NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

INTERVENTIONAL PROCEDURES PROGRAMME

Interventional procedure overview of endovenous mechanochemical ablation for varicose veins

Varicose veins in the legs are swollen and enlarged veins. They develop when the small valves inside a vein stop working properly, allowing blood to pool in the vein. This can cause pain, aching and swelling in the legs, and skin problems including inflammatory dermatitis and ulceration. In endovenous mechanochemical ablation, a tube with a hollow wire at its tip is inserted up the affected vein in the leg. The wire is rotated and a chemical is injected through the tube as it is pulled back out of the vein. This causes the vein to become inflamed, then shrivel and close.

Introduction

The National Institute for Health and Care Excellence (NICE) has prepared this interventional procedure (IP) overview to help members of the interventional procedures advisory committee (IPAC) make recommendations about the safety and efficacy of an interventional procedure. It is based on a rapid review of the medical literature and specialist opinion. It should not be regarded as a definitive assessment of the procedure.

Date prepared

This IP overview was prepared in October 2015 and updated in March 2016.

Procedure name

- Endovenous mechanochemical ablation for varicose veins

Specialist societies

- The Vascular Society of Great Britain and Ireland
- British Society of Interventional Radiology
- British Association of Sclerotherapists

Description

Indications and current treatment

Varicose veins are a sign of underlying venous insufficiency and affect 20–30% of adults. Most people with varicose veins have no symptoms, but venous insufficiency may cause fatigue, heaviness, aching, throbbing, itching and cramps in the legs. Chronic venous insufficiency can lead to skin discoloration, inflammatory dermatitis and ulceration. Great saphenous vein insufficiency is the most common form of venous insufficiency in people presenting with symptoms.

A NICE guideline describes recommendations for the diagnosis and management of varicose veins (Varicose veins in the legs: The diagnosis and management of varicose veins, NICE guidelines [CG168]). Many people have varicose veins that do not cause any symptoms or need treatment on medical grounds. However, some people will need treatment for the relief of symptoms or if there is evidence of skin discolouration, inflammation or ulceration. Treatment options include endothermal ablation, ultrasound guided foam sclerotherapy, and surgery (usually stripping and ligation of the great and small saphenous veins, and phlebectomies).

What the procedure involves

Endovenous mechanochemical ablation for varicose veins combines mechanical ablation with the use of sclerosing agents to close veins without the need for tumescent anaesthesia (infusion of a large volume of dilute local anaesthetic around and along the entire length of vein to be treated).

The procedure is carried out using local anaesthesia at the catheter insertion site. Ultrasound imaging is used to identify the target vein (usually the great saphenous vein), its diameter and the treatment length, which depends on perforators and tributaries. An infusion catheter with a motor drive is introduced percutaneously into the distal end of the target vein and, in the case of the long saphenous vein, the catheter tip is advanced to the saphenofemoral junction. A dispersion wire that extends through the catheter lumen is rotated to damage the epithelium and a sclerosant is infused simultaneously as the catheter is slowly pulled back through the vein. Patients are advised to wear compression stockings for approximately 2 weeks after the procedure.

Clinical assessment

The CEAP (clinical, etiological, anatomic and pathophysiologic) classification from the American Venous Forum is often used to classify venous disease of the lower limb. Clinical signs are classified as: C0 – no signs of venous disease; C1 –

telangiectasias or reticular veins; C2 – varicose veins; C3 – oedema; C4a – pigmentation or eczema; C4b – lipodermatosclerosis or atrophie blanche; C5 – healed venous ulcer; C6 – active venous ulcer.

Outcome measures

Aberdeen Varicose Vein Questionnaire (AVVQ)

AVVQ is a 13-point questionnaire covering multiple elements of varicose vein disease (including pain, patient satisfaction and limitations on daily activity) on a scale of 0–100, with a higher score indicating severe effect.

Venous Clinical Severity Score (VCSS)

VCSS includes 9 clinical characteristics of chronic venous disease scores graded from 0 (absent) to 3 (severe), with the current version having an additional category for compression, with a maximum score of 30 (indicating severe disease).

Literature review

Rapid review of literature

The medical literature was searched to identify studies and reviews relevant to endovenous mechanochemical ablation for varicose veins. The following databases were searched, covering the period from their start to 1 February 2016: MEDLINE, PREMEDLINE, EMBASE, Cochrane Library and other databases. Trial registries and the Internet were also searched. No language restriction was applied to the searches (see appendix C for details of search strategy). Relevant published studies identified during consultation or resolution that are published after this date may also be considered for inclusion.

The following selection criteria (table 1) were applied to the abstracts identified by the literature search. Where selection criteria could not be determined from the abstracts the full paper was retrieved.

Table 1 Inclusion criteria for identification of relevant studies

Characteristic	Criteria
Publication type	Clinical studies were included. Emphasis was placed on identifying good quality studies. Abstracts were excluded where no clinical outcomes were reported, or where the paper was a review, editorial, or a laboratory or animal study. Conference abstracts were also excluded because of the difficulty of appraising study methodology, unless they reported specific adverse events that were not available in the published literature.
Patient	Patients with varicose veins.
Intervention/test	Endovenous mechanochemical ablation.
Outcome	Articles were retrieved if the abstract contained information relevant to the safety and/or efficacy.
Language	Non-English-language articles were excluded unless they were thought to add substantively to the English-language evidence base.

List of studies included in the IP overview

This IP overview is based on approximately 930 patients from 1 randomised controlled trial, 2 non-randomised comparative studies, 5 case series and 1 case report[1–9].

Other studies that were considered to be relevant to the procedure but were not included in the main extraction table (table 2) have been listed in appendix A.

Table 2 Summary of key efficacy and safety findings on endovenous mechanochemical ablation for varicose veins

Study 1 Bootun R (2014)

Details

Study type	**Randomised controlled trial**
Country	UK
Recruitment period	Not reported
Study population and number	**n=117 patients; 119 legs (60 mechanochemical ablation versus 59 radiofrequency ablation)** Adult patients with primary great saphenous vein or small saphenous vein incompetence.
Age and sex	Mean age=54 versus 49 years (p=0.12), range 18–90 years 59% female
Patient selection criteria	Age>18 years and reflux greater than 0.5 seconds in the saphenous veins. Exclusion criteria: current deep vein thrombosis; recurrent varicose veins; arterial disease (ankle brachial pressure index<0.8); veins less than 3 mm in diameter; hypercoagulability; patients who are unwilling to participate; inability or unwillingness to complete questionnaires.
Technique	All procedures were done under