stockings"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Dropouts reported
Selective reporting (reporting bias)	Unclear risk	Study authors indicated they would report on analgesia use for pain; this was not reported in the results
Other bias	Unclear risk	"...there were 31 missing or uninterruptible USS reports at 3/12 (14%)" Primary end point analysed under various models for imputing missing data were performed Study authors work for Sapheon

Nordon 2011

Study characteristics	
Methods	***Study design:*** prospective, double-blind RCT ***Country:*** UK ***Setting/Location:*** a National Health Service vascular unit ***Source of funding:*** St George's, University of London Charitable Trust (UK) ***Intention-to-treat analysis:*** yes
Participants	***No of participants randomised:*** 159 randomised ***No of participants analysed:*** EVLA = 78; RFA = 79 ***Exclusions post-randomisation:*** 2 EVLA failed cannulation ***Losses to follow-up:*** EVLA = 10; RFA = 9 ***Age years mean (SD):*** EVLA 46.7 (± 14.4); RFA 46.9 (± 15.1) ***Sex - F/M:*** EVLA 54/26; RFA 45/34 ***Inclusion criteria:*** 18 – 80 yrs, primary varicose veins, GSV territory, symptomatic varicose veins and able to attend follow-up ***Exclusion criteria:*** unable to provide consent, pregnancy, age < 18 or > 80 yrs, tortuosity of GSV not amenable to endovenous treatment, recurrent varicose veins, recent DVT/PE, on anticoagulants, intolerance of nonsteroidal anti-inflammatory drugs, SSV reflux, deep venous reflux, people with bilateral symptomatic varicose veins and people not fit for day case were excluded
Interventions	***Treatment description:*** EVLA *:* performed under general anaesthesia. Vari-Lase Bright tip laser fibre (810 nm diode laser, EVLT, Pyramed, Vascular Solutions). The fibre was withdrawn continuously at 2 mm/s (12 W power) with a target 80 J/cm energy. Standard tumescent anaesthesia used. Full-length compression wool (Formflex, Natural, Lantor, UK) and crepe bandage (Multi-crepe, Frontier Multigate, UK) applied post-operatively then exchanged for thigh-length compression hosiery after 24 hrs, worn for a minimum of 2 weeks The median energy delivery in the EVLT group was 77.1 J/cm Phlebectomy hooks were used for simultaneous avulsion of infragenicular varicosities that had been marked before surgery ***Control description:*** RFA: performed under general and tumescent anaesthesia VNUSClosureFAST (Covidien, USA) segmental RFA. Double treatment of the most proximal segment was performed. External compression of the treated segment was applied with target power less than 20 W at 120 °C. Bandaging and compression stocking applied as above. ***Duration:*** 1 week and 3 months
Outcomes	***Primary outcomes:*** GSV occlusion at 7 days and GSV occlusion at 3 months, DUS was performed to confirm GSV occlusion. Disease recurrence/treatment failure was defined as a 5 cm segment of GSV with reflux, identified on DUS. Performed by blinded physician. ***Secondary outcomes:*** post-operative pain – pain diary visual analogue pain chart (0 – 100) daily (validated) and the number of analgesics taken at 1 week. Percentage area of bruising based on 2 views. Complications at 1 week and QoL score pre-operatively (AVVQ and EQ- 5D) and 3 months. Return to work assessed at 3 months
Notes	

Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**

Nordon 2011 *(Continued)*

Random sequence generation (selection bias)	Low risk	"Randomization was performed on the day of surgery. Patients were randomised to receive either laser therapy or RFA" Envelopes were ordered using binary random number tables.
Allocation concealment (selection bias)	Low risk	By sealed opaque envelopes
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Participants were blinded to the endovenous treatment received
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Physician performing post-procedural DUS blinded until after scan at 3 months
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Dropouts recorded, no reasons provided
Selective reporting (reporting bias)	Low risk	All outcomes reported
Other bias	Unclear risk	At 80% power (α-error 5%, β-error 20%), 138 participants were required. Assuming a 10% dropout rate, a minimum of 152 participants were to be recruited In contrast to other studies, Nordon 2011 performed all interventions under general anaesthesia in addition to tumescent anaesthesia

Pronk 2010

Study characteristics	
Methods	***Study design:*** single-centre, prospective, non-blinded, RCT ***Country:*** the Netherlands ***Setting/Location:*** outpatient clinic specialising in venous disease ***Source of funding:*** in article as 'None' ***Intention-to-treat analysis:*** unclear - but most likely as analyses 68 in the HL/S group, although two were lost to follow-up
Participants	***No of participants randomised:*** total n = 122; legs = 130 (EVLT legs = 62; HL/S legs = 68) ***No of participants analysed:*** total n = 122; legs = 130 (EVLT legs = 62; HL/S legs = 68) ***Exclusions post-randomisation:*** not indicated ***Losses to follow-up:*** total = 9 (EVLT n = 1; HL/S n = 8) ***Age - mean years (SD):*** EVLT 49 (11.0); HL/S 50 (10.5) ***Sex - M/F:*** EVLT 16/46; HL/S 15/53 ***No bilateral limbs randomised:*** EVLT 8, HL/S 0

Pronk 2010 *(Continued)*

	Inclusion criteria: age > 18 years at randomisation,CEAP classification C2, GSV and SFJ incompetence defined as reflux > 0.5 s seen on DUS imaging with an intrafascial length of at least 15 cm measured from the SFJ downwards, and GSV diameter between 0.3 and 1.5 cm ***Exclusion criteria:*** previous surgical treatment of the GSV; intrafascial GSV reflux length ≤ 15 cm measure from SFJ downwards; GSV diameter ≤ 0.3 or ≥ 1.5 cm; pregnancy; immobility; intolerance of lidocaine; active superficial phlebitis; previous or active DVT; deep venous insufficiency
Interventions	***Treatment(s):*** EVLT (980 nm diode laser; Biolitec): DUS-guided; perivenous tumescent anaesthesia under ultrasonographic guidance ***Control:*** HL/S of the GSV; perivenous tumescent anaesthesia; ligation of GSV followed by ligation of all tributaries then stripping by PIN-stripper through small incision just below or above the knee ***Duration:*** followed up at 1 week and 6 weeks, 6 months, 1 yr, 3 yrs and 5 yrs
Outcomes	***Primary outcomes:*** recurrent varicose veins in follow-up of 10 yrs (current publication only focuses on 1 yr results) ***Secondary outcomes:*** QoL (EQ-5D), post-operative pain (visual analogue scale from 0 - 10) and complications ***Recurrence definition:*** visible, palpable varicosities in the area of the treated GSV, classified as CEAP greater than or equal to C2; after surgery a new refluxing vein less than 3 mm and clinically visible was also considered recurrent; after EVLT a recurrent varicose vein on DUS was defined as the ability to compress the GSV, or as reflux > 0.5 s in a vein originating in the groin and connected with the femoral vein
Notes	June 2007 to December 2008 "Patients with bilateral GSV incompetence were randomised only once" "Directly after SFL/S and EVLA treatment, sclerotherapy (Aethoxysclerol 0.5 - 3.0%, Kreussler) of residual superficial varicose veins was performed by a phlebologist"

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Used computer randomisation, per participant
Allocation concealment (selection bias)	Low risk	Used computer randomisation (1:1)
Blinding of participants and personnel (performance bias) All outcomes	High risk	No blinding of participants and personnel
Blinding of outcome assessment (detection bias) All outcomes	High risk	No blinding of assessors
Incomplete outcome data (attrition bias) All outcomes	High risk	Although it was stated that two participants were lost to follow-up at six weeks, there is no explanation of the numbers used to analyse the one-year outcomes or the participant satisfaction outcome
Selective reporting (reporting bias)	Low risk	All outcomes reported on

Pronk 2010 *(Continued)*

Other bias	Unclear risk	Possibly underpowered; power calculation described a need for 120 participants in each group, but only 113 were available for follow-up in the surgery group. Also, study authors say participants with dual incompetencies were only randomised once, but the number randomised (130) is legs, and not participants, which is n = 122. This is confusing and possibly misleading. All procedures performed under local tumescent anaesthesia.

Rasmussen 2007

Study characteristics	
Methods	***Study design:*** RCT ***Country:*** Denmark ***Setting/Location:*** office-based setting, private clinic ***Source of funding:*** grant from the Public Health Insurance Research Foundation of Denmark; EVLT catheters provided, in part, by Biolitec AG (Bonn, Germany) and Micronmed (Kristianstad, Sweden) ***Intention-to-treat analysis:*** yes
Participants	***No of participants randomised:*** total n = 121 participants (137 legs) (EVLT n = 62 (69 legs); HL/S n = 59 (68 legs) ***No of participants analysed:*** at 6 months: total n = 88 (EVLT n = 47; HL/S n = 41) (all meta-analyses performed on an ITT basis by all legs randomised) ***Exclusions post-randomisation:*** none ***Losses to follow-up:*** 12 days - EVLT 2, HL/S 0; 1 month - EVLT 4, HL/S 2; 3 months - EVLT 6, HL/S 5; 6 months - EVLT 15, HL/S 18 ***Age - mean years (range):*** EVLT 53 (26 - 79); HL/S 54 (22 - 78) ***Sex - (M/F):*** EVLT 21/41; HL/S 16/43 ***No bilateral limbs randomised:*** EVLT 7; HL/S 9 ***Inclusion criteria:*** CEAP class C2 to C4 (Ep, As, Pr); informed consent; age 18 - 80; GSV incompetence confirmed by > 0.5 s reflux on DUS ***Exclusion criteria:*** duplication of GSV or incompetent anterior accessory GSV; SSV reflux (or < 3 months since surgery for SSV incompetence); previous DVT; ABI < 0.9 or Hx arterial disease; femoral or popliteal insufficiency; tortuous GSV
Interventions	***Treatment(s):*** EVLT (DUS guided) 980 nm diode laser, 1.5 s pulses, 1.5 s pause, 12 W energy; EVLT Ceralas D 980 Biolitec, Bonn, Germany ***Control:*** high tie strip and multiple stab avulsion (HL/S) ***Duration:*** follow-up 12 ds, 1, 3, and 6 months, 2 and 5 yrs post-procedure
Outcomes	***Primary outcomes:*** it is not clear what their specific primary or secondary outcomes were. Rasmussen 2007 set out to assess safety, efficacy, post-operative morbidity, sick leave, QoL and costs. They reported results on: absence from work and normal activity; AVVSS; SF-36 score; VVSS; pain VAS; complications (minor e.g. required no treatment versus major e.g. required treatment, hospitalisation, permanent sequelae or death); cost (procedure and days off sick from work)

Rasmussen 2007 *(Continued)*

	Recurrence definition: veins which had not been observed before or not previously marked by the participant on the AVVSS form
Notes	8 participants in each group had previous high ligation i.e. were recurrent. They were permitted as they had a patent refluxing SFJ and GSV. Study author contacted and further information on randomisation process given: "A block of 10 envelopes would ensure that a sufficient number of each treatments were available, i.e. 5 of each all the time. This is like tossing a coin but easier to document. The envelopes were kept in a basket, but the basket was filled by a research nurse when the patients were not present. All envelopes were alike. There was no chance of bias."

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	After contacting the study author, further details on the random sequence generation were confirmed: 'Blocks of 10 envelopes kept in a basket, the basket was filled by a research nurse when the patients were not present. All envelopes were alike.'
Allocation concealment (selection bias)	Low risk	After contacting the study author, further details on allocation concealment were confirmed: 'The envelopes were kept in a basket, but the basket was filled by a research nurse when the patient were not present. All envelopes were alike.'
Blinding of participants and personnel (performance bias) All outcomes	High risk	Impossible to blind operator or participants to treatment. No blinding of participants and personnel.
Blinding of outcome assessment (detection bias) All outcomes	High risk	No mention that outcome assessors were blinded
Incomplete outcome data (attrition bias) All outcomes	Low risk	Losses to follow-up did not have an impact on the outcome measures; the two treatment groups remained similar in numbers despite losses
Selective reporting (reporting bias)	Low risk	The pre-specified outcomes in the study protocol were reported in the pre-specified way Additional outcome measures were reported in a subsequent publication (2-year results) reporting recurrence rates, which were not a pre-specified outcome measure. However, this does not introduce any bias or inaccuracy into the trial.
Other bias	Unclear risk	121 participants (137 limbs): included 16 participants with bilateral varicose veins; no stratification of these participants in the results; all bilaterally treated participants received the same treatment on both legs.

Rasmussen 2011

Study characteristics

Methods	***Study design:*** two-centre, prospective, RCT

Rasmussen 2011 *(Continued)*

	Country: Denmark ***Setting/Location:*** two private surgical centres under contract to the national healthcare system in Denmark: Danish Vein Centre, Naestved, Surgical Centre Roskilde, Denmark ***Source of funding:*** financed by a grant from the Public Health Insurance Research Foundation of Denmark. Radiofrequency equipment was provided by VNUS Medical Technologies ***Intention-to-treat analysis:*** not indicated
Participants	***No of participants randomised:*** total n = 500 (580 legs); (EVLT n = 125 (144 legs); RFA n = 125 (148 legs); UGFS n = 125 (145 legs); HL/S n = 125 (143 legs)) ***No of participants analysed:*** at 3 days: total n = 494 (573 legs); (EVLT n = 124 (143 legs); RFA n = 124 (146 legs); UGFS n = 123 (143 legs); HL/S n = 123 (141 legs) at 1 month: total n = 489 (564 legs); (EVLT n = 125 (144 legs); RFA n = 121 (141 legs); UGFS n = 124 (144 legs); HL/S n = 119 (135 legs) At 1 yr: total n = 417 (476 legs); (EVLT n = 107 (121 legs); RFA n = 106 (124 legs); UGFS n = 107 (123 legs); HL/S n = 97 (108 legs) ***Exclusions post-randomisation:*** total n = 2 (EVLT n = 0; RFA n = 0; UGFS n = 1; HL/S n = 1) ***Losses to follow-up:*** at 3 days 4 losses; (1 in EVLT, 1 in RFA (2 legs), 1 in UGFS, 1 in HLS group), at 3 months 9 losses; (4 (7 legs) from RFA, 5 (7 legs) from HLS). At 1 yr 81 losses; (18 (23 legs) from EVLT, 19 (24 legs) RFA, 17 (21 legs) UGFS, 27 (34 legs) HLS groups) ***Age - mean years (range):*** EVLT 52 (18 - 74); RFA 51 (23 - 75); UGFS 51 (18 - 75); HL/S 50 (19 - 72) ***Sex - percent women:*** EVLT 72%; RFA 70%; UGFS 76%; HL/S 77% ***No bilateral limbs randomised:*** EVLT 19, RFA 23, UGFS 20, HL/S 18 ***Inclusion criteria:*** age 18 - 75; symptomatic varicose veins; CEAP class C2 to C4 (Ep As Pr); GSV incompetence defined by reflux time of more than 0.5 s on DUS; informed consent provided ***Exclusion criteria:*** duplication of the saphenous trunk or an incompetent anterior accessory saphenous vein; SSV reflux (until 3 months after removal of such a vein); previous DVT; history of arterial insufficiency or ABPI < 0.9, or both; axial deep venous insufficiency (femoral, popliteal or both); tortuous GSV rendering the vein unsuitable for endovenous treatment
Interventions	***Treatment(s):*** all performed under tumescent anaesthesia, 'most' with a light sedative EVLT: duplex guidance - 980 nm diode for the first 17 participants, 1470 nm diode for the rest, in one centre (Roskilde) pulse mode was used and continuous mode was used in the other centre; Ceralas D 980 Biolitec, Jeno, Germany and 1470 Ceralas D RFA: performed according to the manufacturer's recommendations; VNUS Medical Technologies Inc USGF: participant in reverse Trendelenburg position, GSV cannulated (5-Fr) just above the knee, foam was 3% polidocanol (2 mL and 8 mL air mix), before injection the table was put into the Trendelenburg position, foam was injected under USS guidance; re-treatment was permitted within 1 month ***Control:*** HLS: under tumescent anaesthesia and 'most with sedation'. Standard groin incision, flush ligation of GSV, division of all tributaries, GSV stripped with a PIN-stripper to below the knee ***Duration:*** follow-up at 3 days, 1 month, 1, 3, 4 and 5 yrs after treatment
Outcomes	***Primary outcomes:*** GSV closure (closed or absent GSV with lack of flow) ***Secondary outcomes:*** pain, absence from work and normal activity, QoL (SF-36, AVVSS) and VCSS and recurrence rates, costs

Rasmussen 2011 *(Continued)*

	Recurrence definition: not provided
Notes	Randomisation took place between February 2007 to July 2009 Bilateral treatment permitted, but both legs received same treatment Mini-phlebectomies performed in all treatment groups to remove varicose veins (mean (range)): EVLT 14 (1 - 43); RFA 16 (10 - 80); UGFS 15 (1 - 43); HL/S 15 (1 - 48))

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	"Consecutive patients referred for varicose vein treatment by the family physician were randomised in the two sites in blocks of 12 sealed envelopes to one of the four treatments". Insufficient description of random sequence generation
Allocation concealment (selection bias)	Low risk	Used sealed envelopes, although do not specify whether these were opaque
Blinding of participants and personnel (performance bias) All outcomes	High risk	No blinding of participants and personnel
Blinding of outcome assessment (detection bias) All outcomes	High risk	No blinding of outcome assessors
Incomplete outcome data (attrition bias) All outcomes	Low risk	Dropouts and reasons were thoroughly reported
Selective reporting (reporting bias)	Low risk	All outcomes were reported on
Other bias	Unclear risk	Different methods, energies and diodes used for EVLT in the two centres, the procedure technique was not uniform; used limbs and not participants in analysis; participants with 'recurrent varicose veins' were also included if the GSV was preserved to the groin on DUS: no report on number of recurrent varicose veins in each group; all procedures performed under local tumescent anaesthesia

Rautio 2002

Study characteristics

Methods	***Study design:*** RCT ***Country:*** Finland ***Setting/Location:*** University of Oulu ***Source of funding:*** Grant from University of Oulu, Finland

Rautio 2002 *(Continued)*

	Intention-to-treat analysis: one participant was excluded after randomisation but not withdrawn from the study, indicating some intention-to-treat process, but which group this participant retired from is not made clear
Participants	***No of participants randomised:*** total n = 33 (RFA n = 16; HL/S n = 17) ***No of participants analysed:*** total n = 28 (RFA n = 15; HL/S n = 13) ***Exclusions post-randomisation:*** 3 participants left as found schedule unsuitable, further 4 refused chosen treatment and 1 excluded due to pregnancy ***Losses to follow-up:*** no ***Age - mean years (SD):*** RFA 33 (6.7); HL/S 38 (6.8) ***Sex - M/F:*** RFA 1/14; HL/S 1/12 ***Inclusion criteria:*** confirmed reflux (USS > 2 s GSV reflux); person suitable for day case; symptomatic previously untreated uncomplicated GSV tributary varicosities and isolated unilateral SFJ incompetence ***Exclusion criteria:*** coagulopathies; pregnancy; multiple, tortuous (> 90 degree bend) large-diameter GSV trunks; bilateral varicose veins; concomitant SSV varicosities
Interventions	***Treatment(s):*** RFA: VNUS Closure system, inserted into GSV at ankle level; no ligation of SFJ, EVLA, UGFS ***Control:*** HL/S:open surgery; SFJ ligation of all tributaries and stripping of GSV to just below knee ***Duration:*** follow-up for 3 yrs
Outcomes	***Primary outcomes:*** it is not clear what their specific primary or secondary outcomes were, aimed to evaluate outcome in terms of pain, sick leave, health-related QoL and cost ***Secondary outcomes:*** assessed further outcomes at 3 yrs including recurrence, satisfaction, VCSS, VSDS and the VDS, patency of GSV and presence of neovascularisation ***Recurrence definition:*** not provided
Notes	Study author contacted 2 February 2010 Replied 8 February 2010: "The 36 patients had their preoperative diagnostic done in an earlier trial (Accuracy of HHD in planning the operating for primary varicose veins. Eur J Vasc Endovasc Surg 2002). After examining these patients and ensuring their suitability to the study they were included. The patients were given the study information and after getting informed consent from all of them, I put 36 named tags to identical envelopes, which were sealed. After shuffling the envelopes I numbered them randomly. List of numbers for randomisation was done earlier according to instructions of the biostatistician of our department. I opened the envelopes in numerical order. Randomisation was done this way, because our strict schedule. Resource allocations (operating theatres, angiography suites etc.) forced us to perform the operations and procedures during a period of two weeks. We also thought, that it was better to inform the result of randomisation to patients in good time beforehand. Four patients withdrew because of the disappointment of having been assigned to the stripping group. Three patients discontinued the study because of an unsuitable schedule. One patient was excluded because of pregnancy. As a result we missed three patients from the RFA group and five patients from the stripping group. I do not see any chance of bias because of selection process itself. Withdrawal of eight patients might have had some influence to the results."

Risk of bias

Bias	Authors' judgement	Support for judgement

Rautio 2002 *(Continued)*

Random sequence generation (selection bias)	Low risk	After contacting the study author, the sequence generation details were clarified: "....36 named tags to identical envelopes, which were sealed. After shuffling the envelopes they were numbered randomly. List of numbers for randomisation was done earlier according to instructions of the biostatistician of our department. The envelopes were opened in numerical order"
Allocation concealment (selection bias)	Low risk	As above
Blinding of participants and personnel (performance bias) All outcomes	High risk	Impossible to blind operator or participants to treatment. No blinding of participants and personnel
Blinding of outcome assessment (detection bias) All outcomes	High risk	No mention that post-operative assessors were blinded
Incomplete outcome data (attrition bias) All outcomes	Low risk	In a later publication (three-year outcome measures), the study authors claim 'all patients also underwent 3 year follow up'; They report no long-term losses to follow-up
Selective reporting (reporting bias)	Low risk	The pre-specified outcomes in the study protocol were reported in the pre-specified way. Additional outcome measures were reported in a subsequent publication (3yr results): recurrence rates, an additional outcome which was not a pre-specified outcome measure. However, this does not introduce any bias or inaccuracy into the trial.
Other bias	Low risk	States "competition of interest: nil" Small study groups

Recovery 2009

Study characteristics	
Methods	***Study design:*** prospective, single-blinded, RCT comparing Laser (EVL) and RFA ***Country:*** USA (5 centres) Germany (1 centre) ***Setting/Location:*** Miami Vein Center; Dotter Interventional Institute, Oregon; Venenzentrum Elsterpark Germany; Midwest Institute for Minimally Invasive Therapies, Illinois; Vein Solutions, Virginia; Community Surgical Associates, Montana ***Source of funding:*** VNUS Medical Technologies provided financial support for data collection and clinical monitoring and participated in the protocol design ***Intention-to-treat analysis:*** not reported
Participants	***No of participants randomised:*** 87 veins in 69 participants ***No of participants analysed:*** 46 limbs were randomised to undergo RFA treatment and 41 to undergo EVLA ***Exclusions post-randomisation*** : not reported ***Losses to follow-up:*** none reported ***Intention-to-treat analysis:*** not reported ***Age: mean years (SD):*** EVLA: 51.6 (12.8); RFA: 52.4 (15.3)

Recovery 2009 *(Continued)*

	Sex F/M: EVLA 31:10 ; RFA 29:17 ***Inclusion criteria:*** age 18 - 80 yrs with incompetent GSV documented on DUS (US; B-mode and colour Doppler imaging) NB: reflux = significant if reversal of flow > 0.5 s after distal compression in the standing position ***Exclusion criteria:*** thrombus in the vein of interest, previous GSV treatment, pregnancy, known malignancy, and use of anticoagulant medication except low dose aspirin
Interventions	***Treatment description:*** EVLA US-guided percutaneous access followed by perivenous tumescent anaesthesia (0.1% lidocaine with epinephrine): EVLA with 980 nm wavelength in continuous mode at 12 W of power with a linear endovenous energy density of 80 J/cm. After treatment: limbs wrapped in compression bandages and class II compression stockings for 24 – 72 hrs then compression stockings for 2 weeks ***Control description:*** RFA US-guided percutaneous access followed by perivenous tumescent anaesthesia (0.1% lidocaine with epinephrine): RFA was performed with an intraluminally placed Closure-FAST 7-cm tip device placed 2 cm from SFJ, segmental energy delivery at 120 °C in 20 s cycles. 2 cycles to proximal GSV, then 1 cycle to the remaining GSV. After treatment: limbs wrapped in compression bandages and class II compression stockings for 24 – 72 hrs then compression stockings for 2 weeks ***Duration:*** 48 hrs, 1 week, 2 weeks, and 1 month after treatment
Outcomes	***Primary outcomes:*** post-operative pain (measured by the subject on a validated VAS (0 (no pain) to 10 (most severe pain)); ecchymosis measured by clinic staff (0 (no ecchymosis) to 5 (ecchymosis over the entire segment and extension above or below the treatment segment)); incidence of adverse procedural sequelae (e.g. DVT, paraesthesia, phlebitis, hyperpigmentation, and infection) ***Secondary outcomes:*** technical success: DUS assessment of which veins were closed within 3 cm of the SFJ at 48 hs and 1 month; reflux = present if reversal of flow > 0.5 s after distal compression in the standing position; VCSS was recorded during each follow-up visit; limb tenderness (scale: 0 (no tenderness) to 10 (acutely severe tenderness)) the use of periprocedural analgesic agents (limited to ibuprofen with a maximum dose of 800 mg twice daily) QoL using CIVIQ
Notes	March to December 2007 Phlebectomy was not permitted until at least 30 ds had elapsed after the procedure Results reported as number of limbs NOT number of participants which is confusing Phlebitis was defined as induration and erythema along the course of the target vein Small study sample size

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	"Randomization was performed within 24 hours before the procedure and was accomplished by the investigators accessing a Web site and downloading the procedure to be performed."
Allocation concealment (selection bias)	Unclear risk	Study authors mention the actual "treatment procedure was not discussed with the participants."

Recovery 2009 *(Continued)*

Blinding of participants and personnel (performance bias) All outcomes	Low risk	Participants were blinded. "…..the actual treatment procedure was not discussed with the participants", thus maintaining the "single-blind nature of the study"
Blinding of outcome assessment (detection bias) All outcomes	High risk	No blinding of assessors
Incomplete outcome data (attrition bias) All outcomes	High risk	Dropouts were not discussed
Selective reporting (reporting bias)	Low risk	All pre-defined outcomes were reported
Other bias	Unclear risk	Use of private centres and sponsorship by VNUS Technologies (RFA manufacturers). Limbs rather than participants reported

RELACS 2012

Study characteristics	
Methods	***Study design:*** two-centre, prospective, RCT ***Country:*** Germany ***Setting/Location:*** university dermatology department (EVLT-treated group) and a specialised vein clinic (HL/S-treated group); Homburg and Bad Bertrich vascular centres ***Source of funding:*** not indicated ***Intention-to-treat analysis:*** not indicated
Participants	***No of participants randomised:*** total n = 400 (EVLT n = 200; HL/S n = 200) ***No of participants analysed:*** total n = 316 (EVLT n = 173; HL/S n = 143) ***Exclusions post-randomisation:*** total n = 54 (EVLT n = 15; HL/S n = 39). All declined to participate. ***Losses to follow-up:*** total n = 30 (EVLT n = 12; HL/S n = 18); at 5 yrs n = 65 (EVLA n = 33; HL/S n = 32) ***Age - mean years (SD):*** EVLT 47.9 (10.9); HL/S 48.0 (10.7) ***Sex - percent female:*** EVLT 67%; HL/S 70% ***Inclusion criteria:*** GSV insufficiency with saphenofemoral incompetence and reflux at least down to the knee level; CVI and/or symptoms caused by GSV incompetence and or severe clinical finding at risk of varicose vein bleeding, thrombophlebitis or DVT; age 18 to 65 yrs; performance status (according to criteria of the American Society of Anesthesiologists, of class I - II) ***Exclusion criteria:*** previous surgical interventions in the groin area with the exception of inguinal herniotomy; anterior or posterior accessory saphenous vein incompetence; small saphenous vein insufficient requiring treatment at the same limb; acute DVT or PTS; known thrombophilia associated with a high risk of thromboembolism; arterial occlusive disease classified as at least Fontaine stage IIA, and/or ABI below 0.8; active malignant disease (diagnosed during the past 5 yrs); poor compliance or inability to understand the study-related procedures; women who are pregnant or nursing

RELACS 2012 *(Continued)*

Interventions	***Treatment(s):*** EVLT (810 nm bare fibres): laser power delivered in a continuous pull-back fashion, performed with tumescent local anaesthetic and sedation at surgeon's discretion; model 435 MedArt A/S Hvidovre, Denmark ***Control:*** HL/S: transection of all tributaries, flush ligation of SFJ with non-absorbable Ethibond 0-0 suture and neoreflux protection with an invaginating continuous Prolene 4-0 stump suture followed by invagination of GSV to just below the knee. Performed under tumescent local anaesthetic and sedation at surgeon's discretion ***Duration:*** follow-up at 1 week (days 1 to 7), 3 months, 1 yr, 2 yrs and 5 yrs
Outcomes	***Primary outcomes:*** 5-year clinical recurrence-free rate according to the classification of REVAS ***Secondary outcomes:*** 5-year DUS recurrence-free rate at the SFJ, treatment-related adverse effects, HVVSS, QoL (CIVIQ-2), participant satisfaction, cosmetic outcome and recovery using questionnaires and VAS (range 1 - 5) ***Recurrence definition:*** REVAS criteria, which defined recurrence as the presence of any new visible or palpable varicosity on the study leg noticed by the examining clinician, originating form the operated site linked to a saphenofemoral recurrence, to an incompetent GSV or perforator at medial thigh level with medical indication for re-operation
Notes	Randomisation took place between September 2004 to March 2007 One limb per participant was randomised (for participants with both limbs being eligible, the one more affected by CVI was chosen for study participation) Incompetent perforators were ligated and peripheral side branches were removed with multiple stab avulsions. After 3 months, those with apparent residual varices and perforators could be treated with additional phlebectomies or sclerotherapy (exclusively at this time point).

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient description of random sequence generation - only described as "blocks of 10" but: "Independent randomisation was conducted via fax from a remote site"
Allocation concealment (selection bias)	High risk	No mention of allocation concealment
Blinding of participants and personnel (performance bias) All outcomes	High risk	No blinding of participants and personnel reported
Blinding of outcome assessment (detection bias) All outcomes	High risk	No blinding of assessors reported
Incomplete outcome data (attrition bias) All outcomes	Low risk	Dropouts and reasons were thoroughly reported
Selective reporting (reporting bias)	Low risk	All outcomes reported on
Other bias	Unclear risk	EVLT and HL/S performed at 2 separate clinics; possibly underpowered: needed 180 participants per group but after dropouts and losses to follow-up, the

RELACS 2012 *(Continued)*

	EVLT group had only 173 and HL/S had 143; no agreed protocol on number of additional phlebectomies - this could affect pain, cosmesis, QoL etc; all procedures performed under local tumescent anaesthesia

Shepherd 2010

Study characteristics	
Methods	***Study design:*** single centre, single-blinded, RCT ***Country:*** UK ***Setting/Location:*** NHS hospital London ***Source of funding:*** "funded by the Mason Medical Research Foundation (registered charity), the Royal Society of Medicine Venous Forum and Imperial College London; these bodies had no input into the study design, data collection, data analysis, manuscript preparation or publication decisions. The authors declare no conflict of interest" ***Intention-to-treat analysis:*** yes
Participants	***No of participants randomised:*** n = 131; RFA = 67; EVLA = 64 ***No of participants analysed:*** RFA 3 day analysis n = 66; 10 day analysis n = 59; 6 week analysis n = 60; EVLA 3 day analysis n = 61; 10 day analysis n = 51; 6 week analysis n = 55 ***Exclusions post-randomisation:*** RFA 3 day excluded n = 1; 10 day analysis excluded n = 8; 6 week analysis excluded n = 7 EVLA 3 day analysis excluded n = 3; 10 day analysis excluded n = 13; 6 week analysis excluded n = 9 ***Losses to follow-up:*** RFA 3 day analysis lost to follow-up n = 1; 10 day analysis lost to follow-up n = 1; 6 week analysis lost to follow-up n = 7 EVLA 3 day analysis lost to follow-up n = 2; 10 day analysis lost to follow-up n = 0; 6 week analysis lost to follow-up n = 8 ***Age years (SD):*** RFA 49 (15); EVLA 48 (16) ***Sex M/F:*** RFA 47:20 EVLA 42:22 ***Inclusion criteria:*** people over 18 yrs of age with primary GSV incompetence were invited to participate ***Exclusion criteria:*** people with current DVT, significant arterial disease (ABI below 0.8) or who were unsuitable for general anaesthesia were excluded
Interventions	***Treatment:*** VNUS ClosureFAST (RFA), in an operating theatre under general anaesthesia, performed by 1 of 3 vascular surgeons. Standard tumescent local anaesthesia (50 mL 1% lidocaine with 1:200,000 adrenaline (epinephrine) in 1000 mL normal saline). In participants treated with segmental RFA, the first segment was treated with two RFA cycles, and the remainder of the vein was treated with one RFA cycle per 7-cm segment. Extrinsic pressure was applied over the vein during treatment cycles. TED stocking continuously for 1 week ***Control:*** 980-nm laser (EVLA) using a bare fibre, in an operating theatre under general anaesthesia, performed by 1 of 3 vascular surgeons. Standard tumescent local anaesthesia (50 mL 1% lidocaine with 1:200,000 adrenaline (epinephrine) in 1000 mL normal saline). In patients who had EVLA, the laser was continually withdrawn with the aim to deliver energy greater than 60 J/cm; power setting 11 W. TED stocking continuously for 1 week ***Duration:*** 3 and 10 days, 6 weeks, 6 months
Outcomes	***Primary outcomes:*** mean post-procedural pain over the first 3 days (number of tablets taken, ratings on 100 mm visual analogue scale) first 3 days ***Secondary outcomes:*** AVVQ and SF-12 at 6 weeks (compare with baseline). The VCSS at week 6, complications at 1 week and 6 weeks. Assessment of vein occlusion rates 6 months after the intervention
Notes	12 months from July 2008 to July 2009 Participants with additional small saphenous or anterior thigh vein incompetence were treated with the allocated treatment modality at the same sitting. This will impact on QoL scores and return to work.

Shepherd 2010 *(Continued)*

"Patients with varicosities were treated with concomitant phlebectomies using a standard technique with an Oesch hook and all phlebectomy sites were sutured with 6/0 polypropylene."

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Used an Internet randomisation service
Allocation concealment (selection bias)	Unclear risk	Used an Internet randomisation service
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Participants were blinded
Blinding of outcome assessment (detection bias) All outcomes	High risk	No blinding of assessors
Incomplete outcome data (attrition bias) All outcomes	Low risk	Dropouts and reasons were thoroughly reported
Selective reporting (reporting bias)	Low risk	All outcomes reported on
Other bias	Unclear risk	Phlebectomies also performed as was SSV and anterior thigh vein incompetence as required. Report pain analysis was adjusted to make allowances for this. RFA 36 bilateral limbs EVLA 30 performed concurrently - subsequently impacts on pain and return to work. In participants with bilateral disease, the leg that was most symptomatic according to the participant was randomised, and both legs received the same treatment.

Subramonia 2010

Study characteristics

Methods	***Study design:*** RCT ***Country:*** UK ***Setting/Location:*** hospital ***Source of funding:*** VNUS Medical Technologies funded some of the Closure PLUS radiofrequency ablation catheters used in the trial. They were not involved in the running of the trial, data collection, interpretation or analyses. ***Intention-to-treat analysis:*** "There was no crossover of patients between the treatment arms after randomisation and before treatment." However, authors do not explicitly state if there was going to be ITT analysis.
Participants	***No of participants randomised:*** total n = 93 (RFA n = 48; HL/S n = 45) ***No of participants analysed:*** total n = 88 (RFA n = 47; HL/S n = 41)

Subramonia 2010 *(Continued)*

	Exclusions post-randomisation: 2 RFA participants (1 taken off waiting list, 1 did not receive any treatment); 4 surgery (1 taken off waiting list, 1 developed atrial fibrillation, 1 developed hypertension, 1 operated on a non-trial list) ***Losses to follow-up:*** none at 6 weeks; 53 participants (61 limbs) available at 20 months ***Age - median years (IQR):*** RFA 47 (38 - 58); HL/S 45 (37 - 53) ***Sex - M/F:*** RFA 13/34; HL/S 14/27 ***No bilateral limbs randomised:*** no bilateral limbs were included ***Inclusion criteria:*** age 18 - 70 yrs; primary or recurrent GSV reflux on DUS; DUS confirmed suitable for RFA; fit for GA; physical condition allowing ambulation after surgery; can give informed consent; individual and surgeon agree intervention is required; availability for follow-up ***Exclusion criteria:*** varicose veins without GSV incompetence on DUS; associated small saphenous or deep venous incompetence; tortuous GSV unsuitable for RFA; GSV diameter < 3 mm and > 12 mm in supine position; GSV thrombus; people with permanent pacemaker or internal defibrillator; concomitant PVD (ABI < 0.9); pregnancy; unable to complete QoL questionnaire due to poor English language skills
Interventions	***Treatment(s):*** RFA; the VNUS Closure PLUS intravascular catheter with bipolar electrodes ***Control:*** HL/S - open surgery ***Duration:*** 1 week and 5 weeks follow-up
Outcomes	***Primary outcomes:*** time taken to return to normal household activities ***Secondary outcomes:*** intraoperative complications; duration of the procedure; post-operative morbidity (pain, analgesic requirements, sensory abnormalities, wound problems, phlebitis, skin burns, pigmentation); time to return to driving; participant satisfaction and QoL ***Recurrence definition:*** not evaluated
Notes	Article was written and designed by two vascular surgeons who perform both procedures regularly and both authors declare no personal conflict of interests in either treatment. The study authors standardised their anaesthetic and inter-operator variability thus reducing bias. Age and sex variables were controlled in the randomisation process, thus reducing potential confounding.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Age and sex were 'judged most likely to influence outcome in the two groups'. Study author contacted for further details: "A web-based randomisation method was used (with assistance from the Institute of Health and Society, Newcastle University, UK) with stratification to ensure appropriate balance between the arms with respect to variables that might influence outcome in the two groups and to minimise the risk of confounding. The method used two stratification variables, age and sex, that were judged most likely to influence the outcome in the two groups. Two levels of each stratification variable were employed: Age: ≤ 50 years and > 50 years Sex: male or female Simple randomisation without stratification does not guarantee equivalence between the two groups and several levels of stratification can make the randomisation system more complicated and also result in some small strata. The

Subramonia 2010 *(Continued)*

		same procedure was allocated to those with bilateral varicose veins both of which were suitable for the trial with a minimum period of 3 months between the procedures. Access to the web site was protected by password and the file server maintained by the University of Newcastle had high security protocols. The researcher alone had knowledge of the password to access the web site. No problems were encountered either in accessing the web site or in randomising patients during the trial."
Allocation concealment (selection bias)	Low risk	Used web-based randomisation
Blinding of participants and personnel (performance bias) All outcomes	High risk	Unable to blind surgeon or participant to treatment. No blinding of participants and personnel
Blinding of outcome assessment (detection bias) All outcomes	High risk	No mention that assessors post-operatively were blinded
Incomplete outcome data (attrition bias) All outcomes	Low risk	Missing outcome data fully reported and balanced in numbers across intervention groups; all participants were followed up at 5 weeks.
Selective reporting (reporting bias)	Low risk	The pre-specified outcomes in the study protocol were reported in the pre-specified way
Other bias	Unclear risk	Included five participants with recurrent varicose veins. No stratification of these participants in the results. This could introduce a potential bias into results such as pain, time to return to normal activities, QoL, etc. Included 12 participants with bilateral varicose veins (randomised on one occasion to the same treatment, but had their limbs treated with a minimum of 6 weeks in between treatments, thus treating each limb as a separate case).

Syndor 2017

Study characteristics	
Methods	***Study design:*** prospective, single-blinded, RCT ***Country:*** USA ***Setting/Location:*** clinic ***Source of funding:*** not stated, study authors received no financial support ***Intention-to-treat analysis***: not stated
Participants	***No of participants randomised:*** 200 participants; RFA = 100; EVLA = 100 ***No of participants analysed:*** RFA = 100, EVLA = 100 ***Exclusions post-randomisation:*** nil ***Losses to follow-up:*** 6 weeks RFA = 97, EVLA = 96; 6 months EVLA = 79, RFA = 74 ***Age mean (range):*** RFA = 47 (19 - 86); EVLA = 48.5 (23 - 86) ***Sex - F/M:*** EVLA 77/23; RFA 80/20 ***Inclusion criteria:*** CVI symptoms caused by GSV reflux (reversed flow in GSV > 0.5 s after calf compression in a standing position); CEAP > 2; prior attempt of at least 6 weeks of compression stockings for CVI ***Exclusion criteria:*** previous vein surgery/EVTA/phlebectomy in target extremity excluding sclerosant injection for spider veins; active or prior DVT; active or prior hypercoagulability; people who are breast-feeding; people who are non-ambulatory; age < 18 yrs; prisoners

Syndor 2017 *(Continued)*

Interventions	***Treatment description:*** RFA: office-based majority without conscious sedation, tumescent anaesthesia. Heat (120 ºC) segmentally 20 s cycles spaced 6.5 cm apart via VNUS ClosureFAST technology (2 consecutive cycles delivered 1 - 2 cm distal to the SFJ and all other segments were treated with 1 cycle. Stockings continuously 24 hrs then during day for 14 days ***Control description:*** EVLA: office-based majority without conscious sedation, tumescent anaesthesia. 980 nm diode laser system (AngioDynamics, Qeensbury NY) at a fluence range of 50 - 80 J and power back power of 10 W with a constant continuous pullback. Stockings continuously 24 hrs then during day for 14 days. ***Duration:*** post-procedure review within 7 days, 6 weeks, 6 months
Outcomes	***Primary outcomes:*** technical success (closure of GSV with no new reflux, neovascularity or other refluxing truncal veins) ***Secondary outcomes:*** pain during procedure (1 - 10), haematoma, paraesthesia, thermal injury, overall satisfaction, satisfaction within 7 days, 6 weeks and 6 months
Notes	Participants were offered ambulatory phlebectomies or UGFS Conscious sedation commonly administered when adjunctive ambulatory phlebectomy performed

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomisation was performed in blocks of two, four or six participants
Allocation concealment (selection bias)	Low risk	"Objective data recorded by nurse practitioner blinded with regards to which EVTA procedure the patient had undergone. All patient charts with photographs were kept in a locked office and the patient database was kept in a secure password protected format. Patients were blinded"
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Participants and personnel blinded. "Objective data recorded by nurse practitioner blinded with regards to which EVTA procedure the patient had undergone. All patient charts with photographs were kept in a locked office and the patient database was kept in a secure password protected format. Patients were blinded"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	"Objective data recorded by nurse practitioner blinded with regards to which EVTA procedure the patient had undergone. All patient charts with photographs were kept in a locked office and the patient database was kept in a secure password protected format." Participants were blinded
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Dropouts reported, reasons not given
Selective reporting (reporting bias)	Low risk	All predefined outcomes reported
Other bias	Unclear risk	Phlebectomies and UGFS performed concomitantly Conscious sedation used Wide range in follow-up dates (i.e. some 6-week reviews were done at 1 yr; initial follow-up ranged from 1 to 29 days)

Syndor 2017 *(Continued)*

	No power analysis

Vähäaho 2019

Study characteristics	
Methods	***Study design:*** prospective single centre RCT ***Country:*** Finland ***Setting/Location:*** Helsinki University Hospital ***Source of funding***: none stated ***Intention-to-treat analysis:*** yes
Participants	***No of participants randomised:*** total n = 132; MOCA n = 65; EVLA n = 34; RFA = 33 ***No of participants analysed:*** total n = 124; MOCA n = 55; EVLA n = 33; RFA = 29 ***Exclusions post-randomisation:*** n = 7; MOCA n = 6; EVLA n = 0; RFA n = 1 ***Losses to follow-up:*** total n = 8; MOCA n = 4; EVLA n = 1; RFA = 3 ***Age - mean years (SD):*** MOCA 50.9 (12); EVLA 49.5 (11.9); RFA 50.3 (13.9) ***Sex - M/F:*** not stated ***No bilateral limbs randomised:*** N/A ***Inclusion criteria:*** C2 to C4, US verified reflux in the GSV, mean GSV diameter in thigh 5 mm to 12 mm, age 20 to 75 years, informed consent provided ***Exclusion criteria:*** BMI > 40 kg/m^2, PAD, lymphoedema, pregnancy, allergy to either sclerosant or lidocaine, severe general illness, malignancy, previous DVT, previous varicose vein intervention in the same leg, coagulation disorder
Interventions	***Treatment(s):*** MOCA Clarivein inserted to -2 cm below SFJ, rotation for 2-3 secs at highest setting. Whilst wire rotating, simultaneous injection of sclerosant (Sotradecol 1.5%) inserted. First 10 cm rechecked with ultrasound and further second treatment given if necessary. Additional phlebectomies under tumescent anaesthesia performed if required ***Control:*** EVLA: performed under local TA using 0.1% lidocaine in ringer's acetate (150 mL to 500 mL used) and light sedative (pre-operative diazepam and if required propofol +/- fentanyl). Ultrasound guidance, 1470 nm diode laser comprising 1.5 sec impulse and 10 W energy with a protocol to apply 70 J/cm. Additional phlebectomies under TA. Class 2 compression stockings for 48 h then daily for 2 weeks RFA: performed under local TA using 0.1% lidocaine in ringer's acetate (150 mL to 500 mL used) and light sedative (pre-operative diazepam and if required propofol ± fentanyl). Ultrasound guidance VNUS closure FAST catheter. 120 ºC for 20 s per segment. The first segment is ablated twice. Additional phlebectomies under TA. Class 2 compression stockings for 48 h then daily for 2 weeks ***Duration:*** one year
Outcomes	***Primary outcomes:*** occlusion rate of the GSV at 1 yr ***Secondary outcomes:*** disease-specific QoL, perceived pain during and after treatment, duration of sick leave, amount of pain medication consumed during and after treatment, 30-day occlusion rate and complications.

Vähäaho 2019 *(Continued)*

	Recurrence definition: partial recanalisation defined as the presence of at least 5 cm of compressible patent GSV
Notes	***Additional phlebectomies*** – yes in both EVLA, RFA and MOCA

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Randomisation done by study nurse after appointment and sealed envelopes into EVLA, RFA and MOCA 1:1:2
Allocation concealment (selection bias)	Low risk	Sealed envelopes
Blinding of participants and personnel (performance bias) All outcomes	High risk	No blinding of participants and personnel
Blinding of outcome assessment (detection bias) All outcomes	High risk	No blinding of assessors
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Dropouts reported, no reasons given
Selective reporting (reporting bias)	Low risk	All outcomes reported
Other bias	Unclear risk	Sample size calculations indicated 160 participants would be required. Due to slow recruitment was terminated at 132.

Vernermo 2016

Study characteristics	
Methods	***Study design:*** prospective, multicentre RCT ***Country:*** Finland ***Setting/Location:*** 2 Finnish hospitals ***Source of funding:*** not stated, study authors declare no conflict of interest ***Intention-to-treat analysis*** **:** yes
Participants	***No of participants randomised:*** 233 participants (233 legs) ***No of participants analysed:*** 214 participants: HL/S = 65; EVLA = 73; UGFS =76 ***Exclusions post-randomisation:*** 19 randomised participants were excluded from the study before treatment ***Losses to follow-up:*** 1 yr: HL/S = 4, EVLA = 0, UGFS = 4 ***Age mean (SD, range):*** HL/S 47.3 (11.3, 27 - 75); EVLA 47 (13.4, 20 - 73); UGFS 48.3 (12.7, 20 - 73) ***Sex - F/M:*** HL/S 55/10; EVLA 55/18; UGFS 58/18 ***Inclusion criteria:*** unilateral symptomatic, uncomplicated varicose veins (CEAP clinical classification C2 to C4), DUS-verified reflux in the GSV, mean diameter of the GSV in the thigh 5 – 10 mm, and age 20 – 70 yrs

Vernermo 2016 *(Continued)*

	Exclusion criteria: PAD, lymphoedema, BMI exceeding 40 kg/m^2, pregnancy, allergy to the sclerosant or lidocaine, severe general illness, malignancy, previous DVT and coagulation disorder
Interventions	***Treatment description:*** HL/S - "SFJ was exposed in the groin and side branches were ligated back to the femoral vein. Retrograde invagination stripping of the GSV was done, usually down to below the knee. Tumescent solution was injected into the tunnel of the stripped. Hook phlebectomies performed. Most patients had general anaesthesia". Compression stockings ***Treatment description:*** EVLA - tumescent local anaesthesia under UG. A light sedative was administered before (diazepam) and during the procedure. 980 nm diode laser (Ceralas D 980; Biolitec, Bonn, Germany) was used initially, but during the study replaced with a 1470 nm radial laser (ELVes; Biolitec). Pulsed mode, with a 1.5 s impulse and 12 W of energy, with the aim of applying 70 J/cm to the GSV. The EVLA catheter tip was positioned 1.5 – 2 cm below the SFJ using UG. Hook phlebectomies performed. Same compression bandage protocol used ***Control description:*** UGFS - "The GSV was cannulated under ultrasound guidance, usually at proximal thigh level and immediately below the knee. The sclerosant foam was prepared with a double-syringe technique with a sclerosant to air ratio of 1:2. The sclerosants used were polidocanol 1% (Aetoxysclerol®; Kreussler, Wiesbaden, Germany) and sodium tetradecyl sulphate (STS) 1% and 3% (Fibrovein™; STD Pharmaceutical Products, Hereford, UK). A compression stocking was applied with the instruction to wear it continuously for 3 ds, followed by day time use for 11 ds. At 1 mt follow-up, a duplex ultrasound examination was done and, if any reflux was observed, a second treatment with foam was carried out. These patients were seen again 4 weeks after the second treatment, and the need for a possible third treatment was checked by duplex imaging". ***Duration:*** follow-up at 1 week, 1 month, 1 year, and 5 years after treatment
Outcomes	***Primary outcomes:*** "1 year occlusion (or absence) rate of GSV on routine duplex imaging, changes in disease-specific quality of life according to the Aberdeen Varicose Vein Severity Score (AVVSS). The diameter of the GSV 20 cm below the groin was also measured and compared with preoperative values." ***Secondary outcomes:*** perioperative pain measured using a visual analogue scale (VAS) at the time of discharge and at 1 week after the procedure; duration of sick leave; and rate of complications such as haematoma, pigmentation, thrombophlebitis and paraesthesia
Notes	November 2007 to May 2010 "Owing to the operating surgeon's preference, five patients originally randomised to EVLA were treated with surgery but, because the analysis was made according to intention to treat, these patients were analysed in EVLA group" Changed from 980 nm diode to a 1470 nm diode Foam used was more concentrated (air to sclerosant ratio 2:1) than in other studies Phlebectomies performed in HL/S and EVLA arms. Some 33% also had foam injected into varicose tributaries during UGFS

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Block randomisation. No further information
Allocation concealment (selection bias)	Low risk	Sealed envelopes
Blinding of participants and personnel (performance bias)	High risk	No blinding of participants and personnel

Vernermo 2016 *(Continued)*

All outcomes		
Blinding of outcome assessment (detection bias) All outcomes	High risk	No blinding of assessors
Incomplete outcome data (attrition bias) All outcomes	Low risk	Dropouts rates and reasons given and not analysed
Selective reporting (reporting bias)	Low risk	All outcomes reported
Other bias	Unclear risk	"Owing to the operating surgeon's preference, five patients originally randomised to EVLA were treated with surgery but, because the analysis was made according to intention to treat, these patients were analysed in EVLA group". The EVLA diode was also changed from a 980 nm diode to a 1470 nm diode during the course of the trial.

ABI: ankle brachial index
ABPI: ankle-brachial pressure index
AVVQ: Aberdeen Varicose Vein Questionnaire (also known as AVVSS)
AVVSS: Aberdeen Varicose Vein Symptom Severity Score
BMI: body mass index
CA: cyanoacrylate glue
CAA: cyanoacrylate ablation
cc: cubic centimetre
CDUS: colour duplex ultrasound
CEAP: Clinical, Etiological, Anatomical, Pathological classification score
CIVIQ: Chronic Venous Insufficiency Quality of Life Questionnaire
cm: centimetre
CVI: chronic venous insufficiency
ds: days
DNA: did not attend
DUS: duplex ultrasound
DVT: deep vein thrombosis
EQ-5D: EuroQol 5D
EVLA: endovenous laser ablation (same as EVLT)
EVLT: endovenous laser therapy
GA: general anaesthetic
GSV: great saphenous vein
HHD: hand-held Doppler
HL: high ligation
HL/S: high ligation and stripping
hrs: hours
HVVSS: Homburg Varicose Vein Severity Score
Hx: history
IQR: interquartile range
ITT: intention-to-treat
mins: minutes
mL: millilitre
mm: millimetre
MOCA: mechanochemical endovenous ablation
MRFA: monopolar radiofrequency ablation
N/A: not applicable
no: number
nm: nanomole
PAD: peripheral artery disease
PE: pulmonary embolism

PP: per-protocol
PTS: post-thrombotic syndrome
PVD: peripheral vascular disease
QoL: quality of life
RCT: randomised controlled trial
REVAS: Recurrent Varices After Surgery
RFA: radiofrequency ablation
s: second
SD: standard deviation
SF-36: Medical Outcomes Short Form-36
SFJ: saphenofemoral junction
SFL/S: saphenofemoral ligation and stripping (equivalent to HL/S)
SSV: small saphenous vein
TA: tumescent anaesthesia
TED: thrombo-embolic-deterrent
TCSS: Total Clinical Severity Score
UG: ultrasound guidance
UGFS: ultrasound-guided foam sclerotherapy
USS: ultrasound scan
VAS: visual analogue scale
VCSS: Venous Clinical Severity Score
VDS: Venous Disability Score
W: watts
yr(s): year(s)

Characteristics of excluded studies *[ordered by study ID]*

Study	Reason for exclusion
Basela 2011	Claim randomisation yet a retrospective study
Campos 2015	Inclusion of participants with CEAP C5 and C6 disease
Chant 1972	Used liquid sclerotherapy - not foam sclerotherapy
Christenson 2010	Christenson 2010 included the treatment of 200 limbs, randomised to receive SFJ ligation and stripping or EVLA. After contacting the study author, it was confirmed that 40 participants underwent bilateral varicose vein treatment. It was also confirmed that participants' 'limbs' were randomised, not participants. In fact, eight participants underwent SFJ ligation and stripping on one limb and EVLA on the other. All participants with bilateral varicose veins were treated on the same day. The high proportion of bilaterally treated participants affects pain scores and post-operative QoL scores. Time to return to work is also published, but limbs cannot return to work independently of one another and, consequently, these results are not suitable for this Cochrane Review.
CLASS 2014	Combined GSV and SSV; data not stratified by GSV despite contacting study authors
Compagna 2010	Comparison of UGFS and SFJ ligation against HL/S and SFJ ligation; the former is not standard practice
De Medeiros 2006	Comparison of EVLA and SFJ ligation against HL/S and SFJ ligation; the former is not standard practice
De Oliveira 2018	Wrong participant population; evaluated people with CEAP C6
Desai 2009	Conference presentation, not enough information to extrapolate data. Study author previously contacted by Cochrane Vascular but has not provided data
Disselhoff 2008	Used cryostripping

Study	Reason for exclusion
dos Santos 2020	Wrong intervention: evaluated UGFS with tumescence against UGFS
Einarsson 1993	Used liquid sclerotherapy - not foam - in their comparison to surgery
Eroglu 2018	Combined GSV and SSV; data not stratified by GSV despite contacting study authors
Figueiredo 2009	Combined GSV and SSV; data not stratified by GSV
Honek 2019	Comparing EVLA with different types of laser generator (1060 nm Nd-Yag crystal compared to 1470 nm diode laser generator)
Jindal 2018	All participants had bilateral varicose veins and underwent both MOCA and RFA
Kalodiki 2012	This paper compared foam sclerotherapy plus ligation to open surgery. Foam plus ligation does not represent 'standard' foam sclerotherapy
Karathanos 2019	Study used inclusion criteria CEAP C2 and above; included C5-C6 participants; data not stratified
Kikuchi 2009	Conference abstract only, not enough information provided to determine inclusion
Lattimer 2012	Comparisons included the use of combined interventions (EVLA with phlebectomies vs UGFS)
Leon 2018	Wrong participant population; compared radiofrequency venous ablation and sclerotherapy with polidocanol foam 3% versus only radiofrequency venous ablation in saphenous veins of 1.5 cm of diameter or more
Leung 2019	Inclusion of participants with CEAP C5 and C6 disease and participants with SSV
Lin 2007	This paper was written in Chinese. Unable to extract any meaningful data despite complete translation
Mendes 2016	Simultaneously treated bilateral legs. Each participant was treated with RFA on one leg and SFJ ligation and stripping on the contralateral limb
Mozafar 2014	Surgical arm comprised of SFJ ligation only which is not standard practice
Oster 2018	Included participants with C2 to C6 disease; data not stratified
Ouvry 2008	Compares two different types of foam, no comparison to different treatment techniques
Ovali 2019	Not an RCT
Shadid 2015	Not an RCT
Sincos 2018	Combined GSV and SSV; data not stratified by GSV despite contacting study authors
Stotter 2005	Surgical arm involved cryostripping
Tawfik 2020	Used combined techniques: EVLA with complementary UGFS to treat incompetent perforating veins and superficial varicosities, and MOCA. In all participants, study authors ablated small saphenous veins and straight accessory saphenous veins or used foam injections for severely tortuous anterior saphenous vein, superficial varicosities, and below knee segments
Wright 2006	Participants randomised by medical staff based on severity of symptoms. Study also combined GSV and SSV, data not stratified by GSV

EVLA: endovenous laser ablation (equivalent to EVLT)
EVLT: endovenous laser therapy
GSV: great saphenous vein
MOCA: mechanochemical ablation
RCT: randomised controlled trial
RFA: radiofrequency ablation
SFJ: saphenofemoral junction
SPJ: saphenopopliteal junction
SSV: small saphenous vein
UGFS: ultrasound-guided foam sclerotherapy
vs: versus

Characteristics of studies awaiting classification *[ordered by study ID]*

Belramman 2020

Methods	Randomised controlled trial to assess pain resulting from MOCA compared with cyanoacrylate adhesive
Participants	People who have primary GSV or SSV vein reflux > 0.5 s on DUS scanning and who are aged over 18 years will be included. Exclusion criteria are: current deep vein thrombosis; recurrent varicose veins; arterial disease (ABPI < 0.8); venous diameter < 3 mm; people who are unwilling to participate; inability or unwillingness to complete questionnaires; adverse reaction to sclerosant or cyanoacrylate or involvement in another venous trial in the past 6 months.
Interventions	Participants are randomised to undergo either MOCA or cyanoacrylate adhesive truncal ablation, followed by treatment of any varicosities. Participants are required to wear compression stockings for 4 days post intervention.
Outcomes	"The primary end point is pain score immediately following completion of truncal ablation, measured by a 100mm visual analogue scale (VAS). The secondary end points include entire treatment pain scores, clinical scores and quality of life scores. Additional assessments also include ecchymosis scores, occlusion rates, time to return to usual activities/work at two weeks. Patients are reviewed at 2 weeks, 3 months, 6 months and 12 months"
Notes	Two references, additional references to ongoing study Belramman 2018, were identified from a top-up search and will be incorporated in the next update

Morrison 2020

Methods	60-month extension study of the randomised VeClose study
Participants	Participants with symptomatic moderate to severe varicosities (CEAP class C2 - C4b) and symptomatic GSV incompetence
Interventions	Randomly assigned (1:1) to either CAC or RFA
Outcomes	The primary outcome measure of this 60-month extension study was complete closure of the target vein, with planned exploratory analysis of noninferiority Secondary outcomes included CEAP class; completion of the VCSS, EuroQol-Five Dimension survey, and Aberdeen Varicose Vein Questionnaire; participant satisfaction with treatment; AEs related to target GSV; and details of adjunctive procedures
Notes	This reference, an additional publication presenting follow-up data of included study Morrison 2015, was identified from a top-up search and will be incorporated in the next update

Rai 2019

Methods	Parallel single-blinded randomised clinical trial
Participants	60 adults with primary varicose veins due to incompetent GSV (CEAP classes C2 to C4 (Ep As Pr))
Interventions	RFA or foam sclerotherapy
Outcomes	HRQoL was assessed by the Short Form 36, and the AVVQ was applied to assess the impact of varicose veins on quality of life of the participants. In addition, pain severity after the procedures was investigated by a VAS (range, 0 to 10). The participants were followed at 1 week, 1 month, 3 months, and 6 months post-operation. GSV reflux and recurrence was assessed by colour DUS examination after 6 months
Notes	This reference was identified from a top-up search and will be incorporated in the next update

Vähäaho 2021

Methods	Randomised, three-arm clinical study
Participants	Venous outpatient clinic patients with varicose veins (CEAP class C2 - C4) caused by GSV insufficiency (132 participants)
Interventions	2:1:1 for MOCA, EVLA, and RFA, respectively
Outcomes	"The state of the GSV with duplex Doppler ultrasound examination and the disease-specific quality of life were assessed at 1 month, 1 year, and 3 years after the treatment"
Notes	This reference, an additional publication presenting follow-up data of included study Vähäaho 2019, was identified from a top-up search and will be incorporated in the next update

AVVQ: Aberdeen Varicose Vein Questionnaire
ABPI: ankle-brachial pressure index
AE: adverse events
CAC: cyanoacrylate closure
CEAP: Clinical, Etiological, Anatomical and Pathophysiological
DUS: duplex ultrasound
EVLA: endovenous laser ablation
GSV: great saphenous vein
HRQoL: health-related quality of life
MOCA: mechanochemical ablation
RFA: radiofrequency ablation
SSV: short saphenous vein
VAS: visual analogue scale
VCSS: Venous Clinical Severity Score

Characteristics of ongoing studies *[ordered by study ID]*

Belramman 2018

Study name	Randomised controlled trial of mechanochemical ablation versus cyanoacrylate adhesive for the treatment of varicose veins
Methods	Prospective, multicentre, randomised, double-blind, parallel assignment trial

Belramman 2018 *(Continued)*

Participants	180 participants
Interventions	Procedure 1: Mechanochemical ablation (MOCA). MOCA using the ClariVein mechanochemical ablation (MOCA) device (Vascular Insights, Madison, CT, USA). Procedure 2: Cyanoacrylate adhesive. Cyanoacrylate using the VenaSealTM Closure System (Medtronic, Minneapolis, Minnesota, USA).
Outcomes	Primary outcome • pain score immediately following completion of the endovenous ablation using a 100-mm VAS Secondary outcomes • pain score at the end of the procedure (including tributary treatment) • QoL scores at baseline, 2 weeks, 3 months, 6 months and 12 months using the EuroQol 5-domain Utility Index (EQ-5D), the Aberdeen Varicose Vein Questionnaire (AVVQ) and the Chronic Venous Insufficiency Questionnaire (CIVIQ-14) scores • clinical change using the VCSS at baseline, 2 weeks, 3 months, 6 months and 12 months • pain score over the first 10 days, recorded as a number on a scale of 0–10 (0 means no pain, 10 means worst imaginable pain) • degree of bruising at 2 weeks using an ecchymosis score with a 5-point scale • time taken to return to work and normal activities • occlusion rates at 3 months, 6 months and 12 months • re-intervention rate at 12 months • comparison of the cost-effectiveness of each intervention at 12 months
Starting date	6 November 2017
Contact information	Amjad Belramman: mailto:a.belramman17%40imperial.ac.uk?subject=NCT03392753, 17/LO/1457, Mechanochemical Ablation Compared to Cyanoacrylate Adhesive Roshan Bootun: mailto:r.bootun%40imperial.ac.uk?subject=NCT03392753, 17/LO/1457, Mechanochemical Ablation Compared to Cyanoacrylate Adhesive
Notes	

Cho 2020

Study name	CASS (CyanoAcrylate closure versus Surgical Stripping for incompetent saphenous veins) study: a randomized controlled trial comparing clinical outcomes after cyanoacrylate closure and surgical stripping for the treatment of incompetent saphenous veins
Methods	Open-label, multicenter, prospective, randomised controlled trial evaluating the non-inferior clinical outcomes of cyanoacrylate closure compared to surgical stripping for the treatment of incompetent saphenous veins
Participants	Participants must have identifiable reflux in the GSV for greater than 0.5 s after distal compression and release or Valsalva's maneuver in the standing or reverse Trendelenburg position. Participants must also have a CEAP classification score of C2 through C5.
Interventions	CAC closure or surgical stripping and followed up for a total of 24 months after treatment
Outcomes	Primary outcome: complete closure of the target vein (defined as vein closure along the entire treated vein segment with no discrete segments of patency exceeding 5 cm after cyanoacrylate closure, and the absence of venous reflux or residual venous tissue after surgical stripping)

Cho 2020 *(Continued)*

	Secondaryoutcomes: perioperative pain, post-operative ecchymosis, VCSS score, AVVQ, and EQ-5D at each scheduled follow-up visit; all adverse events during the 24-month follow-up period; and the complete closure rate and absence of venous reflux or residual venous tissue at the 12- and 24-month follow-ups
Starting date	2 April 2018
Contact information	In Mok Jung. Department of Surgery, Seoul Metropolitan Government-Seoul National University Boramae Medical Center, Seoul National University College of Medicine, Seoul, South Korea
Notes	Esimated completion of recruitment 29 February 2020

NCT04526626

Study name	Endovenous radiofrequency ablation versus high ligation and stripping for treatment of varicose veins: a prospective controlled trial
Methods	Single group assignment. No details on allocation. This study was to investigate the outcomes of RFA and stripping for varicose veins
Participants	300 participants with varicose veins
Interventions	High ligation and stripping or RFA for treatment of lower limb varicose veins (ClosureFast, Medtronic)
Outcomes	Technical success, complications, recurrence
Starting date	1 February 2020
Contact information	Principal Investigator: Hailei Li, MD, PhD; University of Hong Kong Shenzhen Hospital
Notes	Estimated completion 30 June 2022

NCT04534244

Study name	Management of tributary veins in superficial venous insufficiency of the lower limbs: impact of endovenous steam treatment versus phlebectomy on quality of life (INVOLVE)
Methods	Randomised, parallel, open label. This study aims to compare two surgical techniques for the treatment of superficial chronic venous insufficiency of the lower limbs: phlebectomy, the gold-standard technique, and endovenous steam treatment
Participants	134 participants with venous insufficiency of the leg
Interventions	Experimental group: endovenous steam treatment of the tributary veins (VBox Hybrid) Control group: treatment of the tributary veins by phlebectomy
Outcomes	QoL, occlusion, return to activity
Starting date	October 2020
Contact information	No contact details provided. Centre Hospitalier Universitaire de Besancon

NCT04534244 *(Continued)*

Notes	Estimated completion February 2023

AVVQ: Aberdeen Varicose Vein Questionnaire
CAC: cyanoacrylate closure
CEAP: Clinical, Etiological, Anatomical and Pathophysiological classification score
CIVIQ-14: Chronic Venous Insufficiency Questionnaire
CVI: chronic venous insufficiency
EQ-5D: EuroQol 5-domain Utility Index
GSV: great saphenous vein
MOCA: mechanochemical ablation
QoL: quality of life
VAS: visual analogue scale
VCSS: Venous Clinical Severity Score

DATA AND ANALYSES

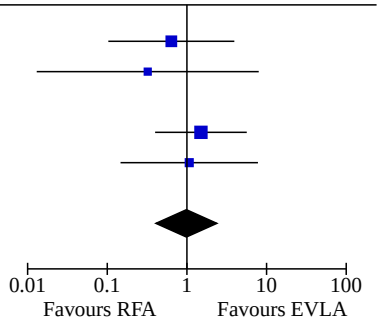
Comparison 1. Endovenous laser ablation versus radiofrequency ablation

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1.1 Technical success < 5 years	5	780	Odds Ratio (M-H, Fixed, 95% CI)	0.98 [0.41, 2.38]
1.2 Long-term technical success > 5 years	1		Odds Ratio (M-H, Fixed, 95% CI)	Totals not selected
1.3 Recurrence	1		Odds Ratio (M-H, Fixed, 95% CI)	Totals not selected
1.4 Long-term recurrence > 5 years	1		Odds Ratio (M-H, Fixed, 95% CI)	Totals not selected

Analysis 1.1. Comparison 1: Endovenous laser ablation versus radiofrequency ablation, Outcome 1: Technical success < 5 years

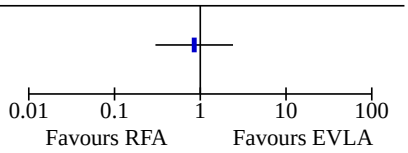
	EVLA		RFA			Odds Ratio	Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI	M-H, Fixed, 95% CI
Nordon 2011	65	68	68	70	29.6%	0.64 [0.10 , 3.94]	
Rasmussen 2011	143	144	148	148	15.2%	0.32 [0.01 , 7.97]	
Recovery 2009	41	41	46	46		Not estimable	
Shepherd 2010	50	54	50	56	36.4%	1.50 [0.40 , 5.64]	
Syndor 2017	77	79	72	74	18.8%	1.07 [0.15 , 7.79]	
Total (95% CI)		**386**		**394**	**100.0%**	**0.98 [0.41 , 2.38]**	
Total events:	376		384				

Heterogeneity: Chi² = 1.08, df = 3 (P = 0.78); I² = 0%
Test for overall effect: Z = 0.03 (P = 0.97)
Test for subgroup differences: Not applicable



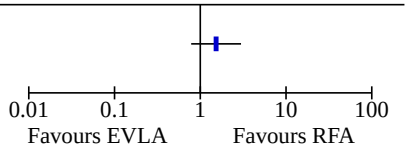
Analysis 1.2. Comparison 1: Endovenous laser ablation versus radiofrequency ablation, Outcome 2: Long-term technical success > 5 years

Study or Subgroup	EVLA Events	EVLA Total	RFA Events	RFA Total	Odds Ratio M-H, Fixed, 95% CI
Rasmussen 2011	136	144	140	147	0.85 [0.30 , 2.41]



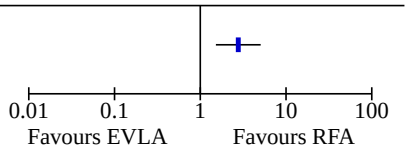
Analysis 1.3. Comparison 1: Endovenous laser ablation versus radiofrequency ablation, Outcome 3: Recurrence

Study or Subgroup	EVLA Events	EVLA Total	RFA Events	RFA Total	Odds Ratio M-H, Fixed, 95% CI
Rasmussen 2011	24	144	17	147	1.53 [0.78 , 2.99]



Analysis 1.4. Comparison 1: Endovenous laser ablation versus radiofrequency ablation, Outcome 4: Long-term recurrence > 5 years

Study or Subgroup	EVLA Events	EVLA Total	RFA Events	RFA Total	Odds Ratio M-H, Fixed, 95% CI
Rasmussen 2011	42	144	19	147	2.77 [1.52 , 5.06]

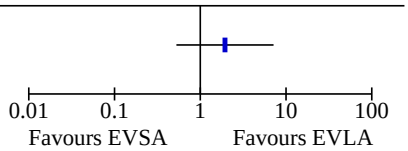


Comparison 2. Endovenous laser ablation versus endovenous steam ablation

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
2.1 Technical success < 5 years	1		Odds Ratio (M-H, Fixed, 95% CI)	Totals not selected

Analysis 2.1. Comparison 2: Endovenous laser ablation versus endovenous steam ablation, Outcome 1: Technical success < 5 years

Study or Subgroup	EVLA Events	EVLA Total	EVSA Events	EVSA Total	Odds Ratio M-H, Fixed, 95% CI
LAST 2014 (1)	88	92	68	74	1.94 [0.53 , 7.15]



Footnotes
(1) high dose of steam

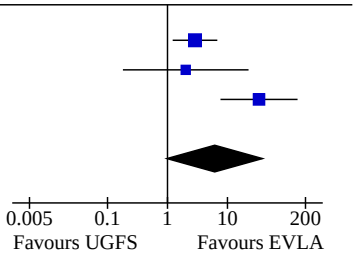
Comparison 3. Endovenous laser ablation versus ultrasound-guided foam sclerotherapy

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
3.1 Technical success < 5 years	3	588	Odds Ratio (M-H, Random, 95% CI)	6.13 [0.98, 38.27]
3.2 Technical success > 5 years	3	534	Odds Ratio (M-H, Random, 95% CI)	6.47 [2.60, 16.10]
3.3 Recurrence	2	443	Odds Ratio (M-H, Random, 95% CI)	0.68 [0.20, 2.36]
3.4 Long-term recurrence > 5 years	2	418	Odds Ratio (M-H, Random, 95% CI)	1.08 [0.40, 2.87]

Analysis 3.1. Comparison 3: Endovenous laser ablation versus ultrasound-guided foam sclerotherapy, Outcome 1: Technical success < 5 years

Study or Subgroup	EVLA Events	EVLA Total	UGFS Events	UGFS Total	Weight	Odds Ratio M-H, Random, 95% CI
Magna 2013	69	78	56	77	40.5%	2.88 [1.22 , 6.77]
Rasmussen 2011	143	144	142	144	25.1%	2.01 [0.18 , 22.46]
Vernermo 2016	71	73	37	72	34.4%	33.58 [7.65 , 147.42]
Total (95% CI)		**295**		**293**	**100.0%**	**6.13 [0.98 , 38.27]**
Total events:	283		235			

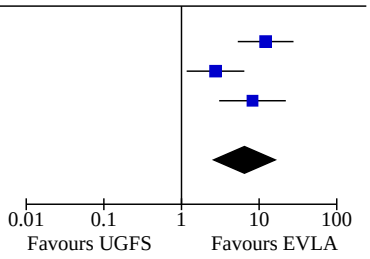
Heterogeneity: Tau² = 1.97; Chi² = 9.10, df = 2 (P = 0.01); I² = 78%
Test for overall effect: Z = 1.94 (P = 0.05)
Test for subgroup differences: Not applicable



Analysis 3.2. Comparison 3: Endovenous laser ablation versus ultrasound-guided foam sclerotherapy, Outcome 2: Technical success > 5 years

Study or Subgroup	EVLA Events	EVLA Total	UGFS Events	UGFS Total	Weight	Odds Ratio M-H, Random, 95% CI
Magna 2013	49	63	15	67	34.8%	12.13 [5.31 , 27.72]
Rasmussen 2011	136	144	124	144	34.1%	2.74 [1.17 , 6.45]
Vernermo 2016	51	57	30	59	31.0%	8.22 [3.06 , 22.07]
Total (95% CI)		**264**		**270**	**100.0%**	**6.47 [2.60 , 16.10]**
Total events:	236		169			

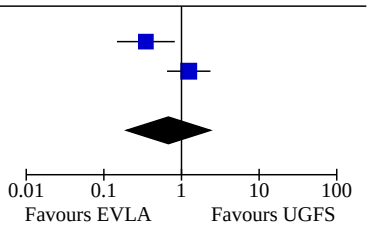
Heterogeneity: Tau² = 0.44; Chi² = 6.33, df = 2 (P = 0.04); I² = 68%
Test for overall effect: Z = 4.02 (P < 0.0001)
Test for subgroup differences: Not applicable



Analysis 3.3. Comparison 3: Endovenous laser ablation versus ultrasound-guided foam sclerotherapy, Outcome 3: Recurrence

Study or Subgroup	EVLA Events	EVLA Total	UGFS Events	UGFS Total	Weight	Odds Ratio M-H, Random, 95% CI
Magna 2013	9	78	21	77	47.4%	0.35 [0.15 , 0.82]
Rasmussen 2011	24	144	20	144	52.6%	1.24 [0.65 , 2.36]
Total (95% CI)		**222**		**221**	**100.0%**	**0.68 [0.20 , 2.36]**
Total events:	33		41			

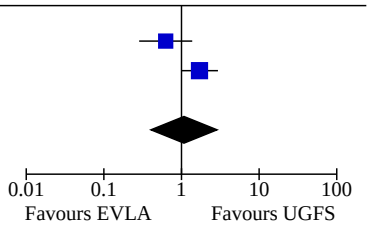
Heterogeneity: Tau² = 0.66; Chi² = 5.41, df = 1 (P = 0.02); I² = 82%
Test for overall effect: Z = 0.61 (P = 0.54)
Test for subgroup differences: Not applicable



Analysis 3.4. Comparison 3: Endovenous laser ablation versus ultrasound-guided foam sclerotherapy, Outcome 4: Long-term recurrence > 5 years

Study or Subgroup	EVLA Events	EVLA Total	UGFS Events	UGFS Total	Weight	Odds Ratio M-H, Random, 95% CI
Magna 2013	14	63	21	67	45.9%	0.63 [0.28 , 1.37]
Rasmussen 2011	42	144	28	144	54.1%	1.71 [0.99 , 2.95]
Total (95% CI)		**207**		**211**	**100.0%**	**1.08 [0.40 , 2.87]**
Total events:	56		49			

Heterogeneity: Tau² = 0.38; Chi² = 4.20, df = 1 (P = 0.04); I² = 76%
Test for overall effect: Z = 0.15 (P = 0.88)
Test for subgroup differences: Not applicable



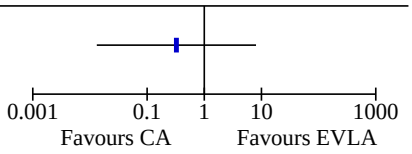
Comparison 4. Endovenous laser ablation versus cyanoacrylate glue

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
4.1 Technical success < 5 years	1		Odds Ratio (M-H, Fixed, 95% CI)	Totals not selected

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
4.2 Recurrence	1		Odds Ratio (M-H, Fixed, 95% CI)	Totals not selected

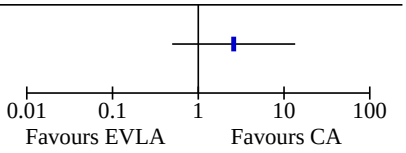
Analysis 4.1. Comparison 4: Endovenous laser ablation versus cyanoacrylate glue, Outcome 1: Technical success < 5 years

Study or Subgroup	EVLA Events	EVLA Total	CA Events	CA Total	Odds Ratio M-H, Fixed, 95% CI
Calik 2019	203	204	208	208	0.33 [0.01 , 8.03]



Analysis 4.2. Comparison 4: Endovenous laser ablation versus cyanoacrylate glue, Outcome 2: Recurrence

Study or Subgroup	EVLA Events	EVLA Total	CA Events	CA Total	Odds Ratio M-H, Fixed, 95% CI
Calik 2019	5	204	2	208	2.59 [0.50 , 13.49]

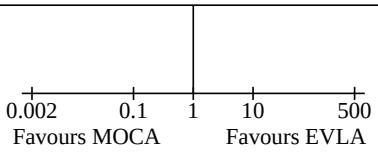


Comparison 5. Endovenous laser ablation versus mechanochemical ablation

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
5.1 Technical success < 5 years	1		Odds Ratio (M-H, Fixed, 95% CI)	Totals not selected
5.2 Recurrence	1		Odds Ratio (M-H, Fixed, 95% CI)	Totals not selected

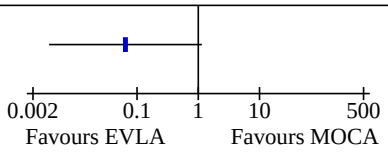
Analysis 5.1. Comparison 5: Endovenous laser ablation versus mechanochemical ablation, Outcome 1: Technical success < 5 years

Study or Subgroup	EVLA Events	EVLA Total	MOCA Events	MOCA Total	Odds Ratio M-H, Fixed, 95% CI
Vähääho 2019	33	33	55	55	Not estimable



Analysis 5.2. Comparison 5: Endovenous laser ablation versus mechanochemical ablation, Outcome 2: Recurrence

Study or Subgroup	EVLA Events	EVLA Total	MOCA Events	MOCA Total	Odds Ratio M-H, Fixed, 95% CI
Vähäaho 2019	0	33	10	55	0.06 [0.00 , 1.14]



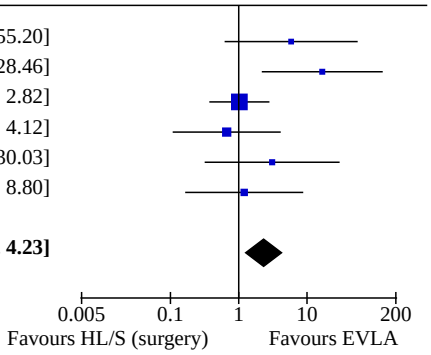
Comparison 6. Endovenous laser ablation versus SFJ ligation and stripping (HL/S, surgery)

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
6.1 Technical success < 5 years	6	1051	Odds Ratio (M-H, Fixed, 95% CI)	2.31 [1.27, 4.23]
6.2 Technical success > 5 years	5	874	Odds Ratio (M-H, Fixed, 95% CI)	0.93 [0.57, 1.50]
6.3 Recurrence	7	1459	Odds Ratio (M-H, Random, 95% CI)	0.78 [0.47, 1.29]
6.4 Long-term recurrence > 5 years	7	1267	Odds Ratio (M-H, Random, 95% CI)	1.09 [0.68, 1.76]

Analysis 6.1. Comparison 6: Endovenous laser ablation versus SFJ ligation and stripping (HL/S, surgery), Outcome 1: Technical success < 5 years

Study or Subgroup	EVLA Events	EVLA Total	HL/S (surgery) Events	HL/S (surgery) Total	Weight	Odds Ratio M-H, Fixed, 95% CI
Darwood 2008	41	42	28	32	5.2%	5.86 [0.62 , 55.20]
HELP-1 2011	136	137	122	137	6.1%	16.72 [2.18 , 128.46]
Magna 2013	69	78	60	68	50.4%	1.02 [0.37 , 2.82]
Rasmussen 2007	66	69	66	68	19.7%	0.67 [0.11 , 4.12]
Rasmussen 2011	143	144	139	142	6.6%	3.09 [0.32 , 30.03]
Vernermo 2016	71	73	59	61	12.0%	1.20 [0.16 , 8.80]
Total (95% CI)		**543**		**508**	**100.0%**	**2.31 [1.27 , 4.23]**
Total events:	526		474			

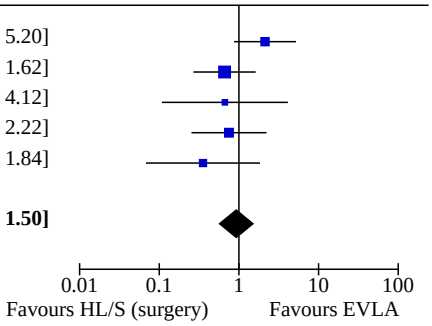
Heterogeneity: Chi² = 9.04, df = 5 (P = 0.11); I² = 45%
Test for overall effect: Z = 2.72 (P = 0.006)
Test for subgroup differences: Not applicable



Analysis 6.2. Comparison 6: Endovenous laser ablation versus SFJ ligation and stripping (HL/S, surgery), Outcome 2: Technical success > 5 years

Study or Subgroup	EVLA Events	EVLA Total	HL/S (surgery) Events	HL/S (surgery) Total	Weight	Odds Ratio M-H, Fixed, 95% CI
HELP-1 2011	100	108	94	110	20.0%	2.13 [0.87 , 5.20]
Magna 2013	49	63	53	63	34.1%	0.66 [0.27 , 1.62]
Rasmussen 2007	66	69	66	68	8.4%	0.67 [0.11 , 4.12]
Rasmussen 2011	136	144	136	142	22.0%	0.75 [0.25 , 2.22]
Vernermo 2016	51	57	48	50	15.6%	0.35 [0.07 , 1.84]
Total (95% CI)		**441**		**433**	**100.0%**	**0.93 [0.57 , 1.50]**
Total events:	402		397			

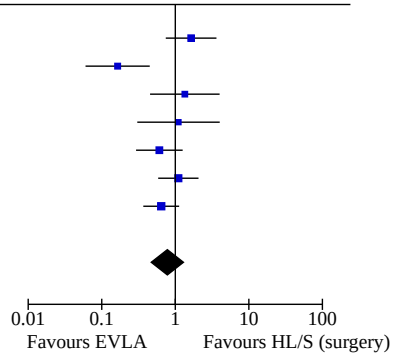
Heterogeneity: Chi² = 5.44, df = 4 (P = 0.24); I² = 27%
Test for overall effect: Z = 0.31 (P = 0.75)
Test for subgroup differences: Not applicable



Analysis 6.3. Comparison 6: Endovenous laser ablation versus SFJ ligation and stripping (HL/S, surgery), Outcome 3: Recurrence

Study or Subgroup	EVLA Events	EVLA Total	HL/S (surgery) Events	HL/S (surgery) Total	Weight	Odds Ratio M-H, Random, 95% CI
Flessenkämper 2013	20	112	11	94	15.1%	1.64 [0.74 , 3.63]
HELP-1 2011	5	124	23	113	12.3%	0.16 [0.06 , 0.45]
Magna 2013	9	78	6	68	11.3%	1.35 [0.45 , 4.00]
Pronk 2010	5	62	5	68	9.3%	1.11 [0.30 , 4.02]
Rasmussen 2007	18	69	25	68	16.0%	0.61 [0.29 , 1.26]
Rasmussen 2011	24	144	22	143	17.5%	1.10 [0.59 , 2.07]
RELACS 2012	28	173	33	143	18.5%	0.64 [0.37 , 1.13]
Total (95% CI)		**762**		**697**	**100.0%**	**0.78 [0.47 , 1.29]**
Total events:	109		125			

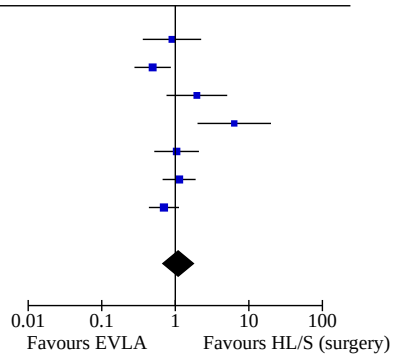
Heterogeneity: Tau² = 0.27; Chi² = 15.95, df = 6 (P = 0.01); I² = 62%
Test for overall effect: Z = 0.97 (P = 0.33)
Test for subgroup differences: Not applicable



Analysis 6.4. Comparison 6: Endovenous laser ablation versus SFJ ligation and stripping (HL/S, surgery), Outcome 4: Long-term recurrence > 5 years

Study or Subgroup	EVLA Events	EVLA Total	HL/S (surgery) Events	HL/S (surgery) Total	Weight	Odds Ratio M-H, Random, 95% CI
Flessenkämper 2013	11	45	14	53	12.1%	0.90 [0.36 , 2.25]
HELP-1 2011	29	108	47	110	16.6%	0.49 [0.28 , 0.87]
Magna 2013	14	63	8	63	11.7%	1.96 [0.76 , 5.08]
Pronk 2010	19	61	4	60	9.6%	6.33 [2.01 , 20.00]
Rasmussen 2007	25	69	24	68	14.8%	1.04 [0.52 , 2.10]
Rasmussen 2011	42	144	38	142	17.3%	1.13 [0.67 , 1.89]
RELACS 2012	69	152	70	129	17.9%	0.70 [0.44 , 1.12]
Total (95% CI)		**642**		**625**	**100.0%**	**1.09 [0.68 , 1.76]**
Total events:	209		205			

Heterogeneity: Tau² = 0.27; Chi² = 19.97, df = 6 (P = 0.003); I² = 70%
Test for overall effect: Z = 0.36 (P = 0.72)
Test for subgroup differences: Not applicable

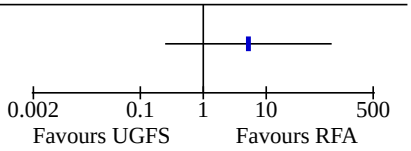


Comparison 7. Radiofrequency ablation versus ultrasound-guided foam sclerotherapy

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
7.1 Technical success < 5 years	1		Odds Ratio (M-H, Fixed, 95% CI)	Totals not selected
7.2 Long-term technical success > 5	1		Odds Ratio (M-H, Fixed, 95% CI)	Totals not selected
7.3 Recurrence	1		Odds Ratio (M-H, Fixed, 95% CI)	Totals not selected
7.4 Long-term recurrence > 5 years	1		Odds Ratio (M-H, Fixed, 95% CI)	Totals not selected

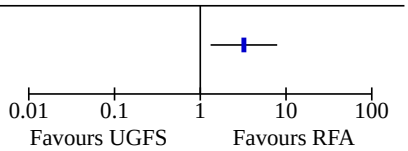
Analysis 7.1. Comparison 7: Radiofrequency ablation versus ultrasound-guided foam sclerotherapy, Outcome 1: Technical success < 5 years

Study or Subgroup	RFA Events	RFA Total	UGFS Events	UGFS Total	Odds Ratio M-H, Fixed, 95% CI
Rasmussen 2011	148	148	142	144	5.21 [0.25 , 109.48]



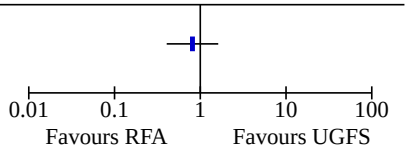
Analysis 7.2. Comparison 7: Radiofrequency ablation versus ultrasound-guided foam sclerotherapy, Outcome 2: Long-term technical success > 5

Study or Subgroup	RFA Events	RFA Total	UGFS Events	UGFS Total	Odds Ratio M-H, Fixed, 95% CI
Rasmussen 2011	140	147	124	144	3.23 [1.32 , 7.89]



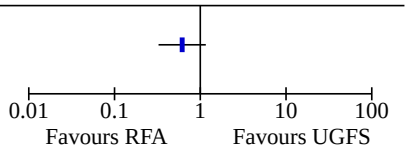
Analysis 7.3. Comparison 7: Radiofrequency ablation versus ultrasound-guided foam sclerotherapy, Outcome 3: Recurrence

Study or Subgroup	RFA Events	RFA Total	UGFS Events	UGFS Total	Odds Ratio M-H, Fixed, 95% CI
Rasmussen 2011	17	147	20	144	0.81 [0.41 , 1.62]



Analysis 7.4. Comparison 7: Radiofrequency ablation versus ultrasound-guided foam sclerotherapy, Outcome 4: Long-term recurrence > 5 years

Study or Subgroup	RFA Events	RFA Total	UGFS Events	UGFS Total	Odds Ratio M-H, Fixed, 95% CI
Rasmussen 2011	19	147	28	144	0.61 [0.33 , 1.16]

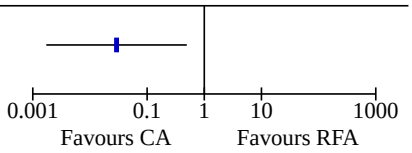


Comparison 8. Radiofrequency ablation versus cyanoacrylate glue

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
8.1 Technical success < 5 years	1		Odds Ratio (M-H, Fixed, 95% CI)	Totals not selected

Analysis 8.1. Comparison 8: Radiofrequency ablation versus cyanoacrylate glue, Outcome 1: Technical success < 5 years

Study or Subgroup	RFA Events	RFA Total	CA Events	CA Total	Odds Ratio M-H, Fixed, 95% CI
Morrison 2015	95	110	105	105	0.03 [0.00 , 0.49]



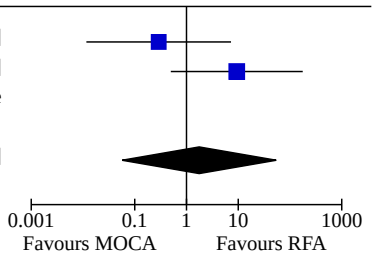
Comparison 9. Radiofrequency ablation versus mechanochemical ablation

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
9.1 Technical success < 5 years	3	435	Odds Ratio (M-H, Random, 95% CI)	1.76 [0.06, 54.15]
9.2 Recurrence	3	389	Odds Ratio (M-H, Random, 95% CI)	1.00 [0.21, 4.81]

Analysis 9.1. Comparison 9: Radiofrequency ablation versus mechanochemical ablation, Outcome 1: Technical success < 5 years

Study or Subgroup	RFA Events	RFA Total	MOCA Events	MOCA Total	Weight	Odds Ratio M-H, Random, 95% CI
Lane 2017	67	68	77	77	48.2%	0.29 [0.01 , 7.25]
MARADONA 2019	103	103	99	103	51.8%	9.36 [0.50 , 176.15]
Vähäaho 2019	29	29	55	55		Not estimable
Total (95% CI)		**200**		**235**	**100.0%**	**1.76 [0.06 , 54.15]**
Total events:	199		231			

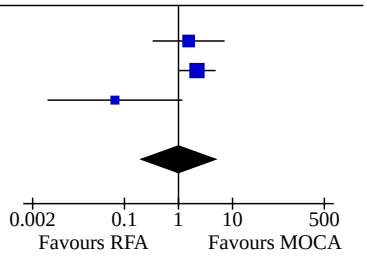
Heterogeneity: Tau² = 3.66; Chi² = 2.48, df = 1 (P = 0.12); I² = 60%
Test for overall effect: Z = 0.32 (P = 0.75)
Test for subgroup differences: Not applicable



Analysis 9.2. Comparison 9: Radiofrequency ablation versus mechanochemical ablation, Outcome 2: Recurrence

Study or Subgroup	RFA Events	RFA Total	MOCA Events	MOCA Total	Weight	Odds Ratio M-H, Random, 95% CI
Lane 2017	4	68	3	77	34.9%	1.54 [0.33 , 7.15]
MARADONA 2019	21	76	12	81	46.1%	2.20 [0.99 , 4.85]
Vähäaho 2019	0	32	10	55	19.0%	0.07 [0.00 , 1.18]
Total (95% CI)		**176**		**213**	**100.0%**	**1.00 [0.21 , 4.81]**
Total events:	25		25			

Heterogeneity: Tau² = 1.23; Chi² = 6.09, df = 2 (P = 0.05); I² = 67%
Test for overall effect: Z = 0.00 (P = 1.00)
Test for subgroup differences: Not applicable



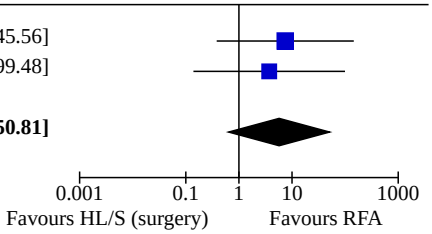
Comparison 10. Radiofrequency ablation versus SFJ ligation and stripping (HL/S, surgery)

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
10.1 Technical success < 5 years	2	318	Odds Ratio (M-H, Fixed, 95% CI)	5.71 [0.64, 50.81]
10.2 Technical success > 5 years	1		Odds Ratio (M-H, Fixed, 95% CI)	Totals not selected
10.3 Recurrence	4	546	Odds Ratio (M-H, Fixed, 95% CI)	0.93 [0.58, 1.51]
10.4 Long-term recurrence > 5 years	1		Odds Ratio (M-H, Fixed, 95% CI)	Totals not selected

Analysis 10.1. Comparison 10: Radiofrequency ablation versus SFJ ligation and stripping (HL/S, surgery), Outcome 1: Technical success < 5 years

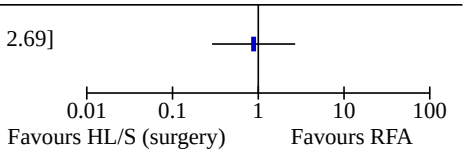
Study or Subgroup	RFA Events	RFA Total	HL/S (surgery) Events	HL/S (surgery) Total	Weight	Odds Ratio M-H, Fixed, 95% CI
Rasmussen 2011	148	148	139	142	53.4%	7.45 [0.38 , 145.56]
Rautio 2002	15	15	12	13	46.6%	3.72 [0.14 , 99.48]
Total (95% CI)		**163**		**155**	**100.0%**	**5.71 [0.64 , 50.81]**
Total events:	163		151			

Heterogeneity: Chi² = 0.10, df = 1 (P = 0.76); I² = 0%
Test for overall effect: Z = 1.56 (P = 0.12)
Test for subgroup differences: Not applicable



Analysis 10.2. Comparison 10: Radiofrequency ablation versus SFJ ligation and stripping (HL/S, surgery), Outcome 2: Technical success > 5 years

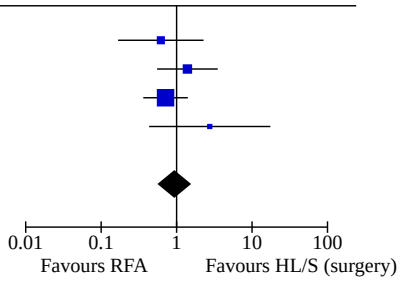
Study or Subgroup	RFA Events	RFA Total	HL/S (surgery) Events	HL/S (surgery) Total	Odds Ratio M-H, Fixed, 95% CI
Rasmussen 2011	140	147	136	142	0.88 [0.29 , 2.69]



Analysis 10.3. Comparison 10: Radiofrequency ablation versus SFJ ligation and stripping (HL/S, surgery), Outcome 3: Recurrence

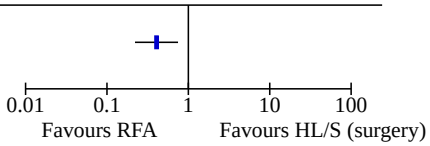
Study or Subgroup	RFA Events	RFA Total	HL/S (surgery) Events	HL/S (surgery) Total	Weight	Odds Ratio M-H, Fixed, 95% CI
EVOLVeS 2003	5	36	6	29	16.5%	0.62 [0.17 , 2.28]
Helmy ElKaffas 2011	12	81	9	81	22.1%	1.39 [0.55 , 3.51]
Rasmussen 2011	17	148	22	143	57.2%	0.71 [0.36 , 1.41]
Rautio 2002	5	15	2	13	4.1%	2.75 [0.43 , 17.49]
Total (95% CI)		**280**		**266**	**100.0%**	**0.93 [0.58 , 1.51]**
Total events:	39		39			

Heterogeneity: Chi² = 3.01, df = 3 (P = 0.39); I² = 0%
Test for overall effect: Z = 0.29 (P = 0.77)
Test for subgroup differences: Not applicable



Analysis 10.4. Comparison 10: Radiofrequency ablation versus SFJ ligation and stripping (HL/S, surgery), Outcome 4: Long-term recurrence > 5 years

Study or Subgroup	RFA Events	RFA Total	HL/S (surgery) Events	HL/S (surgery) Total	Odds Ratio M-H, Fixed, 95% CI
Rasmussen 2011	19	147	38	142	0.41 [0.22 , 0.75]



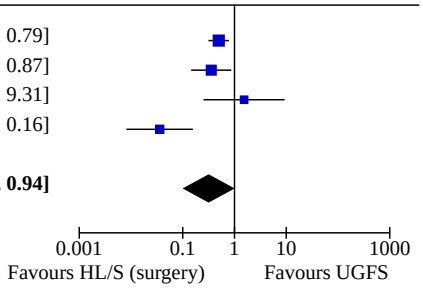
Comparison 11. Ultrasound-guided foam sclerotherapy versus SFJ ligation and stripping (HL/S, surgery)

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
11.1 Technical success < 5 years	4	954	Odds Ratio (M-H, Random, 95% CI)	0.32 [0.11, 0.94]
11.2 Technical success > 5 years	3	525	Odds Ratio (M-H, Random, 95% CI)	0.09 [0.03, 0.30]
11.3 Recurrence	3	822	Odds Ratio (M-H, Random, 95% CI)	1.81 [0.87, 3.77]
11.4 Long-term recurrence (≥ 5 years)	3	639	Odds Ratio (M-H, Random, 95% CI)	1.24 [0.57, 2.71]

Analysis 11.1. Comparison 11: Ultrasound-guided foam sclerotherapy versus SFJ ligation and stripping (HL/S, surgery), Outcome 1: Technical success < 5 years

Study or Subgroup	UGFS Events	UGFS Total	HL/S (surgery) Events	HL/S (surgery) Total	Weight	Odds Ratio M-H, Random, 95% CI
FOAM 2010	139	213	140	177	32.8%	0.50 [0.31 , 0.79]
Magna 2013	56	77	60	68	28.2%	0.36 [0.15 , 0.87]
Rasmussen 2011	142	144	139	142	17.8%	1.53 [0.25 , 9.31]
Vernermo 2016	37	72	59	61	21.2%	0.04 [0.01 , 0.16]
Total (95% CI)		**506**		**448**	**100.0%**	**0.32 [0.11 , 0.94]**
Total events:	374		398			

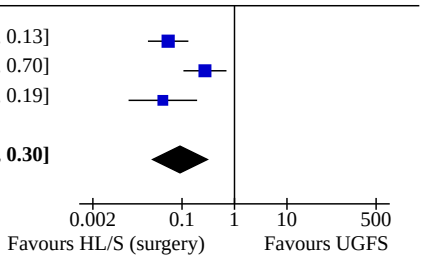
Heterogeneity: Tau² = 0.89; Chi² = 13.78, df = 3 (P = 0.003); I² = 78%
Test for overall effect: Z = 2.07 (P = 0.04)
Test for subgroup differences: Not applicable



Analysis 11.2. Comparison 11: Ultrasound-guided foam sclerotherapy versus SFJ ligation and stripping (HL/S, surgery), Outcome 2: Technical success > 5 years

Study or Subgroup	UGFS Events	UGFS Total	HL/S (surgery) Events	HL/S (surgery) Total	Weight	Odds Ratio M-H, Random, 95% CI
Magna 2013	15	67	53	63	37.1%	0.05 [0.02 , 0.13]
Rasmussen 2011	124	144	136	142	36.1%	0.27 [0.11 , 0.70]
Vernermo 2016	30	59	48	50	26.8%	0.04 [0.01 , 0.19]
Total (95% CI)		**270**		**255**	**100.0%**	**0.09 [0.03 , 0.30]**
Total events:	169		237			

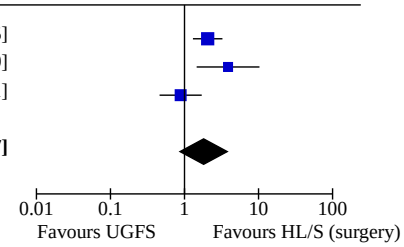
Heterogeneity: Tau² = 0.80; Chi² = 7.37, df = 2 (P = 0.03); I² = 73%
Test for overall effect: Z = 3.92 (P < 0.0001)
Test for subgroup differences: Not applicable



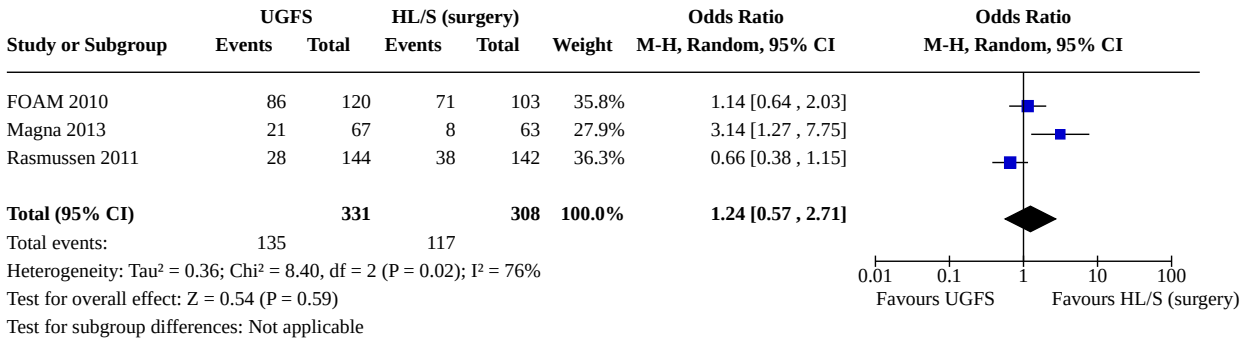
Analysis 11.3. Comparison 11: Ultrasound-guided foam sclerotherapy versus SFJ ligation and stripping (HL/S, surgery), Outcome 3: Recurrence

Study or Subgroup	UGFS Events	UGFS Total	HL/S (surgery) Events	HL/S (surgery) Total	Weight	Odds Ratio M-H, Random, 95% CI
FOAM 2010	75	213	37	177	39.9%	2.06 [1.30 , 3.25]
Magna 2013	21	77	6	68	25.7%	3.88 [1.46 , 10.29]
Rasmussen 2011	20	144	22	143	34.3%	0.89 [0.46 , 1.71]
Total (95% CI)		**434**		**388**	**100.0%**	**1.81 [0.87 , 3.77]**
Total events:	116		65			

Heterogeneity: Tau² = 0.30; Chi² = 7.16, df = 2 (P = 0.03); I² = 72%
Test for overall effect: Z = 1.59 (P = 0.11)
Test for subgroup differences: Not applicable



Analysis 11.4. Comparison 11: Ultrasound-guided foam sclerotherapy versus SFJ ligation and stripping (HL/S, surgery), Outcome 4: Long-term recurrence (≥ 5 years)



ADDITIONAL TABLES

Table 1. Clinical, Etiological, Anatomical and Pathophysiological (CEAP) classification

C0	No visible signs of venous disease
C1	Spider veins, telangiectases or reticular veins (diameter < 3 mm)
C2	Varicose veins (with a diameter > 3 mm)
C3	Varicose veins with oedema
C4	Varicose veins with trophic skin lesions secondary to chronic venous insufficiency
C4a	Pigmentation, purpura, eczema
C4b	Lipodermatosclerosis, atrophie blanche
C5	Healed venous ulcer
C6	Active venous ulcer

Table 2. Study sample sizes

EVLA versus RFA				
Study	**Participants randomised**	**Participants analysed**		
	Overall	**Overall**	**EVLA**	**RFA**
Nordon 2011	159	157	78	79
Rasmussen 2011 [a]	250	213	107	106
	292 legs	245 legs	121 legs	124 legs
Recovery 2009	87 legs	87 legs	41 legs	46 legs

Table 2. Study sample sizes *(Continued)*

Shepherd 2010	131	115	55	60
Syndor 2017	200	153	79	74
EVLA versus EVSA				
Study	**Participants randomised**	**Participants analysed**		
	Overall	**Overall**	**EVLA**	**EVSA**
LAST 2014	217 237 legs	199 legs	92 legs	107 legs
EVLA versus UGFS				
Study	**Participants randomised**	**Participants analysed**		
	Overall	**Overall**	**EVLA**	**UGFS**
Magna 2013 [a]	160 legs	155 legs	78 legs	77 legs
Rasmussen 2011 [a]	250 289 legs	214 244 legs	107 121 legs	107 123 legs
Vernermo 2016 [a]	159	145	73	72
EVLA versus CA				
Study	**Participants randomised**	**Participants analysed**		
	Overall	**Overall**	**EVLA**	**CA**
Calik 2019	400	355	174	181
EVLA versus MOCA				
Study	**Participants randomised**	**Participants analysed**		
	Overall	**Overall**	**EVLA**	**MOCA**
Vähäaho 2019 [a]	99	88	33	55
EVLA versus HL/S (surgery)				
Study	**Participants randomised**	**Participants analysed**		
	Overall	**Overall**	**EVLA**	**HL/S (surgery)**
Darwood 2008	118 136 legs	95 114 legs	80 legs	34 legs
Flessenkämper 2013 [b]	301	255	127	128
HELP-1 2011	280	237	124	113

Table 2. Study sample sizes *(Continued)*

Magna 2013 [a]	160 legs	146 legs	78 legs	68 legs
Pronk 2010	122 130 legs	130 legs	62 legs	68 legs
Rasmussen 2007	121 137 legs	88	47	41
Rasmussen 2011 [a]	250 287 legs	204 229 legs	107 121 legs	97 108 legs
RELACS 2012	400	316	173	143
Vernermo 2016 [a]	152	134	73	61
RFA versus UGFS				
Study	**Participants randomised**	**Participants analysed**		
	Overall	**Overall**	**RFA**	**UGFS**
Rasmussen 2011 [a]	250 292 legs	213 247 legs	106 124 legs	107 123 legs
RFA versus CA				
Study	**Participants randomised**	**Participants analysed**		
	Overall	**Overall**	**RFA**	**CA**
Morrison 2015	222	208	104	104
RFA versus MOCA				
Study	**Participants randomised**	**Participants analysed**		
	Overall	**Overall**	**RFA**	**MOCA**
Lane 2017	170	129	60	69
MARADONA 2019	213	200	99	101
Vähäaho 2019 [a]	98	84	29	55
RFA versus HL/S (surgery)				
Study	**Participants randomised**	**Participants analysed**		
	Overall	**Overall**	**RFA**	**HL/S (surgery)**
EVOLVeS 2003	85 86 legs	80 legs	44 legs	36 legs

Table 2. Study sample sizes *(Continued)*

Helmy ElKaffas 2011	180	162	81	81
Rasmussen 2011 [a]	250 290 legs	203 232 legs	106 124 legs	97 108 legs
Rautio 2002	33	28	15	13
Subramonia 2010	93	88	47	41

UGFS versus HL/S (surgery)

Study	Participants randomised	Participants analysed		
	Overall	Overall	UGFS	HL/S (surgery)
FOAM 2010	460	390	213	177
Magna 2013 [a]	160 legs	145 legs	77 legs	68 legs
Rasmussen 2011 [a]	250 286 legs	204 231 legs	107 123 legs	97 108 legs
Vernermo 2016 [a]	155	133	72	61

[a]Study includes multiple comparisons of different interventions.
[b]Study includes third treatment arm not included within this review.
CA: cyanoacrylate glue
EVLA: endovenous laser ablation
EVSA: endovenous steam ablation
HL/S: high ligation and stripping
MOCA: mechanochemical ablation
RFA: radio frequency ablation
UGFS: ultrasound-guided foam sclerotherapy

Table 3. Age and sex of participants

EVLA versus RFA

Study	Age (years)		Sex (F:M)	
	EVLA	RFA	EVLA	RFA
Nordon 2011	46.7 (14.4) mean (SD)	46.9 (15.1) mean (SD)	54:26	45:34
Rasmussen 2011	52 (18 - 74) mean (range)	51 (23 - 75) mean (range)	90:35	88:37
Recovery 2009	51.6 (12.8) mean (SD)	52.4 (15.3) mean (SD)	31:10	29:17
Shepherd 2010	48 (16)	49 (15)	42:22	47:20

Table 3. Age and sex of participants *(Continued)*

	mean (SD)	mean (SD)		
Syndor 2017	48.5 (23 - 86)	47 (19 - 86)	77:23	80:20
	mean (range)	mean (range)		
EVLA versus EVSA				
Study	**Age (years)**		**Sex (F:M)**	
	EVLA	**EVSA**	**EVLA**	**EVSA**
LAST 2014	55 (12)	56 (13)	61:45	73:39
	mean (SD)	mean (SD)	62:48 (legs)	76:41 (legs)
EVLA versus UGFS				
Study	**Age (years)**		**Sex (F:M)**	
	EVLA	**UGFS**	**EVLA**	**UGFS**
Magna 2013	49 (15.03)	56 (13.30)	54:24	52:25
	mean (SD)	mean (SD)		
Rasmussen 2011	52 (18 - 74)	51 (18 - 75)	90:35	94:30
	mean (range)	mean (range)		
Vernermo 2016	47 (13.4) [20 - 73]	48.3 (12.7) [20 - 73]	55:18	58:18
	mean (SD) [range]	mean (SD) [range]		
EVLA versus CA				
Study	**Age (years)**		**Sex (F:M)**	
	EVLA	**CA**	**EVLA**	**CA**
Calik 2019	38.4 (11.9)	38.6 (11.6)	114:86	109:91
	mean (SD)	mean (SD)		
EVLA versus MOCA				
Study	**Age (years)**		**Ses (F:M)**	
	EVLA	**MOCA**	**EVLA**	**MOCA**
Vähäaho 2019	49.5 (11.9)	50.9 (12.0)	N/A	N/A
	mean (SD)	mean (SD)		
EVLA versus HL/S (surgery)				
Study	**Age (years)**		**Sex (F:M)**	
	EVLA	**HL/S (surgery)**	**EVLA**	**HL/S (surgery)**

Table 3. Age and sex of participants *(Continued)*

Darwood 2008	EVLT1: 42 (30.5 - 54.5); EVLT2: 52 (35 - 59); mean (IQR)	49 (38.5 - 57.5) mean (IQR)	EVLT1: 22:16 EVLT2: 16:11	16:14
Flessenkämper 2013	47.4 (12.9) mean (SD)	47.7 (11.5) mean (SD)	97:45	112:47
HELP-1 2011	49 (14) mean (SD)	49 (13) mean (SD)	85:54	90:47
Magna 2013	49 (15.03) mean (SD)	52 (15.59) mean (SD)	54:24	46:22
Pronk 2010	49 (11.0) mean (SD)	50 (10.5) mean (SD)	46:16	53:15
Rasmussen 2007	53 (26 - 79) mean (range)	54 (22 - 78) mean (range)	41:21	43:16
Rasmussen 2011	52 (18 - 74) mean (SD)	50 (19 - 72) mean (range)	90:35	95:29
RELACS 2012	47.9 (10.9) mean (SD)	48.0 (10.7) mean (SD)	113:48	124:61
Vernermo 2016	47 (13.4) [20 - 73] mean (SD) [range]	47.3 (11.3) [27 - 75] mean (SD) [range]	55:18	55:10
RFA versus UGFS				
Study	**Age (years)**		**Sex (F:M)**	
	RFA	**UGFS**	**RFA**	**UGFS**
Rasmussen 2011	51 (23 - 75) mean (range)	51 (18 - 75) mean (range)	88:37	94:30
RFA versus CA				
Study	**Age (years)**		**Sex (F:M)**	
	RFA	**CA**	**RFA**	**CA**
Morrison 2015	50.5 (25.6 - 70.1) mean (range)	49.0 (26.6 - 70.6) mean (range)	93:21	83:25
RFA versus MOCA				

Table 3. Age and sex of participants *(Continued)*

Study	Age (years)		Sex (F:M)	
	RFA	MOCA	RFA	MOCA
Lane 2017	58 (median)	54.5 (median)	50:33	50:37
MARADONA 2019	53.4 (22.6 - 77.9) median (range)	54.9 (16.3 - 18.2) median (range)	63:43	67:40
Vähääho 2019	50.3 (13.9) mean (SD)	50.9 (12.0) mean (SD)	N/A	N/A
RFA versus HL/S (surgery)				
Study	**Age (years)**		**Sex (F:M)**	
	RFA	**HL/S (surgery)**	**RFA**	**HL/S (surgery)**
EVOLVeS 2003	49 (4) mean (SD)	47 (4) mean (SD)	32:12	26:10
Helmy ElKaffas 2011	33.1 (2.6) mean (SD)	34.9 (3.7) mean (SD)	48:42	45:45
Rasmussen 2011	51 (23 - 75) mean (range)	50 (19 - 72) mean (range)	88:37	95:29
Rautio 2002	33 (6.7) mean (SD)	38 (6.8) mean (SD)	14:1	12:1
Subramonia 2010	47 (38 - 58) median (IQR)	45 (37 - 53) median (IQR)	34:13	27:14
UGFS versus HL/S (surgery)				
Study	**Age (years)**		**Sex (F:M)**	
	UGFS	**HL/S (surgery)**	**UGFS**	**HL/S (surgery)**
FOAM 2010	55.8 (13.4) mean (SD)	54.6 (13.4) mean (SD)	175:58	162:65
Magna 2013	56 (13.30) mean (SD)	52 (15.59) mean (SD)	52:25	46:22
Rasmussen 2011	51 (18 - 75) mean (range)	50 (19 - 72) mean (range)	94:30	95:29

Table 3. Age and sex of participants *(Continued)*

Vernermo 2016	48.3 (12.7) [20 - 73] mean (SD) [range]	47.3 (11.3) [27 - 75] mean (SD) [range]	58:18	55:10

CA: cyanoacrylate glue
EVLA: endovenous laser ablation (same as EVLT)
EVLT: endovenous laser therapy
EVSA: endovenous steam ablation
F: female
HL/S: high ligation and stripping
IQR: interquartile range
M: male
MOCA: mechanochemical ablation
RFA: radio frequency ablation
SD: standard deviation
UGFS: ultrasound-guided foam sclerotherapy

Table 4. Laser technique used

Study	Laser	Pulsed/continuous	Energy	Technique
Calik 2019	1470 nm diode	not stated	15 W	withdrawn at 2.08 ± 0.6 cm/s
Darwood 2008	810 nm diode	1) pulsed	12 W	1 s pulses, 1 s intervals
		2) continuous	14 W	withdrawn 2 - 3 mm/s
Flessenkämper 2013	980 nm diode	continuous	30 W	not indicated
HELP-1 2011	810 nm diode	continuous	14 W	not indicated
LAST 2014	940 nm diode	continuous	12 W	not indicated
Magna 2013	940 nm diode	continuous	not indicated	not indicated
Nordon 2011	810 nm diode	continuous	12 W	withdrawn 2 mm/s
Pronk 2010	980 nm diode	continuous	12 W	not indicated
Rasmussen 2007	980 nm diode	pulsed	12 W	1.5 s pulses, 1.5 s intervals
Rasmussen 2011	980 nm diode	1) pulsed	not indicated	not indicated
		2) continuous		
	1470 nm diode	1) pulsed		
		2) continuous		
Recovery 2009	980 nm diode	continuous	12 W	not indicated
RELACS 2012	810 nm diode	continuous	20 W	not indicated
Shepherd 2010	980 nm diode	continuous	11 W	not indicated
Syndor 2017	980 nm diode	continuous	10 W	not indicated

Table 4. Laser technique used *(Continued)*

Vähäaho 2019	1470 nm diode	pulsed	10 W	1.5 s impulse
Vernermo 2016	980 nm diode	pulsed	12 W	1.5 s impulse
	1470 nm diode	pulsed	12 W	1.5 s impulse

cm: centimetre
mm: millimetre
nm: nanometre
s: seconds
W: watts

Table 5. Outcome measures

Technique	Study	Outcome measure								
		Technical success	Complications	Recurrence/ recanalisation	Pain	QoL Score	VCSS	Duration of procedure	Inpatient/day case	Return to normal activities/work
EVLA versus RFA	Nordon 2011	✓	✓		✓	✓		✓		✓
	Rasmussen 2011		✓	✓	✓	✓	✓	✓		✓
	Recovery 2009	✓	✓		✓		✓			
	Shepherd 2010	✓	✓		✓		✓		✓	✓
	Syndor 2017	✓	✓		✓		✓	✓		
EVLA versus EVSA	LAST 2014	✓	✓		✓	✓	✓			✓
EVLA versus UGFS	Magna 2013	✓	✓	✓		✓				
	Rasmussen 2011		✓	✓	✓	✓	✓	✓		✓
	Vernermo 2016	✓	✓		✓	✓				✓
EVLA versus CA	Calik 2019	✓	✓	✓	✓	✓	✓	✓		✓
EVLA versus MOCA	Vähäaho 2019	✓	✓	✓	✓	✓				✓
EVLA versus HL/S (surgery)	Darwood 2008	✓	✓		✓	✓	✓		✓	✓
	Flessenkämper 2013		✓	✓	✓				✓	✓
	HELP-1 2011	✓	✓	✓	✓	✓	✓	✓	✓	✓
	Magna 2013	✓	✓	✓		✓				
	Pronk 2010		✓	✓	✓	✓			✓	✓

Table 5. Outcome measures *(Continued)*

	Rasmussen 2007	✓	✓	✓	✓	✓	✓		✓	✓
	Rasmussen 2011	✓	✓	✓	✓	✓	✓	✓		✓
	RELACS 2012		✓	✓	✓	✓				✓
	Vernermo 2016	✓	✓		✓	✓		✓		✓
RFA versus UGFS	Rasmussen 2011		✓	✓	✓	✓	✓	✓		✓
RFA versus CA	Morrison 2015	✓	✓		✓	✓	✓	✓	✓	
RFA versus MOCA	Lane 2017	✓	✓	✓	✓	✓	✓			✓
	MARADONA 2019	✓	✓	✓	✓	✓	✓	✓		✓
	Vähäaho 2019	✓	✓	✓	✓	✓				✓
RFA versus HL/S (surgery)	EVOLVeS 2003		✓	✓		✓	✓	✓	✓	✓
	Helmy ElKaffas 2011		✓	✓	✓			✓		✓
	Rasmussen 2011		✓	✓	✓	✓	✓	✓		✓
	Rautio 2002	✓	✓	✓	✓	✓	✓	✓		✓
	Subramonia 2010		✓		✓	✓		✓		✓
UGFS versus HL/S (surgery)	FOAM 2010	✓	✓	✓		✓	✓			
	Magna 2013	✓	✓	✓		✓				
	Rasmussen 2011		✓	✓	✓	✓	✓	✓		✓
	Vernermo 2016	✓	✓		✓	✓				✓

CA: cyanoacrylate glue
EVLA: endovenous laser ablation
EVSA: endovenous steam ablation
HL/S: high ligation and stripping
MOCA: mechanochemical ablation

QoL: quality of life
RFA: radio frequency ablation
UGFS: ultrasound-guided foam sclerotherapy
VCSS: Venous Clinical Severity Score

Table 6. Additional phlebectomies

EVLA versus RFA		
Study	**Additional phlebectomies**	
	EVLA	**RFA**
Nordon 2011	yes	yes
Rasmussen 2011	yes	yes
Recovery 2009	after 30 days	after 30 days
Shepherd 2010	yes	yes
Syndor 2017 [a]	yes	yes
EVLA versus EVSA		
Study	**Additional phlebectomies**	
	EVLA	**EVSA**
LAST 2014	after 3 months	after 3 months
EVLA versus UGFS		
Study	**Additional phlebectomies**	
	EVLA	**UGFS**
Magna 2013	yes	yes
Rasmussen 2011	yes	yes
Vernermo 2016	yes	no
EVLA versus CA		
Study	**Additional phlebectomies**	
	EVLA	**CA**
Calik 2019	after 3 months	after 3 months
EVLA versus MOCA		
Study	**Additional phlebectomies**	
	EVLA	**MOCA**
Vähäaho 2019	yes	yes
EVLA versus HL/S (surgery)		
Study	**Additional phlebectomies**	

Table 6. Additional phlebectomies *(Continued)*

	EVLA	HL/S (surgery)
Darwood 2008	yes - at 6 weeks	yes
Flessenkämper 2013	yes	yes
HELP-1 2011	yes	yes
Magna 2013	yes	yes
Pronk 2010	yes	yes
Rasmussen 2007	yes	yes
Rasmussen 2011	yes	yes
RELACS 2012	yes	yes
Vernermo 2016	yes	yes
RFA versus UGFS		
Study	**Additional phlebectomies**	
	RFA	**UGFS**
Rasmussen 2011	yes	yes
RFA versus CA		
Study	**Additional phlebectomies**	
	RFA	**CA**
Morrison 2015	no	no
RFA versus MOCA		
Study	**Additional phlebectomies**	
	RFA	**MOCA**
Lane 2017	yes	yes
MARADONA 2019	no	yes
Vähäaho 2019	yes	yes
RFA versus HL/S (surgery)		
Study	**Additional phlebectomies**	
	RFA	**HL/S (surgery)**
EVOLVeS 2003	yes	yes

Table 6. Additional phlebectomies *(Continued)*

Helmy ElKaffas 2011	yes	yes
Rasmussen 2011	yes	yes
Rautio 2002	yes	yes
Subramonia 2010	yes	yes
UGFS versus HL/S (surgery)		
Study	**Additional phlebectomies**	
	UGFS	**HL/S (surgery**
FOAM 2010	yes	yes
Magna 2013	yes	yes
Rasmussen 2011	yes	yes
Vernermo 2016	no	yes

[a]Participants were offered ambulatory phlebectomy or UGFS.
CA: cyanoacrylate glue
EVLA: endovenous laser ablation
EVSA: endovenous steam ablation
HL/S: high ligation and stripping
RFA: radio frequency ablation
MOCA: mechanochemical ablation
UGFS: ultrasound-guided foam sclerotherapy

Table 7. Technical success

EVLA versus RFA		
Study - time point	**Technical success (%)**	
	EVLA	**RFA**
Nordon 2011 3 months	65/68 (96)	68/70 (97)
Rasmussen 2011 1 month	143/144 (99)	148/148 (100)
5 yr	136/144 (94)	140/147 (95)
Recovery 2009 1 month	41/41 (100)	46/46 (100)
Shepherd 2010 6 months	50/54 (93)	50/56 (89)
Syndor 2017 6 months	77/79 (97)	72/74 (97)
EVLA versus EVSA		
Study - time point	**Technical success (%)**	

Table 7. Technical success *(Continued)*

	EVLA	EVSA
LAST 2014 1 yr	88/92 (96)	all 93/107 (87)
		high[a] 68/74 (92)
EVLA versus UGFS		
Study - time point	**Technical success (%)**	
	EVLA	**UGFS**
Magna 2013 1 yr	69/78 (88)	56/77 (73)
5 yr	49/63 (77)	15/67 (23)
Rasmussen 2011 1 month	143/144 (99)	142/144 (99)
5 yr	136/144 (94)	124/144 (86)
Vernermo 2016 1 yr	71/73 (93)	37/72 (51)
5 yr	51/57 (89)	30/59 (51)
EVLA versus CA		
Study - time point	**Technical success (%)**	
	EVLA	**CA**
Calik 2019 1 yr	203/204 (99)	208/208 (100)
EVLA versus MOCA		
Study - time point	**Technical success (%)**	
	EVLA	**MOCA**
Vähäaho 2019 30 days	33/33 (100)	55/55 (100)
EVLA versus HL/S (surgery)		
Study - time point	**Technical success (%)**	
	EVLA	**HL/S (surgery)**
Darwood 2008 [b] 3 months	EVLT1. 41/42 (97)	28/32 (87)
	EVLT2. 26/29 (89)	
HELP-1 2011 1 yr	136/137 (99)	122/137 (89)
	100/108 (92)	94/110 (85)
Magna 2013 1 yr	69/78 (88)	60/68 (88)
5 yr	49/63 (78)	53/63 (85)
Rasmussen 2007 1 month	66/69 (96)	66/68 (97)

Table 7. Technical success *(Continued)*

5 yr	66/69 (96)	66/68 (97)
Rasmussen 2011 1 month	143/144 (99)	139/142 (98)
5 yr	136/144 (94)	136/142 (96)
Vernermo 2016 1 yr	71/73 (93)	59/61 (97)
5 yr	51/57 (89)	48/50 (96)
RFA versus UGFS		
Study - time point	**Technical success (%)**	
	RFA	**UGFS**
Rasmussen 2011 1 month	148/148 (100)	142/144 (99)
5 yr	140/147 (95)	124/144 (86)
RFA versus CA		
Study - time point	**Technical success (%)**	
	RFA	**CA**
Morrison 2015 1 month	95/110 (85)	115/115 (100)
RFA versus MOCA		
Study - time point	**Technical success (%)**	
	RFA	**MOCA**
Lane 2017 6 months	67/68 (98)	77/77 (100)
MARADONA 2019 30 days	103/103 (100)	99/103 (96)
Vähäaho 2019 30 days	29/29 (100)	55/55 (100)
RFA versus HL/S (surgery)		
Study - time point	**Technical success (%)**	
	RFA	**HL/S (surgery)**
Rasmussen 2011 1 months	148/148 (100)	139/142 (98)
5 yr	140/147 (95)	136/142 (96)
Rautio 2002 mean 50 days	15/15 (100)	12/13 (92)
UGFS versus HL/S (surgery)		
Study - time point	**Technical success (%)**	
	UGFS	**HL/S (surgery)**

Table 7. Technical success *(Continued)*

FOAM 2010 2 yr	139/213 (65)	140/177 (79)
Magna 2013 1 yr	56/77 (73)	60/68 (88)
5 yr	15/67 (22)	53/63 (84)
Rasmussen 2011 1 month	142/144 (99)	139/142 (98)
5 yr	124/144 (86)	136/142 (96)
Vernermo 2016 1 yr	37/72 (51)	59/61 (97)
5 yr	30/59 (51)	48/50 (96)

[a]High dose of steam
[b]Reported as limbs and not participants
CA: cyanoacrylate glue
EVLA: endovenous laser ablation (same as EVLT)
EVLT: endovenous laser therapy
EVSA: endovenous steam ablation
HL/S: high ligation and stripping
MOCA: mechanochemical ablation
RFA: radiofrequency ablation
UGFS: ultrasound-guided foam sclerotherapy
yr: year(s)

Table 8. Recurrence

EVLA versus RFA		
Study - final time point	**Recurrence noted at final time point (%) < 5 yr**	
	EVLA	**RFA**
Nordon 2011	No results	
Rasmussen 2011 3 yr	24/144 (17)	17/147 (12)
Recovery 2009	No results	
Shepherd 2010	No results	
Syndor 2017	Mention 'recurrent symptoms' but do not specify what this entails	
EVLA versus EVSA		
Study - final time point	**Recurrence noted at final time point (%) < 5 yr**	
	EVLA	**EVSA**
LAST 2014	No results	
EVLA versus UGFS		
Study - final time point	**Recurrence noted at final time point (%) < 5 yrs**	

Table 8. Recurrence *(Continued)*

	EVLA	**UGFS**
Magna 2013 1 yr	9/78 (12)	21/77 (27)
Rasmussen 2011 3 yr	24/144 (17)	20/144 (14)
Vernermo 2016	No results	
EVLA versus CA		
Study - final time point	**Recurrence noted at final time point (%) < 5 yrs**	
	EVLA	**CA**
Calik 2019 1 yr	5/204 (2)	2/208 (1)
EVLA versus MOCA		
Study - final time point	**Recurrence noted at final time point (%) < 5 yrs**	
	EVLA	**MOCA**
Vähäaho 2019 1 yr	0/33 (0)	10/55 (18)
EVLA versus HL/S (surgery)		
Study - final time point	**Recurrence noted at final time point (%) < 5 yrs**	
	EVLA	**HL/S (surgery)**
Darwood 2008 [a] 1 yr	No results	
Flessenkämper 2013 2 yr	20/112 (17.8)	11/94(11.7)
HELP-1 2011 1 yr	5/124 (4)	23/113 (20)
Magna 2013 1 yr	9/78 (12)	6/68 (9)
Pronk 2010 1 yr	5/62 (8)	5/68 (7)
Rasmussen 2007 2 yr	18/69 (26)	25/68 (37)
Rasmussen 2011 [a] 3 yr	24/144 (17)	22/143 (15)
RELACS 2012 2 yr	28/173 (16)	33/143 (23)
Vernermo 2016	no results	
RFA versus UGFS		
Study - final time point	**Recurrence noted at final time point (%) < 5 yrs**	
	RFA	**UGFS**
Rasmussen 2011	17/147 (12)	20/144 (14)

Table 8. Recurrence *(Continued)*

RFA versus CA		
Study - final time point	**Recurrence noted at final time point (%) < 5 yrs**	
	RFA	**CA**
Morrison 2015	no results	
RFA versus MOCA		
Study - final time point	**Recurrence noted at final time point (%) < 5 yrs**	
	RFA	**MOCA**
Lane 2017	4/68 (6)	3/77 (4)
MARADONA 2019 2 yr	21/76 (28)	12/81 (15)
Vähäaho 2019 1 yr	0/32 (0)	10/55 (18)
RFA versus HL/S (surgery)		
Study - final time point	**Recurrence noted at final time point (%) < 5 yrs**	
	RFA	**HL/S (surgery)**
EVOLVeS 2003 2 yr	5/36 (14)	6/29 (21)
Helmy ElKaffas 2011 2 yr	12/81 (15)	9/81 (11)
Rasmussen 2011 [a] 3 yr	17/148 (11)	22/143 (15)
Rautio 2002 2 yr	5/15 (33)	2/13 (15)
Subramonia 2010	not reported	
UGFS versus HL/S (surgery)		
Study - final time point	**Recurrence noted at final time point (%) < 5 yrs**	
	UGFS	**HL/S (surgery)**
FOAM 2010 2 yr	75/213 (35)	37/177 (21)
Magna 2013 1 yr	21/77 (27)	6/68 (9)
Rasmussen 2011 [a] 3 yr	20/144 (14)	22/143 (15)
Vernermo 2016	not reported	

[a]Reported as limbs and not participants
CA: cyanoacrylate glue
EVLA: endovenous laser ablation
EVSA: endovenous steam ablation
HL/S: high ligation and stripping
MOCA: mechanochemical ablation

RFA: radio frequency ablation
UGFS: ultrasound-guided foam sclerotherapy
yr: year(s)

Table 9. Five-year recurrence

EVLA versus RFA		
Study - final time point	**Recurrence noted at final time point (%)**	
	EVLA	**RFA**
Rasmussen 2011 [a]	42/144 (29)	19/147 (13)
EVLA versus EVSA - no data		
EVLA versus UGFS		
Study - final time point	**Recurrence noted at final time point (%)**	
	EVLA	**UGFS**
Magna 2013	14/63 (22)	21/67 (31)
Rasmussen 2011 [a]	42/144 (29)	28/144(19)
EVLA versus CA - no data		
EVLA versus MOCA - no data		
EVLA versus HL/S (surgery)		
Study - final time point	**Recurrence noted at final time point (%)**	
	EVLA	**HL/S (surgery)**
Flessenkämper 2013	11/45 (24)	14/53 (26)
HELP-1 2011	29/108 (27)	47/110 (43)
Magna 2013	14/63 (22)	8/63 (13)
Pronk 2010	19/61 (31)	4/60 (7)
Rasmussen 2007	25/69 (36)	24/68 (35)
Rasmussen 2011 [a]	42/144 (29)	38/142 (27)
RELACS 2012	69/152 (45)	70/129 (54)
RFA versus UGFS		
Study - final time point	**Recurrence noted at final time point (%)**	
	RFA	**UGFS**
Rasmussen 2011 [a]	19/147 (13)	28/144 (19)

Table 9. Five-year recurrence *(Continued)*

RFA versus CA - no data		
RFA versus MOCA - no data		
RFA versus HL/S (surgery)		
Study - final time point	**Recurrence noted at final time point (%)**	
	RFA	**HL/S (surgery)**
Rasmussen 2011 [a]	19/147 (13)	38/142 (27)
UGFS versus HL/S (surgery)		
Study - final time point	**Recurrence noted at final time point (%)**	
	UGFS	**HL/S (surgery)**
FOAM 2010 8 yr	86/120 (72)	71/103 (69)
Magna 2013	21/67 (31)	8/63 (13)
Rasmussen 2011 [a]	28/144 (19)	38/142 (27)

[a]Reported as limbs and not participants
CA: cyanoacrylate glue
EVLA: endovenous laser ablation
EVSA: endovenous steam ablation
HL/S: high ligation and stripping
MOCA: mechanochemical ablation
RFA: radiofrequency ablation
UGFS: ultrasound-guided foam sclerotherapy

Table 10. Post-operative complications within three months

Early post-operative complications (within three months)																
EVLA versus RFA																
Study	**Minor (not requiring intervention) (%)**												**Major (requiring intervention) (%)**			
Adverse event	**Haematoma (wound or thigh)**		**Saphenous nerve injury**		**Thermal injury/ inflammation**		**Wound problems (groin/ stab)**		**Bruising and pigmentation**		**Phlebitis**		**Wound problems**		**Other**	
Technique	**EVLA**	**RFA**	**EVLA**	**RFA**	**EVLA**	**RFA**	**EVLA**	**RFA**	**EVLA**	**RFA**	**EVLA**	**RFA**	**EVLA**	**RFA**	**EVLA**	**RFA**
Nordon 2011			2/78 (2.6)	1/77 (1.3)	2/78 (2.6)	1/76 (1.3)	0/78 (0)	0/76 (0)			2/78 (2.6)	1/76 (1.3)	0/78 (0)	0/76 (0)		
Rasmussen 2011 [a]	1/125 (0.8)	0/121 (0)	3/125 (2.4)	6/121 (5)					3/125 (2.4)	8/121 (6.6	4/125 (3.2)	12/121 (9.9)	0/125 (0)	1/121 (0.8)	0/125 (0)	0/121 (0)
Recovery 2009			2/41 (4.9)	1/46 (2.2)					0/41 (0)	1/46 (2.2)	6/41 (14.6)	0/46 (0)			1/41 (2.2)	0/46 (0)
Shepherd 2010	2/64 (3)	0/67 (0)	5/64 (8)	8/67 (12)			1/64 (2)	2/67 (3)	2/64 (3)	6/67 (9)	5/64 (7)	5/67 (7)	2/64 (3)	4/67 (6)	0/64 (0)	1/67 (1) PE
Syndor 2017			9/96 (9.4)	13/97 (13.7)	0/96 (0)	0/97 (0)			3/96 (3.1)	3/97 (3.1)	1/96 (1)	1/97 (1.0)	3/96 (3.1)	2/97 (2.1)	0/96 (0)	0/97 (0)
EVLA versus EVSA																
Study	**Minor (not requiring intervention) (%)**												**Major (requiring intervention) (%)**			
Adverse event	**Haematoma (wound or thigh)**		**Saphenous nerve injury**		**Thermal injury/ inflammation**		**Wound problems (groin/ stab)**		**Bruising and pigmentation**		**Phlebitis**		**Wound problems**		**Other**	
Technique	**EVLA**	**EVSA**	**EVLA**	**EVSA**	**EVLA**	**EVSA**	**EVLA**	**EVSA**	**EVLA**	**EVSA**	**EVLA**	**EVSA**	**EVLA**	**EVSA**	**EVLA**	**EVSA**

Table 10. Post-operative complications within three months *(Continued)*

LAST 2014			0/109	1/117	0/109	0/117	0/109	0/117			10/109	10/117	0/109	0/117	1/109	0/117
			(0)	(0.9)	(0)	(0)	(0)	(0)			(9.2)	(8.5)	(0)	(0)	(0.9) DVT	(0)
EVLA versus UGFS																
Study	**Minor (not requiring intervention) (%)**												**Major (requiring intervention) (%)**			
Adverse event	**Haematoma (wound or thigh)**		**Saphenous nerve injury**		**Thermal injury/ inflammation**		**Wound problems (groin/ stab)**		**Bruising and pigmentation**		**Phlebitis**		**Wound problems**		**Other**	
Technique	**EVLA**	**UGFS**	**EVLA**	**UGFS**	**EVLA**	**UGFS**	**EVLA**	**UGFS**	**EVLA**	**UGFS**	**EVLA**	**UGFS**	**EVLA**	**UGFS**	**EVLA**	**UGFS**
Magna 2013			2/78	1/77					2/78	1/77			0/78	0/77	0/78	0/77
			(2.6)	(1.3)					(2.6)	(1.3)			(0)	(0)	(0)	(0)
Rasmussen 2011 [a]	1/125	1/124	3/125	2/124					3/125	8/124	4/125	17/124	0/125	4/124	0/125	1/124
	(0.8)	(0.8)	(2.4)	(1.6)					(2.4)	(6.5)	(3.2)	(13.7)	(0)	(3.2)	(0)	(0.8)
Vernermo 2016	31/73	14/72	1/73	2/72					3/73	50/72			3/73	0/72		
	(42)	(20)	(1)	(2)					(5)	(67)			(4)	(0)		
EVLA versus CA																
Study	**Minor (not requiring intervention) (%)**												**Major (requiring intervention) (%)**			
Adverse event	**Haematoma (wound or thigh)**		**Saphenous nerve injury**		**Thermal injury/ inflammation**		**Wound problems (groin/ stab)**		**Bruising and pigmentation**		**Phlebitis**		**Wound problems**		**Other**	
Technique	**EVLA**	**CA**	**EVLA**	**CA**	**EVLA**	**CA**	**EVLA**	**CA**	**EVLA**	**CA**	**EVLA**	**CA**	**EVLA**	**CA**	**EVLA**	**CA**
Calik 2019 [b]			28/200	6/200					63/200	31/200	14/200	7/200			2/200	
			(11)	(3)					(31)	(15.5)	(7)	(3.5)			(1)	
EVLA versus MOCA																

Table 10. Post-operative complications within three months *(Continued)*

Study	Minor (not requiring intervention) (%)												Major (requiring intervention) (%)			
Adverse event	**Haematoma (wound or thigh)**		**Saphenous nerve injury**		**Thermal injury/ inflammation**		**Wound problems (groin/ stab)**		**Bruising and pigmentation**		**Phlebitis**		**Wound problems**		**Other**	
Technique	**EVLA**	**MOCA**	**EVLA**	**MOCA**	**EVLA**	**MOCA**	**EVLA**	**MOCA**	**EVLA**	**MOCA**	**EVLA**	**MOCA**	**EVLA**	**MOCA**	**EVLA**	**MOCA**
Vähääho 2019			4/34 (12)	0/65 (0)									0/34 (0)	1/65 (1.5)		

EVLA versus HL/S (surgery)

Study	Minor (not requiring intervention) (%)												Major (requiring intervention) (%)			
Adverse event	**Haematoma (wound or thigh)**		**Saphenous nerve injury**		**Thermal injury/ inflammation**		**Wound problems (groin/ stab)**		**Bruising and pigmentation**		**Phlebitis**		**Wound problems**		**Other**	
Technique	**EVLA**	**HL/S**	**EVLA**	**HL/S**	**EVLA**	**HL/S**	**EVLA**	**HL/S**	**EVLA**	**HL/S**	**EVLA**	**HL/S**	**EVLA**	**HL/S**	**EVLA**	**HL/S**
Darwood 2008 [a]	0/80 (0)	0/32 (0)	1/80 (1)	4/32 (13)					1/80 (1)	2/32 (6)	9/80 (11)	0/32 (0)	0/80 (0)	2/32 (6)	0/80 (0)	1/32[c] (3)
Flessenkämper 2013			24/142 (17)	23/159 (15)					68/142 (48)	108/159 (68)					1/142 (0.7)	1/159 (0.6)
HELP-1 2011	1/137 (0.7)	11/133 (8.3)	4/137 (2.9)	13/133 (9.8)					5/137 (3.6)	3/133 (2.2)	4/137 (2.9)	6/133 (4.5)	2/137 (1.5)	8/133 (6)		
Magna 2013			2/78 (2.6)	4/68 (5.9)					2/78 (2.6)	0/68 (0)			0/78 (0)	3/68 (4.4)	0/78 (0)	0/68 (0)
Pronk 2010			2/62 (3)	1/68 (1)												

Table 10. Post-operative complications within three months *(Continued)*

Rasmussen 2007 [a]	3/69[d] (5)	5/68 (8)	1/69 (2)	1/68 (5.9)	0/69 (0)	0/68 (0)	0/69 (0)	1/68 (2)	7/69 (11)	15/68 (25)	2/69 (3)	2/68 (3)	0/69 (0)	1/68[e] (2)	0/69 (0)	0/68 (0)
Rasmussen 2011 [a]	1/125 (0.8)	1/119 (0.8)	3/125 (2.4)	5/119 (4.2)					3/125 (2.4)	6/119 (5)	4/125 (3.2)	5/119 (4.2)	0/125 (0)	0/119 (0.8)	0/125 (0)	1/119 (0.8)
RELACS 2012									169/185 (91)	145/161 (90)	20/185 (10.8)	4/161 (2.5)	1/185 (0.5)	0/161 (0)	3/185 (1.6)	1/161 (0.6)
Vernermo 2016	31/73 (42)	40/65 (62)	1/73 (1)	2/65 (3)					3/73 (4)	3/65 (4)			3/73 (4)	3/65 (4)		
RFA versus UGFS																
Study	**Minor (not requiring intervention) (%)**												**Major (requiring intervention) (%)**			
Adverse event	**Haematoma (wound or thigh)**		**Saphenous nerve injury**		**Thermal injury/ inflammation**		**Wound problems (groin/ stab)**		**Bruising and pigmentation**		**Phlebitis**		**Wound problems**		**Other**	
Technique	**RFA**	**UGFS**	**RFA**	**UGFS**	**RFA**	**UGFS**	**RFA**	**UGFS**	**RFA**	**UGFS**	**RFA**	**UGFS**	**RFA**	**UGFS**	**RFA**	**UGFS**
Rasmussen 2011 [a]	0/121 (0)	1/124 (0.8)	6/121 (0.8)	2/124 (1.6)					8/121 (6.6)	8/124 (6.5)	12/121 (9.9)	17/124 (13.7)	1/121 (0.8)	4/124 (3.2)	0/121 (0)	1/124 (0.8)
RFA versus CA																
Study	**Minor (not requiring intervention) (%)**												**Major (requiring intervention) (%)**			
Adverse event	**Haematoma (wound or thigh)**		**Saphenous nerve injury**		**Thermal injury/ inflammation**		**Wound problems (groin/ stab)**		**Bruising and pigmentation**		**Phlebitis**		**Wound problems**		**Other**	
Technique	**RFA**	**CA**	**RFA**	**CA**	**RFA**	**CA**	**RFA**	**CA**	**RFA**	**CA**	**RFA**	**CA**	**RFA**	**CA**	**RFA**	**CA**
Morrison 2015			3/114	3/108	1/114	0/108					16/114	22/108	1/114	1/114	0/114	0/108

Table 10. Post-operative complications within three months *(Continued)*

	(3)	(3)	(1)	(0)							(14)	(20)	(1)	(1)	(0)	(0)
RFA versus MOCA																
Study	**Minor (not requiring intervention) (%)**												**Major (requiring intervention) (%)**			
Adverse event	**Haematoma (wound or thigh)**		**Saphenous nerve injury**		**Thermal injury/ inflammation**		**Wound problems (groin/ stab)**		**Bruising and pigmentation**		**Phlebitis**		**Wound problems**		**Other**	
Technique	**RFA**	**MOCA**	**RFA**	**MOCA**	**RFA**	**MOCA**	**RFA**	**MOCA**	**RFA**	**MOCA**	**RFA**	**MOCA**	**RFA**	**MOCA**	**RFA**	**MOCA**
Lane 2017																
MARADONA 2019	15/104 (14)	14/105 (13)	3/104 (3)	1/105 (1)	0/104 (0)	0/105 (0)	0/105 (0)	1/104 (1)	2/104 (2)	7/105 (7)	8/104 (8)	12/105 (11)			3/104 (3)	
Vähäaho 2019													1/65 (1.5)	0/65 (0)		
RFA versus HL/S (surgery)																
Study	**Minor (not requiring intervention) (%)**												**Major (requiring intervention) (%)**			
Adverse event	**Haematoma (wound or thigh)**		**Saphenous nerve injury**		**Thermal injury/ inflammation**		**Wound problems (groin/ stab)**		**Bruising and pigmentation**		**Phlebitis**		**Wound problems**		**Other**	
Technique	**RFA**	**HL/S**	**RFA**	**HL/S**	**RFA**	**HL/S**	**RFA**	**HL/S**	**RFA**	**HL/S**	**RFA**	**HL/S**	**RFA**	**HL/S**	**RFA**	**HL/S**
EVOLVeS 2003	6/44 (14)	18/36 (50)	10/44 (23)	5/36 (4.2)					14/44 (32)	23/36 (64)			0/44 (0)	2/36 (6)[f]	0/44 (0)	0/36 (0)
Helmy ElKaffas 2011	1/90 (1.1)	30/90 (33.3)	9/90 (10)	3/90 (3.3)	0/90 (0)	0/90 (0)					6/90 (6.6)	0/90 (0)	0/90 (0)	3/90 (3.3)	0/90 (0)	1/90 (1.1)
Rasmussen 2011 [a]	0/121	1/119	6/121	5/119					8/121	6/119	12/121	5/119	1/121	1/119	0/121	1/119

Table 10. Post-operative complications within three months *(Continued)*

	(0)	(0.8)	(4.9)	(4.2)					(6.6)	(5)	(9.9)	(4.2)	(0.8)	(0.8)	(0)	(0.8)
Rautio 2002	1/15	4/13	2/15	3/13	1/15	0/13	0/15	0/13	0/15	0/13	3/15	0/13	0/15	0/13	0/15	0/13
	(7)	(31)	(13)	(23)	(7)	(0)	(0)	(0)	(0)	(0)	(20)	(0)	(0)	(0)	(0)	(0)
Subramonia 2010	0/47	0/47	9/47	20/41	0/47	0/41	0/47	7/41	5/47	0/41	0/47	0/41	0/47	0/41	0/47	0/41
	(0)	(0)	(19)	(49)	(0)	(0)	(0)	(17)	(11)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
UGFS versus HL/S (surgery)																
Study	**Minor (not requiring intervention) (%)**												**Major (requiring intervention) (%)**			
Adverse event	**Haematoma (wound or thigh)**		**Saphenous nerve injury**		**Thermal injury/ inflammation**		**Wound problems (groin/ stab)**		**Bruising and pigmentation**		**Phlebitis**		**Wound problems**		**Other**	
Technique	**UGFS**	**HL/S**	**UGFS**	**HL/S**	**UGFS**	**HL/S**	**UGFS**	**HL/S**	**UGFS**	**HL/S**	**UGFS**	**HL/S**	**UGFS**	**HL/S**	**UGFS**	**HL/S**
FOAM 2010	0/217	3/176	0/217	6/176							17/217	0/176	0/217	4/176	0/176	0/217
	(0)	(1.7)	(0)	(3.4)							(7.8)	(0)	(0)	(2.3)	(0)	(0.9)
Magna 2013			1/77	4/68					1/77	0/68			0/77	3/68	0/77	0/68
			(1.3)	(5.9)					(1.3)	(0)			(0)	(4.4)	(0)	(0)
Rasmussen 2011 [a]	1/124	1/119	2/124	5/119					8/124	6/119	17/124	5/119	4/124	1/119	1/124	1/119
	(0.8)	(0.8)	(1.6)	(4.2)					(6.5)	(5)	(14)	(4.2)	(3.2)	(0.8)	(0.8)	(0.8)
Vernermo 2016	14/72	40/65	2/72	2/65					5/72	3/65			0/72	3/65		
	(20)	(62)	(2)	(3)					(7)	(4)			(0)	(4)		

[a]Results only available per limb, not per participant
[b]Two participants developed DVTs.
[c]Post-operative acute respiratory distress syndrome (requiring seven days intensive therapy unit (ITU) support) following aspiration post-operatively
[d]In one participant, the saphenous thrombus extended into the femoral vein; it resolved without intervention.
[e]Groin infection requiring antibiotics
[f]Includes one participant who required debridement and intravenous antibiotics for a 'thigh and calf infection'
CA: cyanoacrylate glue

DVT: deep vein thrombosis
EVLA: endovenous laser ablation
EVSA: endovenous steam ablation
HL/S: high ligation and stripping
MOCA: mechanochemical ablation
PE: pulmonary embolism
RFA: radio frequency ablation
UGFS: ultrasound-guided foam sclerotherapy

Table 11. Post-operative complications after three months

Late post-operative complications (after three months)																
EVLA versus RFA																
Study	**Minor (not requiring intervention) (%)**												**Major (requiring intervention) (%)**			
Adverse event	**Haematoma (wound or thigh)**		**Saphenous nerve injury**		**Thermal injury/ inflammation**		**Wound problems (groin/ stab)**		**Bruising and pigmentation**		**Phlebitis**		**Wound problems**		**Other**	
Technique	**EVLA**	**RFA**	**EVLA**	**RFA**	**EVLA**	**RFA**	**EVLA**	**RFA**	**EVLA**	**RFA**	**EVLA**	**RFA**	**EVLA**	**RFA**	**EVLA**	**RFA**
Nordon 2011																
Rasmussen 2011 [a]																
Recovery 2009																
Shepherd 2010																
Syndor 2017			8/79 (10.3)	6/74 (8.33)	0/79 (0)	0/74 (0)			10/79 (12.66)	6/74 (8.11)	0/79 (0)	2/74 (2.7)	0/79 (0)	0/74 (0)	0/79 (0)	0/74 (0)
EVLA versus EVSA																
Study	**Minor (not requiring intervention) (%)**												**Major (requiring intervention) (%)**			
Adverse event	**Haematoma (wound or thigh)**		**Saphenous nerve injury**		**Thermal injury/ inflammation**		**Wound problems (groin/ stab)**		**Bruising and pigmentation**		**Phlebitis**		**Wound problems**		**Other**	

Table 11. Post-operative complications after three months *(Continued)*

Technique	EVLA	EVSA	EVLA	EVSA	EVLA	EVSA	EVLA	EVSA	EVLA	EVSA	EVLA	EVSA	EVLA	EVSA	EVLA	EVSA
LAST 2014			0/98	2/107							0/98	3/107				
			(0)	(1.9)							(0)	(2.8)				
EVLA versus UGFS																
Study	**Minor (not requiring intervention) (%)**												**Major (requiring intervention) (%)**			
Adverse event	**Haematoma (wound or thigh)**		**Saphenous nerve injury**		**Thermal injury/ inflammation**		**Wound problems (groin/ stab)**		**Bruising and pigmentation**		**Phlebitis**		**Wound problems**		**Other**	
Technique	**EVLA**	**UGFS**	**EVLA**	**UGFS**	**EVLA**	**UGFS**	**EVLA**	**UGFS**	**EVLA**	**UGFS**	**EVLA**	**UGFS**	**EVLA**	**UGFS**	**EVLA**	**UGFS**
Magna 2013			0/78	1/77					1/78	1/77						
			(0)	(1.3)					(1.3)	(1.3)						
Rasmussen 2011 [a]																
Vernermo 2016																
EVLA versus CA																
Study	**Minor (not requiring intervention) (%)**												**Major (requiring intervention) (%)**			
Adverse event	**Haematoma (wound or thigh)**		**Saphenous nerve injury**		**Thermal injury/ inflammation**		**Wound problems (groin/ stab)**		**Bruising and pigmentation**		**Phlebitis**		**Wound problems**		**Other**	
Technique	**EVLA**	**CA**	**EVLA**	**CA**	**EVLA**	**CA**	**EVLA**	**CA**	**EVLA**	**CA**	**EVLA**	**CA**	**EVLA**	**CA**	**EVLA**	**CA**
Calik 2019			13/200	2/200					3/200	1/200	0/200	0/200			2/200	0/200
			(7)	(1.1)					(1.6)	(0.5)	(0)	(0)			(1.1)	(0)
EVLA versus MOCA																

Table 11. Post-operative complications after three months *(Continued)*

Study	Minor (not requiring intervention) (%)												Major (requiring intervention) (%)			
Adverse event	**Haematoma (wound or thigh)**		**Saphenous nerve injury**		**Thermal injury/ inflammation**		**Wound problems (groin/ stab)**		**Bruising and pigmentation**		**Phlebitis**		**Wound problems**		**Other**	
Technique	**EVLA**	**MOCA**	**EVLA**	**MOCA**	**EVLA**	**MOCA**	**EVLA**	**MOCA**	**EVLA**	**MOCA**	**EVLA**	**MOCA**	**EVLA**	**MOCA**	**EVLA**	**MOCA**
Vähäaho 2019			3/33 (11)	0/55 (0)					3/33 (11)	6/55 (11)						

EVLA versus HL/S (surgery)

Study	Minor (not requiring intervention) (%)												Major (requiring intervention) (%)			
Adverse event	**Haematoma (wound or thigh)**		**Saphenous nerve injury**		**Thermal injury/ inflammation**		**Wound problems (groin/ stab)**		**Bruising and pigmentation**		**Phlebitis**		**Wound problems**		**Other**	
Technique	**EVLA**	**HL/S**	**EVLA**	**HL/S**	**EVLA**	**HL/S**	**EVLA**	**HL/S**	**EVLA**	**HL/S**	**EVLA**	**HL/S**	**EVLA**	**HL/S**	**EVLA**	**HL/S**
Darwood 2008 [a]	0/80 (0)	0/34 (0)	0/80 (0)	1/34 (3)	0/80 (0)	0/34 (0)	0/80 (0)	0/34 (0)	0/80 (0)	0/34 (0)	0/80 (0)	0/34 (0)	0/80 (0)	0/34 (0)	0/80 (0)	0/34 (0)
Flessenkämper 2013			23/127 (18)	5/128 (4)					12/127 (9.4)	14/128 (11)						
HELP-1 2011																
Magna 2013			0/78 (0)	1/68 (1.5)					1/78 (1.3)	0/68 (0)						
Pronk 2010																
Rasmussen 2007 [a]	0/96 (0)	0/68 (0)	0/96 (0)	1/68 (2)	0/96 (0)	0/68 (0)	0/96 (0)	0/68 (0)	0/96 (0)	0/68 (0)	0/96 (0)	0/68 (0)	0/96 (0)	0/68 (0)	0/96 (0)	0/68 (0)

Table 11. Post-operative complications after three months *(Continued)*

Rasmussen 2011 [a]																
RELACS 2012																
Vernermo 2016																
RFA versus UGFS																
Study	**Minor (requiring intervention) (%)**												**Major (requiring intervention) (%)**			
Adverse event	**Haematoma (wound or thigh)**		**Saphenous nerve injury**		**Thermal injury/ inflammation**		**Wound problems (groin/ stab)**		**Bruising and pigmentation**		**Phlebitis**		**Wound problems**		**Other**	
Technique	**RFA**	**UGFS**	**RFA**	**UGFS**	**RFA**	**UGFS**	**RFA**	**UGFS**	**RFA**	**UGFS**	**RFA**	**UGFS**	**RFA**	**UGFS**	**RFA**	**UGFS**
Rasmussen 2011 [a]																
RFA versus CA																
Study	**Minor (requiring intervention) (%)**												**Major (requiring intervention) (%)**			
Adverse event	**Haematoma (wound or thigh)**		**Saphenous nerve injury**		**Thermal injury/ inflammation**		**Wound problems (groin/ stab)**		**Bruising and pigmentation**		**Phlebitis**		**Wound problems**		**Other**	
Technique	**RFA**	**CA**	**RFA**	**CA**	**RFA**	**CA**	**RFA**	**CA**	**RFA**	**CA**	**RFA**	**CA**	**RFA**	**CA**	**RFA**	**CA**
Morrison 2015					0/84 (0)	1/86 (1.2)										
RFA versus MOCA																
Study	**Minor (not requiring intervention) (%)**												**Major (requiring intervention) (%)**			
Adverse event	**Haematoma (wound or thigh)**		**Saphenous nerve injury**		**Thermal injury/ inflammation**		**Wound problems (groin/ stab)**		**Bruising and pigmentation**		**Phlebitis**		**Wound problems**		**Other**	

Table 11. Post-operative complications after three months *(Continued)*

Technique	RFA	MO-CA	RFA	MOCA	RFA	MO-CA	RFA	MO-CA	RFA	MOCA	RFA	MO-CA	RFA	MO-CA	RFA	MO-CA
Lane 2017																
MARADONA 2019																
Vähäaho 2019			2/29	0/55					4/29							
			(6.9)	(0)					(13.8)							
RFA versus HL/S (surgery)																
Study	**Minor (not requiring intervention) (%)**												**Major (requiring intervention) (%)**			
Adverse event	**Haematoma (wound or thigh)**		**Saphenous nerve injury**		**Thermal injury/ inflammation**		**Wound problems (groin/ stab)**		**Bruising and pigmentation**		**Phlebitis**		**Wound problems**		**Other**	
Technique	**RFA**	**HL/S**	**RFA**	**HL/S**	**RFA**	**HL/S**	**RFA**	**HL/S**	**RFA**	**HL/S**	**RFA**	**HL/S**	**RFA**	**HL/S**	**RFA**	**HL/S**
EVOLVeS 2003	0/43	3/34	0/43	0/34	0/43	0/34	0/43	0/34	0/43	1/34	0/43	2/34	0/43	0/34	0/43	0/34
	(0)	(9)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(3)	(0)	(6)	(0)	(0)	(0)	(0)
Helmy ElKaffas 2011																
Rasmussen 2011 [a]																
Rautio 2002	0/15	0/13	1/15	5/13	0/15	0/13	0/15	0/13	0/15	0/13	0/15	0/13	0/15	0/13	0/15	0/13
	(0)	(0)	(0)	(38)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
Subramonia 2010																
UGFS versus HL/S (surgery)																
Study	**Minor (not requiring intervention) (%)**												**Major (requiring intervention) (%)**			

Table 11. Post-operative complications after three months *(Continued)*

Adverse event	Haematoma (wound or thigh)		Saphenous nerve injury		Thermal injury/ inflammation		Wound problems (groin/ stab)		Bruising and pigmentation		Phlebitis		Wound problems		Other	
Technique	**UGFS**	**HL/S**	**UGFS**	**HL/S**	**UGFS**	**HL/S**	**UGFS**	**HL/S**	**UGFS**	**HL/S**	**UGFS**	**HL/S**	**UGFS**	**HL/S**	**UGFS**	**HL/S**
FOAM 2010									12/213 (5.6)	2/177 (1.1)						
Magna 2013			1/77 (1.3)	1/68 (1.5)												
Rasmussen 2011 [a]																
Vernermo 2016																

[a]Results only available per limb, not per participant
CA: cyanoacrylate glue
EVLA: endovenous laser ablation
EVSA: endovenous steam ablation
HL/S: high ligation and stripping
MOCA: mechanochemical ablation
RFA: radio frequency ablation
UGFS: ultrasound-guided foam sclerotherapy

Table 12. Quality of life scores

Technique	Study	Quality of life score							
		V-Q/SymQ	**AVVSS**	**CIVIQ2**	**SF-12**	**SF-36**	**RAND-36**	**EQ-5D**	**SF-6D**
EVLA versus RFA	Nordon 2011							✓	
	Rasmussen 2011	✓				✓			
	Recovery 2009							✓	
	Shepherd 2010				✓				
EVLA versus EVSA	LAST 2014							✓	

Table 12. Quality of life scores *(Continued)*

EVLA versus UGFS	Magna 2013		✓			✓		
	Rasmussen 2011	✓			✓			
	Vernermo 2016		✓					
EVLA versus CA	Calik 2019			✓				
EVLA versus MOCA	Vähäaho 2019		✓					
EVLA versus HL/S (surgery)	Darwood 2008		✓					
	Flessenkämper 2013					✓		
	HELP-1 2011		✓		✓	✓	✓	
	Magna 2013		✓			✓		
	Pronk 2010					✓		
	Rasmussen 2007		✓		✓			
	Rasmussen 2011	✓			✓			
	RELACS 2012			✓				
	Vernermo 2016		✓					
RFA versus UGFS	Rasmussen 2011	✓			✓			
RFA versus CA	Morrison 2015		✓			✓		
RFA versus MOCA	Lane 2017		✓			✓		
	MARADONA 2019		✓				✓	
	Vähäaho 2019		✓					
RFA versus HL/S (surgery)	EVOLVeS 2003			✓				
	Rasmussen 2011	✓			✓			

Table 12. Quality of life scores *(Continued)*

	Rautio 2002					✓	
	Subramonia 2010	✓	✓				
RFA versus UGFS	Rasmussen 2011	✓			✓		
UGFS versus HL/S (surgery)	FOAM 2010						✓
	Magna 2013		✓				✓
	Rasmussen 2011	✓			✓		
	Vernermo 2016		✓				

AVVSS: Aberdeen Varicose Vein Symptom Severity Score
CA: cyanoacrylate glue
CIVIQ2: Chronic Venous Insufficiency Quality of Life Questionnaire
EQ-5D: EuroQol-5D
EVLA: endovenous laser ablation
EVSA: endovenous steam ablation
HL/S: high ligation and stripping
MOCA: mechanochemical ablation
RAND-36: Short term RAND-36 (validated for Finland)
RFA: radiofrequency ablation
SF-12: Medical Outcomes Study Short Form 12
SF-36: Medical Outcomes Study Short Form 36
SF-6D: variation of the Medical Outcomes Study Short Form 36
UGFS: ultrasound-guided foam sclerotherapy
V-Q/SymQ: VEINES-QoL/Sym questionnaire

Table 13. Change in Venous Clinical Severity Score (VCSS)

EVLA versus RFA						
Study - final time point	**Initial VCSS**		**Final VCSS**		**Change in VCSS**	
	EVLA	**RFA**	**EVLA**	**RFA**	**EVLA**	**RFA**
Recovery 2009 mean (SD) 1 month	4.9 (2.8)	4.7 (3.1)	3.2 (1.8)	2.7 (2.2)		
Rasmussen 2011 mean (SD) 3 yr	2.68 (2.25)	2.95 (2.06)	0.34 (1.3)	0.44 (1.82)	3.3	3.7
Shepherd 2010 mean (SD) 6 months	4.7 (2.1)	5.1 (2.1)	1.4 (1.8)	1.4 (1.7)		
Syndor 2017 median (range) 6 months	5 (2 - 26)	5 (1 - 20)	1 (0 - 18)	1 (0 - 6)		
EVLA versus EVSA						
Study - final time point	**Initial VCSS**		**Final VCSS**		**Change in VCSS**	
	EVLA	**EVSA**	**EVLA**	**EVSA**	**EVLA**	**EVSA**
LAST 2014 change after 12 weeks (95% CI)	not given	not given	not given	not given	-2.5 (-2.1 to -2.93)	all -2.9 (-2.4 to -3.5) hIgh[a] -2.69 (-2.34 to -3.04)
EVLA versus UGFS						
Study - final time point	**Initial VCSS**		**Final VCSS**		**Change in VCSS**	
	EVLA	**UGFS**	**EVLA**	**UGFS**	**EVLA**	**UGFS**
Rasmussen 2011 mean (SD) 3 yr	2.68 (2.25)	2.66 (1.45)	0.34 (1.3)	0.15 (0.4)		
EVLA versus CA						
Study - final time point	**Initial VCSS**		**Final VCSS**		**Change in VCSS**	
	EVLA	**CA**	**EVLA**	**CA**	**EVLA**	**CA**
Calik 2019 mean (SD) 1 yr	5.8 (1.9)	5.7 (1.9)	1.3 (0.9)	1.3 (0.9)		
EVLA versus MOCA - no data						
EVLA versus HL/S (surgery)						
Study - final time point	**Initial VCSS**		**Final VCSS**		**Change in VCSS**	
	EVLA	**HL/S (surgery)**	**EVLA**	**HL/S (surgery)**	**EVLA**	**HL/S (surgery)**

Table 13. Change in Venous Clinical Severity Score (VCSS) *(Continued)*

Rasmussen 2007 mean (SD) 5 yr	2.8 (1.7)	2.4 (1.4)	0.4 (0.9)	2.4 (1.4)		
Rasmussen 2011 mean (SD) 3 yr	2.68 (2.25)	2.75 (1.62)	0.34 (1.3)	0.3 (0.5)		
RFA versus UGFS						
Study - final time point	**Initial VCSS**		**Final VCSS**		**Change in VCSS**	
	RFA	**UGFS**	**RFA**	**UGFS**	**RFA**	**UGFS**
Rasmussen 2011 mean (SD) 3 yr	2.95 (2.06)	2.66 (1.45)	0.44 (1.82)	0.15 (0.4)		
RFA versus CA						
Study - final time point	**Initial VCSS**		**Final VCSS**		**Change in VCSS**	
	RFA	**CA**	**RFA**	**CA**	**RFA**	**CA**
Morrison 2015 mean (SD) 3 months	5.6 (2.6)	5.5 (2.6)	2.0 (2.0)	1.9 (1.6)		
RFA versus MOCA						
Study - final time point	**Initial VCSS**		**Final VCSS**		**Change in VCSS**	
	RFA	**MOCA**	**RFA**	**MOCA**	**RFA**	**MOCA**
Lane 2017 median (range) 6 months	5	6	2 (1 - 5)	2 (1 - 4)		
MARADONA 2019 median (IQR) 2 yr	individually reported	individually reported	individually reported	individually reported	4 (3 - 5)	3 (2 - 5)
RFA versus HL/S (surgery)						
Study - final time point	**Initial VCSS**		**Final VCSS**		**Change in VCSS**	
	RFA	**HL/S (surgery)**	**RFA**	**HL/S (surgery)**	**RFA**	**HL/S (surgery)**
EVOLVeS 2003 mean (SD) 2 yr	4.8 (0.34)	4.39 (0.38)	unable to read from graph			
Rasmussen 2011 mean (SD) 3 yr	2.95 (2.06)	2.75 (1.62)	0.44 (1.82)	0.3 (0.5)		
Rautio 2002 median (range) 3 yr change - mean (SD)	4 (4 - 6)	5 (4 - 9)			- 4.3 (2.3)	-4 (-1.2)
UGFS versus HL/S (surgery)						
Study - final time point	**Initial VCSS**		**Final VCSS**		**Change in VCSS**	
	UGFS	**HL/S (surgery)**	**UGFS**	**HL/S (surgery)**	**UGFS**	**HL/S (surgery)**
FOAM 2010 mean (SD) 2 yr	3.2 (1.9)	3.5 (2.2)	1.7 (1.2)	1.9 (1.4)	-1.49	-1.75
Rasmussen 2011 mean (SD) 3 yr	2.66 (1.45)	2.75 (1.62)	0.15 (0.4)	0.3 (0.5)		

[a]High dose of steam
CA: cyanoacrylate glue
CI: confidence interval
EVLA: endovenous laser ablation
EVSA: endovenous steam ablation
HL/S: high ligation and stripping
IQR: interquartile range
MOCA: mechanochemical ablation
RFA: radiofrequency ablation
SD: standard deviation
UGFS: ultrasound-guided foam sclerotherapy
yr: year(s)

Table 14. Length of procedure or operative time

EVLA versus RFA		
Study	**Time (min)**	
	EVLA	**RFA**
Nordon 2011 median (range)	30 (10 - 60)	30 (15 - 60)
Rasmussen 2011 mean (range)[a]	26 (12 - 80)	27 (12 - 80)
Syndor 2017 median (range)	total procedure 23.5 (8 - 95) total ablation time 5 (1 - 18)	total procedure 21 (6 - 64) total ablation time 4 (1 - 14)
EVLA versus EVSA - no data		
EVLA versus UGFS		
Study	**Time (min)**	
	EVLA	**UGFS**
Rasmussen 2011 mean (range)[a]	26 (12 - 80)	19 (5 - 145)
EVLA versus CA		
Study	**Time (min)**	
	EVLA	**CA**
Calik 2019 mean (SD)	31.7 (8.8)	13 (3.4)
EVLA versus MOCA - no data		
EVLA versus HL/S (surgery)		
Study	**Time (min)**	
	EVLA	**HL/S (surgery)**
HELP-1 2011 mean (SD)	61 (14)	67 (16)
Rasmussen 2011 mean (range)[a]	26 (12 - 80)	32 (15 - 80)

Table 14. Length of procedure or operative time *(Continued)*

Vernermo 2016 mean (SD) [range]	83 (17) [50 - 139]	95 (19) [62 - 155]
RFA versus UGFS		
Study	**Time (min)**	
	RFA	**UGFS**
Rasmussen 2011 mean (range)[a]	27 (12 - 80)	19 (5 - 145)
RFA versus CA		
Study	**Time (min)**	
	RFA	**CA**
Morrison 2015 mean (range)	19 (5 - 46)	24 (11 - 40)
RFA versus MOCA		
Study	**Time (min) procedural time**	
	RFA	**MOCA**
MARADONA 2019 mean (IQR)	13 (4 - 85)	12 (5 - 45)
RFA versus HL/S (surgery)		
Study	**Time (min)**	
	RFA	**HL/S (surgery)**
EVOLVeS 2003 mean (SD)	74 (10)	89 (12)
Helmy ElKaffas 2011 mean (SD)	40 (12)	45 (13)
Rasmussen 2011 mean (range)[a]	27 (12 - 80)	32 (15 - 80)
Rautio 2002 mean (SD)	Operating time: 75 (16.6) Operating room time: 115 (18.3) Recovery room time: 227 (57.6)	Operating time: 57 (11) Operating room time: 99 (12.9) Recovery room time: 198 (40.7)
Subramonia 2010 median (IQR)	Theatre time: 82 (73 - 91) Procedure time: 76 (67 - 84)	Theatre time: 55 (48 - 63) Procedure time: 48 (39 - 54)
UGFS versus HL/S (surgery)		
Study	**Time (min)**	
	UGFS	**HL/S (surgery)**
Rasmussen 2011 mean (range)[a]	19 (5 - 145)	32 (15 - 80)

[a]Surgeon's time
CA: cyanoacrylate glue
EVLA: endovenous laser ablation
EVSA: endovenous steam ablation
HL/S: high ligation and stripping
IQR: interquartile range
min: minutes
MOCA: mechanochemical ablation
RFA: radiofrequency ablation
SD: standard deviation
UGFS: ultrasound-guided foam sclerotherapy

Table 15. Duration of hospital stay

EVLA versus RFA		
Study	**Length of hospital stay % day case**	
	EVLA	**RFA**
Shepherd 2010	98[a]	95.5[b]
EVLA versus EVSA - no data		
EVLA versus UGFS - no data		
EVLA versus CA - no data		
EVLA versus MOCA - no data		
EVLA versus HL/S (surgery)		
Study	**Length of hospital stay % day case**	
	EVLA	**HL/S (surgery)**
Darwood 2008	100	100
Flessenkämper 2013	~100	~100
HELP-1 2011	100	78.8
Pronk 2010	100	100
Rasmussen 2007	100	100
RFA versus UGFS - no data		
RFA versus CA		
Study	**Length of hospital stay % day case**	
	RFA	**CA**
Morrison 2015	100	100
RFA versus MOCA - no data		

Table 15. Duration of hospital stay *(Continued)*

RFA versus HL/S (surgery)

Study	Length of hospital stay % day case	
	RFA	HL/S (surgery)
EVOLVeS 2003	95[c]	86[d]
Helmy ElKaffas 2011 hours in hospital mean (SD) [range]	14 (SD 3.6) [12 to 18]	30 (SD 11.5) [18 to 48]
Rautio 2002	93.3	92.3

UGFS versus HL/S (surgery)

Study	Length of hospital stay % day case	
	UGFS	HL/S (surgery)
FOAM 2010	not indicated	100

[a]One participant required overnight admission due to post-operative nausea.
[b]One participant required overnight admission for pain requiring opioids, one for nausea and one for hypotension secondary to general anaesthesia.
[c]Two participants kept overnight
[d]Five participants kept overnight
CA: cyanoacrylate glue
EVLA: endovenous laser ablation
EVSA: endovenous steam ablation
HL/S: high ligation and stripping
MOCA: mechanochemical ablation
RFA: radiofrequency ablation
UGFS: ultrasound-guided foam sclerotherapy

Table 16. Time to return to work and normal activities

EVLA versus RFA

Study	Time to return to work (days)		Time to return normal activities (days)	
	EVLA	RFA	EVLA	RFA
Nordon 2011 median (range)	7 (1 - 60)[a]	9 (0 - 28)		
Rasmussen 2011 median (range)	3.6 (0 - 46)	2.9 (0 - 14)	3.6 (0 - 46)	1 (0 - 30)
Shepherd 2010	n returned to work at 3 days 14 (41%) 7 days 27 (71%)	n returned to work at 3 days 15 (37%) 7 days 29 (71%)	n returned to normal at 3 days 25 (50%) 7 days 37 (74%)	n returned to normal at 3 days 37 (60%) 7 days 48 (77%)

Table 16. Time to return to work and normal activities *(Continued)*

EVLA versus EVSA

Study	Time to return to work (days)		Time to return normal activities (days)	
	EVLA	EVSA	EVLA	EVSA
LAST 2014 mean (95% CI)			4.2 (3.4 - 5)	all 1.6 (1 - 2.1) high[b] 1.6 (0.9 - 2.3)

EVLA versus UGFS

Study	Time to return to work (days)		Time to return normal activities (days)	
	EVLA	UGFS	EVLA	UGFS
Rasmussen 2011 median (range)	3.6 (0 - 46)	2.9 (0 - 33)	2 (0 - 25)	1 (0 - 30)
Vernermo 2016 mean (SD) [range]	8 (5) [0 - 29]	1 (3) [0 - 21]		

EVLA versus CA

Study	Time to return to work (days)		Time to return normal activities (days)	
	EVLA	CA	EVLA	CA
Calik 2019 mean (SD)	2.9 (1.8)	1.5 (0.6)		

EVLA versus MOCA

Study	Time to return to work (days)		Time to return normal activities (days)	
	EVLA	MOCA	EVLA	MOCA
Vähäaho 2019 [c] mean	actual 5.3 perceived 8.6	actual 4.3 perceived 7.8		

EVLA versus HL/S (surgery)

Study	Time to return to work (days)		Time to return normal activities (days)	
	EVLA	HL/S (surgery)	EVLA	HL/S (surgery)
Darwood 2008 [d] median (IQR)	EVLT1: 4 (2.5 - 7) EVLT2: 4 (1 - 12)	17 (7.25 - 33.25)	EVLT1: 2 (0 - 7) EVLT2: 2 (0 - 7)	7 (2 - 26)
HELP-1 2011 median (range)	4 (2 - 14)	14 (13 - 28)	3 (1 - 10)	14 (7 - 25)
Pronk 2010 mean (SD)	4.38 (5.43)	4.15 (3.72)	3.16 (4.34)	3.20 (4.01)
Rasmussen 2007 mean (SD)	7 (6)	7.6 (4.9)	6.9 (7)	7.7 (6.1)

Table 16. Time to return to work and normal activities *(Continued)*

Rasmussen 2011 median (range)	3.6 (0 - 46)	4.3 (0 - 42)	2 (0 - 25)	4 (0 - 30)
RELACS 2012 mean	10.4	11.8	4.8	4
Vernermo 2016 mean (SD) [range]	8 (5) [0 - 29]	12 (6) [0 - 33]		
RFA versus UGFS				
Study	**Time to return to work (days)**		**Time to return normal activities (days)**	
	RFA	**UGFS**	**RFA**	**UGFS**
Rasmussen 2011 median (range)	2.9 (0 - 14)	2.9 (0 - 33)	1 (0 - 30)	1 (0 - 30)
RFA versus CA - no data				
RFA versus MOCA				
Study	**Time to return to work (days)**		**Time to return normal activities**	
	RFA	**MOCA**	**RFA**	**MOCA**
Lane 2017 median (IQR)	2 (2 - 7)	3 (1 - 7)	2 (1 - 7)	2 (1 - 4)
MARADONA 2019 mean (range)	2.98 (0 - 15)	2.28 (0 -13)	1.43 (0 - 6)	1 (0 - 6)
Vähäaho 2019 [c] mean	actual 4.7 perceived 6.4	actual 4.3 perceived 7.8		
RFA versus HL/S (surgery)				
Study	**Time to return to work (days)**		**Time to return normal activities**	
	RFA	**HL/S (surgery)**	**RFA**	**HL/S (surgery)**
EVOLVeS 2003 [e] mean	4.7	12.4	1.15	3.89
Helmy ElKaffas 2011 mean (SD)			3 (3)	7 (2.6)
Rasmussen 2011 median (range)	2.9 (0 - 14)	4.3 (0 - 42)	1 (0 - 30)	4 (0 - 30)
Rautio 2002 [c] mean (SD)	actual: 6.5 (3.3) perceived: 6.1 (4.4)	actual: 15.6 (6) perceived: 19.2 (10)	no data	no data
Subramonia 2010 median (IQR)	10 (4 - 13)	18.5 (11 - 28)	3 (0 - 7)	12.5 (4 - 21)
UGFS versus HL/S (surgery)				

Table 16. Time to return to work and normal activities *(Continued)*

Study	Time to return to work (days)		Time to return normal activities	
	UGFS	HL/S (surgery)	UGFS	HL/S (surgery)
Rasmussen 2011 median (range)	2.9 (0 - 33)	4.3 (0 - 42)	1 (0 - 30)	4 (0 - 30)
Vernermo 2016 mean (SD) [range]	1 (3) [0 - 21]	12 (6) [0 - 33]		

[a]Three outliers at 42, 60, 60 days
[b]High dose of steam
[c]Sick leave days taken and participant's own perception of required sick leave
[d]Presented both laser techniques separately
[e]Adjusted according to the number of phlebectomies performed, and the type of anaesthetic used
CA: cyanoacrylate glue
CI: confidence interval
EVLA: endovenous laser ablation (same as EVLT)
EVLT: endovenous laser therapy
EVSA: endovenous steam ablation
HL/S: high ligation and stripping
IQR: interquartile range
MOCA: mechanochemical ablation
RFA: radiofrequency ablation
SD: standard deviation
UGFS: ultrasound-guided foam sclerotherapy

APPENDICES

Appendix 1. Database searches Nov 2017 and Jan 2018

Search 1: EVLA and foam sclerotherapy vs open surgery

Source	Search strategy	Hits retrieved
VASCULAR REGISTER IN CRS WEB	great saphenous vein AND VVeins*	14 Nov 2017: 136
CENTRAL via CRSO	#1 MESH DESCRIPTOR Sclerotherapy EXPLODE ALL TREES 447 #2 MESH DESCRIPTOR Sclerosing Solutions EXPLODE ALL TREES 385 #3 sclero*:TI,AB,KY 10085 #4 (tetradecyl adj2 (sulfate or sulphate)):TI,AB,KY 62 #5 MESH DESCRIPTOR Sodium Tetradecyl Sulfate EXPLODE ALL TREES 37 #6 MESH DESCRIPTOR Saline Solution, Hypertonic EXPLODE ALL TREES 442 #7 MESH DESCRIPTOR Ethanolamines 1499 #8 (polydocanol or polidocanol):TI,AB,KY 216 #9 saline:TI,AB,KY 20656	13 Nov 2017: 402

(Continued)

	#10 (ethanolamine adj2 oleate):TI,AB,KY 65 #11 (sodium adj2 morrhuate):TI,AB,KY 19 #12 sotradecol:TI,AB,KY 6 #13 (aetoxisclerol or aethoxysclerol):TI,AB,KY 15 #14 Turbofoam:TI,AB,KY 2 #15 (foam* or microfoam*):TI,AB,KY 1440 #16 varisolve:TI,AB,KY 2 #17 MESH DESCRIPTOR Laser Therapy EXPLODE ALL TREES 3452 #18 (endovenous or EVLA or EVLT or radiofrequency or laser* or ablation* or obliteration* or RFA):TI,AB,KY 16990 #19 MESH DESCRIPTOR Catheter Ablation EXPLODE ALL TREES 1211 #20 aetoxiskerol or aethoxyskerol 1 #21 21 #1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9 or #10 or #11 or #12 or #13 or #14 or #15 or #16 or #17 or #18 or #19 or #20 49890 #22 MESH DESCRIPTOR Vascular Surgical Procedures EXPLODE ALL TREES 13303 #23 MESH DESCRIPTOR Ligation EXPLODE ALL TREES 559 #24 (surg* or ligat* or strip* or phlebectomy):TI,AB,KY 149800 #25 #22 or #23 or #24 155224 #26 #21 and #25 15863 #27 MESH DESCRIPTOR Varicose Veins EXPLODE ALL TREES 803 #28 MESH DESCRIPTOR Saphenous Vein EXPLODE ALL TREES WITH QUALIFIERS SU 207 #29 (varic* or incomp* or insuffici* or tortuous or sapheno* or GSV or CVI):TI,AB,KY 23616 #30 MESH DESCRIPTOR Venous Insufficiency EXPLODE ALL TREES 405 #31 #27 or #28 or #29 or #30 23650 #32 #26 and #31 1011 #33 01/01/2014 TO 13/11/2017:CD 370986 #34 #32 AND #33 402	
Clinicaltrials.gov	Varicose Veins OR VARICES | ablation OR foam | First posted from 01/01/2014 to 11/14/2017	14 Nov 2017: 35
ICTRP Search Portal	Varicose Veins OR VARICES | ablation OR foam | 01/01/2014 to 11/14/2017	14 Nov 2017: 17
MEDLINE VIA OVID	1 exp Sclerotherapy/ 5411 2 exp Sclerosing Solutions/ 10832 3 sclero*.ti,ab. 180324	14 Nov 2017: 76

(Continued)

4 (tetradecyl adj2 (sulfate or sulphate)).ti,ab. 455

5 exp Sodium Tetradecyl Sulfate/ 460

6 exp Saline Solution, Hypertonic/ 5645

7 Ethanolamines/ 11813

8 (polydocanol or polidocanol).ti,ab. 752

9 saline.ti,ab. 170166

10 (ethanolamine adj2 oleate).ti,ab. 332

11 (sodium adj2 morrhuate).ti,ab. 179

12 sotradecol.ti,ab. 55

13 (aetoxisclerol or aethoxysclerol).ti,ab. 50

14 (aetoxiskerol or aethoxyskerol).ti,ab. 1

15 Turbofoam.ti,ab. 2

16 (foam* or microfoam*).ti,ab. 23577

17 varisolve.ti,ab. 2

18 exp Laser Therapy/ 60498

19 (endovenous or EVLA or EVLT or radiofrequency or laser* or ablation* or obliteration* or RFA).ti,ab. 341596

20 exp Catheter Ablation/ 31195

21 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 743792

22 exp Vascular Surgical Procedures/ 242140

23 exp Ligation/ 23767

24 (surg* or ligat* or strip* or phlebectomy).ti,ab. 1911449

25 22 or 23 or 24 2073066

26 21 and 25 97099

27 exp Varicose Veins/ 17830

28 exp Venous Insufficiency/ 7384

29 exp Saphenous Vein/su [Surgery] 3241

30 (varic* or incomp* or insuffici* or tortuous or sapheno* or GSV or CVI).ti,ab. 445791

31 27 or 28 or 29 or 30 455898

32 26 and 31 6917

33 randomized controlled trial.pt. 505234

34 controlled clinical trial.pt. 100418

35 randomized.ab. 441461

36 placebo.ab. 205236

(Continued)

	37 drug therapy.fs. 2146561	
	38 randomly.ab. 304739	
	39 trial.ab. 464951	
	40 groups.ab. 1882251	
	41 33 or 34 or 35 or 36 or 37 or 38 or 39 or 40 4444149	
	42 32 and 41 1865	
	43 2017*.ed. 946724	
	44 42 and 43 76	
	45 from 44 keep 1-76 76	
EMBASE	1 exp Sclerotherapy/ 8991	13 Nov 2017: 179
	2 exp Sclerosing Solutions/ 7438	
	3 sclero*.ti,ab. 184740	
	4 (tetradecyl adj2 (sulfate or sulphate)).ti,ab. 412	
	5 exp Sodium Tetradecyl Sulfate/ 1098	
	6 exp Saline Solution, Hypertonic/ 138036	
	7 Ethanolamines/ 1673	
	8 (polydocanol or polidocanol).ti,ab. 755	
	9 saline.ti,ab. 161243	
	10 (ethanolamine adj2 oleate).ti,ab. 297	
	11 (sodium adj2 morrhuate).ti,ab. 96	
	12 sotradecol.ti,ab. 57	
	13 (aetoxisclerol or aethoxysclerol).ti,ab. 41	
	14 (aetoxiskerol or aethoxyskerol).ti,ab. 1	
	15 Turbofoam.ti,ab. 3	
	16 (foam* or microfoam*).ti,ab. 23376	
	17 varisolve.ti,ab. 5	
	18 exp Laser Therapy/ 18342	
	19 (endovenous or EVLA or EVLT or radiofrequency or laser* or ablation* or obliteration* or RFA).ti,ab. 307984	
	20 exp Catheter Ablation/ 27168	
	21 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 741625	
	22 exp Vascular Surgical Procedures/ 332738	
	23 exp Ligation/ 43062	
	24 (surg* or ligat* or strip* or phlebectomy).ti,ab. 1839209	

(Continued)

	25 22 or 23 or 24 2038357 26 21 and 25 112846 27 exp Varicose Veins/ 31021 28 exp Venous Insufficiency/ 6660 29 exp Saphenous Vein/su [Surgery] 261 30 (varic* or incomp* or insuffici* or tortuous or sapheno* or GSV or CVI).ti,ab. 407337 31 27 or 28 or 29 or 30 421472 32 26 and 31 9311 33 randomized controlled trial/ 434019 34 controlled clinical trial/ 407541 35 random$.ti,ab. 1124569 36 randomization/ 67995 37 intermethod comparison/ 222704 38 placebo.ti,ab. 213793 39 (compare or compared or comparison).ti. 324804 40 ((evaluated or evaluate or evaluating or assessed or assess) and (compare or compared or comparing or comparison)).ab. 1550509 41 (open adj label).ti,ab. 59603 42 ((double or single or doubly or singly) adj (blind or blinded or blindly)).ti,ab. 152470 43 double blind procedure/ 118472 44 parallel group$1.ti,ab. 18844 45 (crossover or cross over).ti,ab. 69732 46 ((assign$ or match or matched or allocation) adj5 (alternate or group$1 or intervention$1 or patient$1 or subject$1 or participant$1)).ti,ab. 239509 47 (assigned or allocated).ti,ab. 280620 48 (controlled adj7 (study or design or trial)).ti,ab. 251185 49 (volunteer or volunteers).ti,ab. 167273 50 trial.ti. 204542 51 33 or 34 or 35 or 36 or 37 or 38 or 39 or 40 or 41 or 42 or 43 or 44 or 45 or 46 or 47 or 48 or 49 or 50 3351318 52 32 and 51 2503 53 2017*.dc. 1594452 54 52 and 53 176	
CINAHL	S39 (EM 2017) AND (S37 AND S38) (15)	14 Nov 2017: 15

(Continued)

S38 EM 2017 (170,959)

S37 S29 AND S36 (235)

S36 S30 OR S31 OR S32 OR S33 OR S34 OR S35 (950,269)

S35 TX randomly (41,411)

S34 TX "treatment as usual" (707)

S33 TX "double-blind*" (754,745)

S32 TX "single-blind*" (8,635)

S31 TX trial (235,674)

S30 MH "Clinical Trials" (90,720)

S29 S19 AND S23 AND S28 (538)

S28 S24 OR S25 OR S26 OR S27 (42,333)

S27 varic* or incomp* or insuffici* or tortuous or sapheno* or GSV or CVI (40,779)

S26 (MH "Saphenous Vein/SU") (120)

S25 (MH "Venous Insufficiency+") (678)

S24 (MH "Varicose Veins+") (2,342)

S23 S20 OR S21 OR S22 (284,406)

S22 surg* or ligat* or strip* or phlebectomy (284,406)

S21 (MH "Ligation") (629)

S20 vascular surgical procedures (42)

S19 S1 OR S2 OR S3 OR S4 OR S5 OR S6 OR S7 OR S8 OR S9 OR S10 OR S11 OR S12 OR S13 OR S14 OR S15 OR S16 OR S17 OR S18 (54,423)

S18 (MH "Catheter Ablation") (6,617)

S17 (endovenous or EVLA or EVLT or radiofrequency or laser* or ablation* or obliteration* or RFA) (22,989)

S16 (MH "Laser Therapy+") (5,466)

S15 varisolve (0)

S14 foam* or microfoam* (2,350)

S13 Turbofoam (0)

S12 aetoxisclerol or aethoxysclerol (0)

S11 sotradecol (2)

S10 sodium n2 morrhuate (11)

S9 ethanolamine n2 oleate (13)

S8 saline (8,211)

S7 polydocanol or polidocanol (33)

S6 (MH "Ethanolamines") (123)

(Continued)

	S5 (MH "Saline Solution, Hypertonic") (527) S4 TX tetradecyl N2 (sulfate or sulphate) (10) S3 TX sclero* (21,277) S2 (MH "Sclerosing Solutions") (181) S1 (MH "Sclerotherapy") (365)	
AMED	1 sclero*.ti,ab. 2212 2 (tetradecyl adj2 (sulfate or sulphate)).ti,ab. 0 3 (polydocanol or polidocanol).ti,ab. 3 4 saline.ti,ab. 528 5 (ethanolamine adj2 oleate).ti,ab. 0 6 (sodium adj2 morrhuate).ti,ab. 1 7 sotradecol.ti,ab. 0 8 (aetoxisclerol or aethoxysclerol).ti,ab. 0 9 (aetoxiskerol or aethoxyskerol).ti,ab. 0 10 Turbofoam.ti,ab. 0 11 (foam* or microfoam*).ti,ab. 269 12 varisolve.ti,ab. 0 13 exp Laser Therapy/ 168 14 (endovenous or EVLA or EVLT or radiofrequency or laser* or ablation* or obliteration* or RFA).ti,ab. 1116 15 (surg* or ligat* or strip* or phlebectomy).ti,ab. 11043 16 exp Varicose Veins/ 63 17 exp Venous Insufficiency/ 49 18 (varic* or incomp* or insuffici* or tortuous or sapheno* or GSV or CVI).ti,ab. 2784 19 or/1-14 4120 20 or/16-18 2845 21 15 and 19 and 20 7 22 "2017".yr. 47 23 21 and 22 0	13 Nov 2017: 0

Search 2: Cyanoacrylate Glue, OR Mechanochemical endovenous Ablation (MOCA) OR Steam treatment versus open surgery for great saphenous vein varices

Source	Search strategy	Hits retrieved
VASCULAR REGISTER IN CRS WEB	#1 STEAM AND INREGISTER #2 Cyanoacrylate AND INREGISTER #3 Mechanochemical AND INREGISTER #4 #1 OR #2 OR #3	20 Nov 2017: 13
CENTRAL via CRSO Issue 10, 2017	#1 MESH DESCRIPTOR Vascular Surgical Procedures EXPLODE TREES 1 13304 #2 MESH DESCRIPTOR Ligation EXPLODE ALL TREES 559 #3 (surg* or ligat* or strip* or phlebectomy):TI,AB,KY 151275 #4 #1 OR #2 OR #3 156699 #5 MESH DESCRIPTOR Varicose Veins EXPLODE ALL TREES 803 #6 MESH DESCRIPTOR Venous Insufficiency EXPLODE ALL TREES 405 #7 MESH DESCRIPTOR Saphenous Vein EXPLODE ALL TREES WITH QUALIFIERS SU 207 #8 (varic* or incomp* or insuffici* or tortuous or sapheno* or GSV or CVI):TI,AB,KY 23850 #9 #5 OR #6 OR #7 OR #8 23884 #10 MESH DESCRIPTOR Cyanoacrylates EXPLODE ALL TREES 178 #11 ("tissue adhesive*"):TI,AB,KY 722 #12 Cyanoacrylate*:TI,AB,KY 314 #13 Enbucrilate:TI,AB,KY 83 #14 VenaSeal:TI,AB,KY 3 #15 VariClose:TI,AB,KY 0 #16 VeClose:TI,AB,KY 5 #17 Histoacryl:TI,AB,KY 39 #18 ("Mechanochemical endovenous Ablation"):TI,AB,KY 6 #19 ("Mechanochemical Ablation"):TI,AB,KY 8 #20 MOCA:TI,AB,KY 265 #21 ClariVein:TI,AB,KY 9 #22 steam:TI,AB,KY 184 #23 #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 1349 #24 #4 AND #9 AND #23 70	20 Nov 2017: 70
Clinicaltrials.gov	varicose OR "Venous Insufficiency" | "tissue adhesives" OR Cyanoacrylates OR Enbucrilate OR Histoacryl OR MOCA OR steam OR Mechanochemical	20 Nov 2017: 19

(Continued)

ICTRP Search Portal	varicose OR "Venous Insufficiency" | "tissue adhesives" OR Cyanoacrylates OR Enbucrilate OR Histoacryl OR MOCA OR steam OR Mechanochemical	20 Nov 2017: 5
MEDLINE VIA OVID	1 exp Vascular Surgical Procedures/ 242206 2 exp Ligation/ 23775 3 (surg* or ligat* or strip* or phlebectomy).ti,ab. 1912818 4 1 or 2 or 3 2074481 5 exp Varicose Veins/ 17833 6 exp Venous Insufficiency/ 7385 7 exp Saphenous Vein/su [Surgery] 3242 8 (varic* or incomp* or insuffici* or tortuous or sapheno* or GSV or CVI).ti,ab. 445981 9 5 or 6 or 7 or 8 456089 10 randomized controlled trial.pt. 505454 11 controlled clinical trial.pt. 100423 12 randomized.ab. 441797 13 placebo.ab. 205350 14 drug therapy.fs. 2147141 15 randomly.ab. 304986 16 trial.ab. 465386 17 groups.ab. 1883715 18 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 4446580 19 exp Cyanoacrylates/ 4846 20 "tissue adhesive*".ti,ab. 1862 21 Cyanoacrylate*.ti,ab. 4342 22 Enbucrilate.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] 1682 23 VenaSeal.ti,ab. 8 24 Enbucrilate.ti,ab. 34 25 VariClose.ti,ab. 6 26 VeClose.ti,ab. 3 27 Histoacryl.ti,ab. 508 28 NBCA.ti,ab. 457 29 "Mechanochemical endovenous Ablation".ti,ab. 20 30 "Mechanochemical Ablation".ti,ab. 25	20 Nov 2017: 106

(Continued)

	31 MOCA.ti,ab. 1410 32 ClariVein.ti,ab. 31 33 "Endovenous steam".ti,ab. 9 34 steam.ti,ab. 7050 35 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34 16144 36 4 and 9 and 18 and 35 106	
EMBASE	1 exp Vascular Surgical Procedures/ 410518 2 exp Ligation/ 53587 3 (surg* or ligat* or strip* or phlebectomy).ti,ab. 2359292 4 1 or 2 or 3 2609911 5 exp Varicose Veins/ 49426 6 exp Venous Insufficiency/ 9594 7 exp Saphenous Vein/su [Surgery] 1007 8 (varic* or incomp* or insuffici* or tortuous or sapheno* or GSV or CVI).ti,ab. 541810 9 exp Cyanoacrylates/ 1798 10 "tissue adhesive*".ti,ab. 2040 11 Cyanoacrylate*.ti,ab. 5292 12 Enbucrilate.mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word] 3938 13 VenaSeal.ti,ab. 24 14 Enbucrilate.ti,ab. 38 15 VariClose.ti,ab. 11 16 VeClose.ti,ab. 5 17 Histoacryl.ti,ab. 712 18 NBCA.ti,ab. 793 19 "Mechanochemical endovenous Ablation".ti,ab. 23 20 "Mechanochemical Ablation".ti,ab. 41 21 MOCA.ti,ab. 3509 22 ClariVein.ti,ab. 36 23 "Endovenous steam".ti,ab. 12 24 STEAM.ti,ab. 9350 25 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 22590	20 Nov 2017: 210

(Continued)

	26 randomized controlled trial/ 483088 27 controlled clinical trial/ 453499 28 random$.ti,ab. 1264147 29 randomization/ 76355 30 intermethod comparison/ 232411 31 placebo.ti,ab. 264252 32 (compare or compared or comparison).ti. 459073 33 ((evaluated or evaluate or evaluating or assessed or assess) and (compare or compared or comparing or comparison)).ab. 1680000 34 (open adj label).ti,ab. 61263 35 ((double or single or doubly or singly) adj (blind or blinded or blindly)).ti,ab. 203375 36 double blind procedure/ 145498 37 parallel group$1.ti,ab. 21082 38 (crossover or cross over).ti,ab. 90507 39 ((assign$ or match or matched or allocation) adj5 (alternate or group$1 or intervention$1 or patient$1 or subject$1 or participant$1)).ti,ab. 272867 40 (assigned or allocated).ti,ab. 321579 41 (controlled adj7 (study or design or trial)).ti,ab. 283958 42 (volunteer or volunteers).ti,ab. 219487 43 trial.ti. 240867 44 or/26-43 3905395 45 5 or 6 or 7 or 8 565240 46 4 and 25 and 44 and 45 210	
CINAHL	S31 S23 AND S30 41 S30 S24 OR S25 OR S26 OR S27 OR S28 OR S29 951,453 S29 TX randomly 41,603 S28 TX "treatment as usual" 707 S27 TX "double-blind*" 755,453) S26 TX "single-blind*" 8,658 S25 TX trial 236,190 S24 MH "Clinical Trials" 90,793 S23 S4 AND S8 AND S22 72 S22 S9 OR S10 OR S11 OR S12 OR S13 OR S14 OR S15 OR S16 OR S17 OR S18 OR S19 OR S20 OR S21 2,012 S21 TX steam 736	20 Nov 2017: 41

(Continued)

	S20 TX ClariVein 2 S19 TX MOCA 470 S18 TX "Mechanochemical Ablation" 3 S17 TX "Mechanochemical endovenous Ablation" 1 S16 TX NBCA 22 S15 TX Histoacryl 25 S14 TX VeClose 0 S13 TX VariClose 0) S12 TX VenaSeal 0 S11 TX Enbucrilate 2 S10 "tissue adhesive*" 593 S9 TX Cyanoacrylates 263 S8 S5 OR S6 OR S7 46,250 S7 TX (varic* or incomp* or insuffici* or tortuous or sapheno* or GSV or CVI 44,693 S6 (MH "Venous Insufficiency+") 678 S5 (MH "Varicose Veins+") 2,349 S4 S1 OR S2 OR S3 392,631 S3 TX surg* or ligat* or strip* or phlebectomy 386,026 S2 (MH "Ligation") 630 S1 (MH "Vascular Surgery+") 13,726	
AMED	1 (surg* or ligat* or strip* or phlebectomy).ti,ab. 11043 2 exp Varicose Veins/ 63 3 exp Venous Insufficiency/ 49 4 (varic* or incomp* or insuffici* or tortuous or sapheno* or GSV or CVI).ti,ab. 2784 5 "tissue adhesive*".ti,ab. 2 6 Cyanoacrylate*.ti,ab. 3 7 Enbucrilate.mp. [mp=abstract, heading words, title] 1 8 Enbucrilate.ti,ab. 1 9 Histoacryl.ti,ab. 2 10 MOCA.ti,ab. 6 11 steam.ti,ab. 72 12 2 or 3 or 4 2845 13 5 or 6 or 7 or 8 or 9 or 10 or 11 85	20 Nov 2017: 0

(Continued)

	14 1 and 12 and 13 0

Search 3: Endovenous ablation, Foam Sclerotherapy, Glue, MOCA, Steam

Source	Search strategy	Hits retrieved
VASCULAR REGISTER IN CRSW	#1 Varicose Veins AND INREGISTER	9 Jan 2018: 209
	#2 foam AND INREGISTER	
	#3 mechanochemical endovenous ablation AND INREGISTER	
	#4 MOCA AND INREGISTER	
	#5 sclerotherapy AND INREGISTER	
	#6 sclerosing solutions AND INREGISTER	
	#7 Laser AND INREGISTER	
	#8 Ablation AND INREGISTER	
	#9 Mechanochemical Ablation AND INREGISTER	
	#10 Cyanoacrylates AND INREGISTER	
	#11 steam AND INREGISTER	
	#12 #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11	
	#13 #1 AND #12	
CENTRAL	#1 MESH DESCRIPTOR Varicose Veins EXPLODE ALL TREES 809	9 Jan 2018: 95
Issue 12, 2017	#2 MESH DESCRIPTOR Venous Insufficiency EXPLODE ALL TREES 406	
	#3 (varic* or incomp* or insuffici* or tortuous or sapheno* or GSV or CVI):TI,AB,KY 24143	
	#4 #1 OR #2 OR #3 24177	
	#5 MESH DESCRIPTOR Laser Therapy EXPLODE ALL TREES 3510	
	#6 MESH DESCRIPTOR Catheter Ablation EXPLODE ALL TREES 1237	
	#7 (endovenous or EVLA or EVLT or radiofrequency or laser* or ablation* or obliteration* or RFA):TI,AB,KY 17365	
	#8 NBCA:TI,AB,KY 13	
	#9 (Mechanochemical endovenous Ablation):TI,AB,KY 6	
	#10 (Mechanochemical Ablation):TI,AB,KY 8	
	#11 #5 OR #6 OR #7 OR #8 OR #9 OR #10 17417	
	#12 MESH DESCRIPTOR Sclerotherapy EXPLODE ALL TREES 448	
	#13 MESH DESCRIPTOR Sclerosing Solutions EXPLODE ALL TREES 385	
	#14 sclero*:TI,AB,KY 10391	

(Continued)

#15 (tetradecyl near2 (sulfate or sulphate)):TI,AB,KY 63

#16 MESH DESCRIPTOR Sodium Tetradecyl Sulfate EXPLODE ALL TREES 37

#17 MESH DESCRIPTOR Saline Solution, Hypertonic EXPLODE ALL TREES 446

#18 MESH DESCRIPTOR Ethanolamines 1503

#19 (polydocanol or polidocanol):TI,AB,KY 217

#20 saline:TI,AB,KY 20996

#21 (ethanolamine near2 oleate):TI,AB,KY 66

#22 (sodium near2 morrhuate):TI,AB,KY 19

#23 sotradecol:TI,AB,KY 6

#24 (aetoxisclerol or aethoxysclerol):TI,AB,KY 15

#25 (aetoxiskerol or aethoxyskerol):TI,AB,KY 1

#26 Turbofoam:TI,AB,KY 2

#27 (foam* or microfoam*):TI,AB,KY 1464

#28 varisolve:TI,AB,KY 2

#29 #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25 OR #26 OR #27 OR #28 34198

#30 MESH DESCRIPTOR Cyanoacrylates EXPLODE ALL TREES 181

#31 ("tissue adhesive*"):TI,AB,KY 730

#32 Cyanoacrylate*:TI,AB,KY 317

#33 Enbucrilate:TI,AB,KY 83

#34 VenaSeal:TI,AB,KY 3

#35 VariClose:TI,AB,KY 0

#36 VeClose:TI,AB,KY 5

#37 Histoacryl:TI,AB,KY 39

#38 #30 OR #31 OR #32 OR #33 OR #34 OR #35 OR #36 OR #37 905

#39 MOCA:TI,AB,KY 278

#40 ClariVein:TI,AB,KY 9

#41 #39 OR #40 284

#42 (Endovenous steam):TI,AB,KY 1

#43 steam:TI,AB,KY 186

#44 #42 OR #43 186

#45 #11 AND #19 34

#46 #11 AND #38 50

#47 #11 AND #41 16

#48 #11 AND #44 16

(Continued)

	#49 #29 AND #38 70 #50 #29 AND #41 17 #51 #29 AND #44 11 #52 #38 AND #41 1 #53 #38 AND #44 0 #54 #41 AND #44 1 #55 #45 OR #46 OR #47 OR #48 OR #49 OR #50 OR #51 OR #52 OR #53 OR #54 184 #56 #4 AND #55 95	
Clinicaltrials.gov	Varicose Veins | steam OR ablation OR sclerotherapy OR Cyanoacrylates OR GLUE OR foam	9 Jan 2018: 99
ICTRP Search Portal	Varicose Veins | steam OR ablation OR sclerotherapy OR Cyanoacrylates OR GLUE OR foam	9 Jan 2018: 68
MEDLINE 2017 and 2018 only	1 exp Varicose Veins/ 17950 2 exp Venous Insufficiency/ 7467 3 (varic* or incomp* or insuffici* or tortuous or sapheno* or GSV or CVI).ti,ab. 454946 4 or/1-3 464353 5 exp Laser Therapy/ 61085 6 exp Catheter Ablation/ 31949 7 (endovenous or EVLA or EVLT or radiofrequency or laser* or ablation* or obliteration* or RFA).ti,ab. 347334 8 NBCA.ti,ab. 475 9 "Mechanochemical endovenous Ablation".ti,ab. 21 10 "Mechanochemical Ablation".ti,ab. 25 11 or/5-10 364051 12 exp Sclerotherapy/ 5483 13 exp Sclerosing Solutions/ 10961 14 sclero*.ti,ab. 185374 15 (tetradecyl adj2 (sulfate or sulphate)).ti,ab. 461 16 exp Sodium Tetradecyl Sulfate/ 461 17 exp Saline Solution, Hypertonic/ 5748 18 Ethanolamines/ 11982 19 (polydocanol or polidocanol).ti,ab. 770 20 saline.ti,ab. 173305 21 (ethanolamine adj2 oleate).ti,ab. 337	9 Jan 2018: 25

(Continued)

22 (sodium adj2 morrhuate).ti,ab. 179

23 sotradecol.ti,ab. 54

24 (aetoxisclerol or aethoxysclerol).ti,ab. 50

25 (aetoxiskerol or aethoxyskerol).ti,ab. 1

26 Turbofoam.ti,ab. 2

27 (foam* or microfoam*).ti,ab. 24095

28 varisolve.ti,ab. 2

29 or/12-28 403167

30 exp Cyanoacrylates/ 4934

31 "tissue adhesive*".ti,ab. 1886

32 Cyanoacrylate*.ti,ab. 4419

33 Enbucrilate.ti,ab. 35

34 VenaSeal.ti,ab. 9

35 VariClose.ti,ab. 6

36 VeClose.ti,ab. 3

37 Histoacryl.ti,ab. 513

38 or/30-37 7716

39 MOCA.ti,ab. 1488

40 ClariVein.ti,ab. 32

41 or/39-40 1510

42 "Endovenous steam".ti,ab. 9

43 steam.ti,ab. 7174

44 or/42-43 7174

45 11 and 29 8205

46 11 and 38 850

47 11 and 41 42

48 11 and 44 235

49 29 and 38 540

50 29 and 41 58

51 29 and 44 153

52 38 and 41 2

53 38 and 44 1

54 41 and 44 6

55 or/45-54 9670

(Continued)

	56 4 and 55 1693	
	57 randomized controlled trial.pt. 516039	
	58 controlled clinical trial.pt. 101743	
	59 randomized.ab. 453171	
	60 placebo.ab. 210619	
	61 drug therapy.fs. 2199170	
	62 randomly.ab. 312199	
	63 trial.ab. 477783	
	64 groups.ab. 1925728	
	65 or/57-64 4548008	
	66 56 and 65 427	
EMBASE 2017 and 2018 only	1 exp Varicose Veins/ 30954	9 Jan 2018: 65
	2 exp Venous Insufficiency/ 6648	
	3 (varic* or incomp* or insuffici* or tortuous or sapheno* or GSV or CVI).ti,ab. 404745	
	4 or/1-3 418741	
	5 exp Laser Therapy/ 18166	
	6 exp Catheter Ablation/ 27123	
	7 (endovenous or EVLA or EVLT or radiofrequency or laser* or ablation* or obliteration* or RFA).ti,ab. 305281	
	8 NBCA.ti,ab. 777	
	9 "Mechanochemical endovenous Ablation".ti,ab. 24	
	10 "Mechanochemical Ablation".ti,ab. 40	
	11 or/5-10 315178	
	12 exp Sclerotherapy/ 8990	
	13 exp Sclerosing Solutions/ 7375	
	14 sclero*.ti,ab. 185006	
	15 (tetradecyl adj2 (sulfate or sulphate)).ti,ab. 410	
	16 exp Sodium Tetradecyl Sulfate/ 1078	
	17 exp Saline Solution, Hypertonic/ 137265	
	18 Ethanolamines/ 1670	
	19 (polydocanol or polidocanol).ti,ab. 760	
	20 saline.ti,ab. 160073	
	21 (ethanolamine adj2 oleate).ti,ab. 299	
	22 (sodium adj2 morrhuate).ti,ab. 97	

(Continued)

23 sotradecol.ti,ab. 57

24 (aetoxisclerol or aethoxysclerol).ti,ab. 42

25 (aetoxiskerol or aethoxyskerol).ti,ab. 1

26 Turbofoam.ti,ab. 3

27 (foam* or microfoam*).ti,ab. 22781

28 varisolve.ti,ab. 5

29 or/12-28 432105

30 exp Cyanoacrylates/ 1015

31 "tissue adhesive*".ti,ab. 1263

32 Cyanoacrylate*.ti,ab. 4139

33 Enbucrilate.ti,ab. 27

34 VenaSeal.ti,ab. 26

35 VariClose.ti,ab. 11

36 VeClose.ti,ab. 5

37 Histoacryl.ti,ab. 519

38 or/30-37 5714

39 MOCA.ti,ab. 3454

40 ClariVein.ti,ab. 40

41 or/39-40 3483

42 "Endovenous steam".ti,ab. 12

43 steam.ti,ab. 7068

44 or/42-43 7068

45 11 and 29 10224

46 11 and 38 1029

47 11 and 41 70

48 11 and 44 367

49 29 and 38 666

50 29 and 41 126

51 29 and 44 224

52 38 and 41 10

53 38 and 44 6

54 41 and 44 10

55 or/45-54 12009

56 4 and 55 2299

(Continued)

	57 randomized controlled trial/ 434283 58 controlled clinical trial/ 407173 59 random$.ti,ab. 1117832 60 randomization/ 68256 61 intermethod comparison/ 218276 62 placebo.ti,ab. 213565 63 (compare or compared or comparison).ti. 322736 64 ((evaluated or evaluate or evaluating or assessed or assess) and (compare or compared or comparing or comparison)).ab. 1540369 65 (open adj label).ti,ab. 59678 66 ((double or single or doubly or singly) adj (blind or blinded or blindly)).ti,ab. 152435 67 double blind procedure/ 118292 68 parallel group$1.ti,ab. 18718 69 (crossover or cross over).ti,ab. 69418 70 ((assign$ or match or matched or allocation) adj5 (alternate or group$1 or intervention$1 or patient$1 or subject$1 or participant$1)).ti,ab. 238152 71 (controlled adj7 (study or design or trial)).ti,ab. 249992 72 (volunteer or volunteers).ti,ab. 166514 73 trial.ti. 203926 74 or/57-73 3255961 75 56 and 74 561	
AMED 2017 and 2018 only	1 exp Varicose Veins/ 64 2 exp Venous Insufficiency/ 50 3 (varic* or incomp* or insuffici* or tortuous or sapheno* or GSV or CVI).ti,ab. 2794 4 or/1-3 2855 5 exp Laser Therapy/ 169 6 exp Catheter Ablation/ 0 7 (endovenous or EVLA or EVLT or radiofrequency or laser* or ablation* or obliteration* or RFA).ti,ab. 1122 8 NBCA.ti,ab. 0 9 "Mechanochemical endovenous Ablation".ti,ab. 0 10 "Mechanochemical Ablation".ti,ab. 0 11 or/5-10 1133 12 exp Sclerotherapy/ 0	9 Jan 2018: 0

(Continued)

13 exp Sclerosing Solutions/ 0

14 sclero*.ti,ab. 2225

15 (tetradecyl adj2 (sulfate or sulphate)).ti,ab. 0

16 exp Sodium Tetradecyl Sulfate/ 0

17 exp Saline Solution, Hypertonic/ 0

18 Ethanolamines/ 0

19 (polydocanol or polidocanol).ti,ab. 3

20 saline.ti,ab. 532

21 (ethanolamine adj2 oleate).ti,ab. 0

22 (sodium adj2 morrhuate).ti,ab. 1

23 sotradecol.ti,ab. 0

24 (aetoxisclerol or aethoxysclerol).ti,ab. 0

25 (aetoxiskerol or aethoxyskerol).ti,ab. 0

26 Turbofoam.ti,ab. 0

27 (foam* or microfoam*).ti,ab. 270

28 varisolve.ti,ab. 0

29 or/12-28 3024

30 exp Cyanoacrylates/ 0

31 "tissue adhesive*".ti,ab. 2

32 Cyanoacrylate*.ti,ab. 3

33 Enbucrilate.ti,ab. 1

34 VenaSeal.ti,ab. 0

35 VariClose.ti,ab. 0

36 VeClose.ti,ab. 0

37 Histoacryl.ti,ab. 2

38 or/30-37 7

39 MOCA.ti,ab. 6

40 ClariVein.ti,ab. 0

41 or/39-40 6

42 "Endovenous steam".ti,ab. 0

43 steam.ti,ab. 73

44 or/42-43 73

45 11 and 29 14

46 11 and 38 0

(Continued)

	47 11 and 41 0	
	48 11 and 44 1	
	49 29 and 38 0	
	50 29 and 41 0	
	51 29 and 44 0	
	52 38 and 41 0	
	53 38 and 44 0	
	54 41 and 44 0	
	55 or/45-54 15	
	56 4 and 55 2	
CINAHL	S62 S4 AND S54 AND S61 78	9 Jan 2018: 1
2017 and 2018 only	S61 S55 OR S56 OR S57 OR S58 OR S59 OR S60 958,825	
	S60 TX randomly 42,126	
	S59 TX "treatment as usual" 724	
	S58 TX "double-blind*" 760,703	
	S57 TX "single-blind*" 8,730	
	S56 TX trial 238,589	
	S55 MH "Clinical Trials" 91,184	
	S54 S45 OR S46 OR S47 OR S48 OR S49 OR S50 OR S51 OR S52 OR S53 840	
	S53 S38 AND S44 0	
	S52 S38 AND S41 0	
	S51 S29 AND S44 22	
	S50 S29 AND S41 9	
	S49 S29 AND S38 45	
	S48 S11 AND S44 40	
	S47 S11 AND S41 5	
	S46 S11 AND S38 51	
	S45 S11 AND S29 696	
	S44 S42 OR S43 749	
	S43 TX steam 749	
	S42 TX "Endovenous steam" 0	
	S41 S39 OR S40 482	
	S40 TX ClariVein 2	
	S39 TX MOCA 482	

(Continued)

S38 S30 OR S31 OR S32 OR S33 OR S34 OR S35 OR S36 OR S37 822

S37 TX Histoacryl 25

S36 TX VeClose 0

S35 TX VariClose 0

S34 TX VenaSeal 0

S33 TX Enbucrilate 2

S32 TX Cyanoacrylate* 270

S31 TX "tissue adhesive*" 610

S30 TX Cyanoacrylates 270

S29 S12 OR S13 OR S14 OR S15 OR S16 OR S17 OR S18 OR S19 OR S20 OR S21 OR S22 OR S23 OR S24 OR S25 OR S26 OR S27 OR S28 38,921

S28 TX varisolve 0

S27 TX foam* or microfoam* 2,605

S26 TX Turbofoam 0

S25 TX aetoxiskerol or aethoxyskerol 0

S24 TX aetoxisclerol or aethoxysclerol 0

S23 TX sotradecol 2

S22 TX sodium N2 morrhuate 12

S21 TX ethanolamine N2 oleate 13

S20 TX saline 8,727

S19 TX polydocanol or polidocanol 33

S18 (MH "Ethanolamines+") 6,503

S17 (MH "Saline Solution, Hypertonic") 533

S16 TX Sodium Tetradecyl Sulfate 6

S15 TX (tetradecyl N2 (sulfate or sulphate)) 10

S14 TX sclero* 21,475

S13 (MH "Sclerosing Solutions") 182

S12 (MH "Sclerotherapy") 365

S11 S5 OR S6 OR S7 OR S8 OR S9 OR S10 24,433

S10 TX "Mechanochemical Ablation" 3

S9 TX "Mechanochemical endovenous Ablation" 1

S8 TX NBCA 22

S7 TX endovenous or EVLA or EVLT or radiofrequency or laser* or ablation* or obliteration* or RFA 24,345

S6 (MH "Catheter Ablation") 6,674

(Continued)

	S5 (MH "Laser Therapy+") 5,572
	S4 (S1 OR S2 OR S3) 46,802
	S3 TX varic* or incomp* or insuffici* or tortuous or sapheno* or GSV or CVI 45,221
	S2 (MH "Venous Insufficiency+") 686
	S1 (MH "Varicose Veins+") 2,378

Appendix 2. Database searches Jan 2019 and Nov 2020

Source	Search strategy	Hits retrieved
VASCULAR REGISTER IN CRSW	#1 Venous Insufficiency AND	25 Jan 2019: 27
	#2 Varicose Veins AND	2 Nov 2020: 93
	#3 Saphenous Vein AND	
	#4 varic* or incomp* or insuffici* or tortuous or sapheno* or GSV or CVI	
	#5 #1 OR #2 OR #3 OR #4	
	#6 Catheter Ablation AND	
	#7 CYANOACRYLATES AND	
	#8 ETHANOLAMINES AND	
	#9 Laser Therapy AND	
	#10 LIGATION AND	
	#11 Solution, Hypertonic	
	#12 Sclerosing Solutions AND	
	#13 SCLEROTHERAPY AND	
	#14 Sodium Tetradecyl Sulfate AND	
	#15 Vascular Surgical Procedures AND	
	#16 Mechanochemical Ablation AND	
	#17 endovenous or EVLA or EVLT or radiofrequency or laser* or ablation* or obliteration* or RFA AND	
	#18 foam* or microfoam* AND	
	#19 steam	
	#20 #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19	
	#21 #20 AND #5	
CENTRAL	#1 MESH DESCRIPTOR Varicose Veins EXPLODE ALL TREES 1025	25 Jan 2019: 5
	#2 MESH DESCRIPTOR Venous Insufficiency EXPLODE ALL TREES 514	Nov 2020: 751

(Continued)

#3 MESH DESCRIPTOR Saphenous Vein EXPLODE ALL TREES 651

#4 ((varic* or incomp* or insuffici* or tortuous or sapheno*) and (vein* or venous)).TI,AB,KY 26520

#5 #1 OR #2 OR #3 OR #4 26570

#6 MESH DESCRIPTOR Catheter Ablation EXPLODE ALL TREES 1325

#7 MESH DESCRIPTOR CYANOACRYLATES EXPLODE ALL TREES 194

#8 MESH DESCRIPTOR ETHANOLAMINES EXPLODE ALL TREES 12584

#9 MESH DESCRIPTOR Laser Therapy EXPLODE ALL TREES 3698

#10 MESH DESCRIPTOR LIGATION EXPLODE ALL TREES 581

#11 MESH DESCRIPTOR Saline Solution, Hypertonic EXPLODE ALL TREES 471

#12 MESH DESCRIPTOR Sclerosing Solutions EXPLODE ALL TREES 409

#13 MESH DESCRIPTOR SCLEROTHERAPY EXPLODE ALL TREES 460

#14 MESH DESCRIPTOR Sodium Tetradecyl Sulfate EXPLODE ALL TREES 41

#15 MESH DESCRIPTOR Vascular Surgical Procedures EXPLODE ALL TREES 14037

#16 (Mechanochemical Ablation):TI,AB,KY 11

#17 (Mechanochemical endovenous Ablation):TI,AB,KY 5

#18 (tissue adhesive*):TI,AB,KY 824

#19 (aetoxisclerol or aethoxysclerol):TI,AB,KY 15

#20 (aetoxiskerol or aethoxyskerol):TI,AB,KY 1

#21 (endovenous or EVLA or EVLT or radiofrequency or laser* or ablation* or obliteration* or RFA):TI,AB,KY 20245

#22 (ethanolamine adj2 oleate):TI,AB,KY 68

#23 (foam* or microfoam*):TI,AB,KY 1724

#24 (polydocanol or polidocanol):TI,AB,KY 254

#25 (sodium adj2 morrhuate):TI,AB,KY 21

#26 (surg* or ligat* or strip* or phlebectomy):TI,AB,KY 174252

#27 (tetradecyl adj2 (sulfate or sulphate)):TI,AB,KY 65

#28 ClariVein:TI,AB,KY 14

#29 Cyanoacrylate*:TI,AB,KY 369

#30 Enbucrilate:TI,AB,KY 74

#31 Histoacryl:TI,AB,KY 42

#32 MOCA:TI,AB,KY 308

#33 NBCA:TI,AB,KY 10

#34 saline:TI,AB,KY 21059

#35 sclero*:TI,AB,KY 12043

(Continued)

	#36 sotradecol:TI,AB,KY 7 #37 steam:TI,AB,KY 184 #38 Turbofoam:TI,AB,KY 2 #39 VariClose:TI,AB,KY 0 #40 varisolve:TI,AB,KY 2 #41 VeClose:TI,AB,KY 6 #42 VenaSeal:TI,AB,KY 6 #43 #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25 OR #26 OR #27 OR #28 OR #29 OR #30 OR #31 OR #32 OR #33 OR #34 OR #35 OR #36 OR #37 OR #38 OR #39 OR #40 OR #41 OR #42 228556 #44 #5 AND #43 8028 #45 VenaSeal:TI,AB,KY AND 01/01/2018 TO 25/01/2019:CD 5	
Clinicaltrials.gov	Varicose Veins OR Venous Insufficiency OR Saphenous Vein OR varic* OR incomp* OR tortuous OR sapheno* | surg* OR ligat* OR strip* OR foam OR ablation* OR endovenous OR glue OR SCLERO*	25 Jan 2019: 12 2 Nov 2020: 25
ICTRP Search Portal	Varicose Veins OR Venous Insufficiency OR Saphenous Vein OR varic* OR incomp* OR tortuous OR sapheno*AND surg* OR ligat* OR strip* OR foam OR ablation* OR endovenous OR glue OR SCLERO*	25 Jan 2019: 5 2 Nov 2020: N/A
MEDLINE	1 exp Varicose Veins/ 2 exp Venous Insufficiency/ 3 exp Saphenous Vein/su 4 ((varic* or incomp* or insuffici* or tortuous or sapheno*) and (vein* or venous)).ti,ab. 5 or/1-4 6 exp Catheter Ablation/ 7 exp CYANOACRYLATES/ 8 exp ETHANOLAMINES/ 9 exp Laser Therapy/ 10 exp LIGATION/ 11 Saline Solution, Hypertonic/ 12 exp Sclerosing Solutions/ 13 exp SCLEROTHERAPY/ 14 exp Sodium Tetradecyl Sulfate/ 15 exp Vascular Surgical Procedures/ 16 Mechanochemical Ablation.ti,ab. 17 Mechanochemical endovenous Ablation.ti,ab.	25 Jan 2019: 1054 2 Nov 2020: 1890

(Continued)

18 tissue adhesive*.ti,ab.

19 (aetoxisclerol or aethoxysclerol).ti,ab.

20 (aetoxiskerol or aethoxyskerol).ti,ab.

21 (endovenous or EVLA or EVLT or radiofrequency or laser* or ablation* or obliteration* or RFA).ti,ab.

22 (ethanolamine adj2 oleate).ti,ab.

23 (foam* or microfoam*).ti,ab.

24 (polydocanol or polidocanol).ti,ab.

25 (sodium adj2 morrhuate).ti,ab.

26 (surg* or ligat* or strip* or phlebectomy).ti,ab.

27 (tetradecyl adj2 (sulfate or sulphate)).ti,ab.

28 ClariVein.ti,ab.

29 Cyanoacrylate*.ti,ab.

30 Enbucrilate.ti,ab.

31 Histoacryl.ti,ab.

32 MOCA.ti,ab.

33 NBCA.ti,ab.

34 saline.ti,ab.

35 sclero*.ti,ab.

36 sotradecol.ti,ab.

37 steam.ti,ab.

38 Turbofoam.ti,ab.

39 VariClose.ti,ab.

40 varisolve.ti,ab.

41 VeClose.ti,ab.

42 VenaSeal.ti,ab.

43 or/6-42

44 5 and 43

45 randomized controlled trial.pt.

46 controlled clinical trial.pt.

47 randomized.ab.

48 placebo.ab.

49 drug therapy.fs.

50 randomly.ab.

51 trial.ab.

(Continued)

	52 groups.ab.	
	53 or/45-52	
	54 exp animals/ not humans.sh.	
	55 53 not 54	
	56 44 and 55	
	57 (2018* or 2019*).ed.	
	58 56 and 57	
EMBASE	1 exp varicosis/	25 Jan 2019: 3437
	2 exp vein insufficiency/	2 Nov 2020: 4403
	3 exp saphenous vein/	
	4 ((varic* or incomp* or insuffici* or tortuous or sapheno*) and (vein* or venous)).ti,ab.	
	5 or/1-4	
	6 exp catheter ablation/	
	7 exp cyanoacrylate derivative/	
	8 exp ethanolamine derivative/	
	9 exp low level laser therapy/	
	10 exp ligation/	
	11 exp sclerosing agent/	
	12 exp sclerotherapy/	
	13 exp tetradecyl sulfate sodium/	
	14 exp vascular surgery/	
	15 exp ablation therapy/	
	16 tissue adhesive*.ti,ab.	
	17 (aetoxisclerol or aethoxysclerol).ti,ab.	
	18 (aetoxiskerol or aethoxyskerol).ti,ab.	
	19 (endovenous or EVLA or EVLT or radiofrequency or laser* or ablation* or obliteration* or RFA).ti,ab.	
	20 (ethanolamine adj2 oleate).ti,ab.	
	21 (foam* or microfoam*).ti,ab.	
	22 (polydocanol or polidocanol).ti,ab.	
	23 (sodium adj2 morrhuate).ti,ab.	
	24 (surg* or ligat* or strip* or phlebectomy).ti,ab.	
	25 (tetradecyl adj2 (sulfate or sulphate)).ti,ab.	
	26 ClariVein.ti,ab.	

(Continued)

27 Cyanoacrylate*.ti,ab.

28 Enbucrilate.ti,ab.

29 Histoacryl.ti,ab.

30 MOCA.ti,ab.

31 NBCA.ti,ab.

32 saline.ti,ab.

33 sotradecol.ti,ab.

34 steam.ti,ab.

35 Turbofoam.ti,ab.

36 VariClose.ti,ab.

37 varisolve.ti,ab.

38 VeClose.ti,ab.

39 VenaSeal.ti,ab.

40 or/6-39

41 5 and 40

42 randomized controlled trial/

43 controlled clinical trial/

44 random$.ti,ab.

45 randomization/

46 intermethod comparison/

47 placebo.ti,ab.

48 (compare or compared or comparison).ti.

49 ((evaluated or evaluate or evaluating or assessed or assess) and (compare or compared or comparing or comparison)).ab.

50 (open adj label).ti,ab.

51 ((double or single or doubly or singly) adj (blind or blinded or blindly)).ti,ab.

52 double blind procedure/

53 parallel group$1.ti,ab.

54 (crossover or cross over).ti,ab.

55 ((assign$ or match or matched or allocation) adj5 (alternate or group$1 or intervention$1 or patient$1 or subject$1 or participant$1)).ti,ab.

56 (assigned or allocated).ti,ab.

57 (controlled adj7 (study or design or trial)).ti,ab.

58 (volunteer or volunteers).ti,ab.

59 trial.ti.

(Continued)

	60 or/42-59	
	61 41 and 60	
	62 (2018* or 2019*).em.	
	63 61 and 62	
	64 from 63 keep 3001-3437	
AMED	1 exp Varicose veins/	25 Jan 2019: 1
	2 exp Venous insufficiency/	2 Nov 2020: 1
	3 (varic* or incomp* or insuffici* or tortuous or sapheno* or GSV or CVI).ti,ab.	
	4 or/1-3	
	5 tissue adhesive*.ti,ab.	
	6 (aetoxisclerol or aethoxysclerol).ti,ab.	
	7 (aetoxiskerol or aethoxyskerol).ti,ab.	
	8 (endovenous or EVLA or EVLT or radiofrequency or laser* or ablation* or obliteration* or RFA).ti,ab.	
	9 (ethanolamine adj2 oleate).ti,ab.	
	10 (foam* or microfoam*).ti,ab.	
	11 (polydocanol or polidocanol).ti,ab.	
	12 (sodium adj2 morrhuate).ti,ab.	
	13 (surg* or ligat* or strip* or phlebectomy).ti,ab.	
	14 (tetradecyl adj2 (sulfate or sulphate)).ti,ab.	
	15 ClariVein.ti,ab.	
	16 Cyanoacrylate*.ti,ab.	
	17 Enbucrilate.ti,ab.	
	18 Histoacryl.ti,ab.	
	19 MOCA.ti,ab.	
	20 NBCA.ti,ab.	
	21 saline.ti,ab.	
	22 sotradecol.ti,ab.	
	23 steam.ti,ab.	
	24 Turbofoam.ti,ab.	
	25 VariClose.ti,ab.	
	26 varisolve.ti,ab.	
	27 VeClose.ti,ab.	
	28 VenaSeal.ti,ab.	

(Continued)

	29 or/5-28	
	30 4 and 29	
	31 exp CLINICAL TRIALS/	
	32 RANDOM ALLOCATION/	
	33 DOUBLE BLIND METHOD/	
	34 Clinical trial.pt.	
	35 (clinic* adj trial*).tw.	
	36 ((singl* or doubl* or trebl* or tripl*) adj (blind* or mask*)).tw.	
	37 PLACEBOS/	
	38 placebo*.tw.	
	39 random*.tw.	
	40 PROSPECTIVE STUDIES/	
	41 or/31-40	
	42 30 and 41	
	43 ("2018" or "2019").yr.	
	44 42 and 43	
CINAHL	S56 S53 AND S54	25 Jan 2019: 493
	S55 S53 AND S54	2 Nov 2020: 699
	S54 EM 2018 OR EM 2019	
	S53 S39 AND S52	
	S52 S40 OR S41 OR S42 OR S43 OR S44 OR S45 OR S46 OR S47 OR S48 OR S49 OR S50 OR S51	
	S51 MH "Random Assignment"	
	S50 MH "Single-Blind Studies" or MH "Double-Blind Studies" or MH "Triple-Blind Studies"	
	S49 MH "Crossover Design"	
	S48 MH "Factorial Design"	
	S47 MH "Placebos"	
	S46 MH "Clinical Trials"	
	S45 TX "multi-centre study" OR "multi-center study" OR "multicentre study" OR "multicenter study" OR "multi-site study"	
	S44 TX crossover OR "cross-over"	
	S43 AB placebo*	
	S42 TX random*	
	S41 TX trial*	

(Continued)

S40 TX "latin square"

S39 S5 AND S38

S38 S6 OR S7 OR S8 OR S9 OR S10 OR S11 OR S12 OR S13 OR S14 OR S15 OR S16 OR S17 OR S18 OR S19 OR S20 OR S21 OR S22 OR S23 OR S24 OR S25 OR S26 OR S27 OR S28 OR S29 OR S30 OR S31 OR S32 OR S33 OR S34 OR S35 OR S36 OR S37

S37 TX VenaSeal

S36 TX VeClose

S35 TX varisolve

S34 TX VariClose

S33 TX Turbofoam

S32 TX steam

S31 TX sotradecol

S30 TX sclero*

S29 TX saline

S28 TX NBCA

S27 TX MOCA

S26 TX Histoacryl

S25 TX Enbucrilate

S24 TX Cyanoacrylate*

S23 TX ClariVein

S22 TX tetradecyl N2 (sulfate or sulphate)

S21 TX surg* or ligat* or strip* or phlebectomy

S20 TX sodium N2 morrhuate

S19 TX polydocanol or polidocanol

S18 TX foam* or microfoam*

S17 TX ethanolamine N2 oleate

S16 TX endovenous or EVLA or EVLT or radiofrequency or laser* or ablation* or obliteration* or RFA

S15 TX aetoxisclerol or aethoxysclerol

S14 TX aetoxiskerol or aethoxyskerol

S13 TX aetoxisclerol or aethoxysclerol

S12 TX tissue adhesive*

S11 TX Mechanochemical endovenous Ablation

S10 TX Mechanochemical Ablation

S9 (MH "Sclerotherapy")

(Continued)

S8 (MH "Sclerosing Solutions")

S7 (MH "Saline Solution, Hypertonic")

S6 (MH "Catheter Ablation")

S5 S1 OR S2 OR S3 OR S4

S4 TX varic* or incomp* or insuffici* or tortuous or sapheno* or GSV or CVI

S3 (MH "Saphenous Vein/SU")

S2 (MH "Venous Insufficiency")

S1 (MH "Varicose Veins+")

WHAT'S NEW

Date	Event	Description
2 November 2020	New search has been performed	New search run. Eleven new studies included and 20 new studies excluded. Four new ongoing studies identified. Four studies awaiting classification.
2 November 2020	New citation required and conclusions have changed	New search run. Eleven new studies included and 20 new studies excluded. Four new ongoing studies identified. Four studies awaiting classification. New authors joined review team. Scope amended to reflect the range of interventions currently available. Text amended to reflect current Cochrane standards, 'Summary of findings' tables added. Conclusions changed.

HISTORY

Protocol first published: Issue 1, 2006
Review first published: Issue 10, 2011

Date	Event	Description
3 June 2014	New citation required but conclusions have not changed	Searches re-run. Eight additional included studies and 12 additional excluded studies identified. Review text updated accordingly. New author joined review team.
3 June 2014	New search has been performed	Searches re-run. Eight additional included studies and 12 additional excluded studies identified.

CONTRIBUTIONS OF AUTHORS

JW: conducted the review, analysed studies for inclusion, selected trials for inclusion, assessed methodological quality of trials and extracted data, entered the data, developed the analysis plan for the update and drafted the review update, wrote the manuscript and contributed significantly to the overall process (joint first author)
SN: conducted the review of included studies, arbitrated on the selection of trials, assisted with data extraction, assessed methodological quality and assisted in drafting the final review, reviewed and wrote the manuscript, contributed significantly to the overall process (joint first author)

CN: conducted the previous review, contributed to the included studies' analysis, dealt with discrepancies and reviewed the manuscript
GS: conceived the original idea for this review, supervised the review, developed the protocol, helped with analysis, wrote and proofread this current review

DECLARATIONS OF INTEREST

JW: none known
SN: none known
CN: none known
GS: none known

SOURCES OF SUPPORT

Internal sources

- No sources of support provided

External sources

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DIFFERENCES BETWEEN PROTOCOL AND REVIEW

The title of this review was changed from 'Endovenous ablation (radiofrequency and laser) and foam sclerotherapy versus open surgery for great saphenous vein varices' to 'Interventions for great saphenous vein incompetence'. This was to reflect a widening of scope to include the range of interventions currently available for GSV incompetence. Additional comparisons are listed in Types of interventions. To reflect current clinical relevance, we rearranged outcomes and clarified inclusion and exclusion criteria. Due to new Cochrane Vascular guidelines, we did not perform cost analysis of the interventions within this review, and we included summary of findings tables to present the certainty of the evidence.

INDEX TERMS

Medical Subject Headings (MeSH)

*Catheter Ablation; Randomized Controlled Trials as Topic; Saphenous Vein [pathology] [*surgery]; Sclerotherapy [*methods]; Varicose Veins [*surgery]; Venous Insufficiency [*surgery]

MeSH check words

Female; Humans; Male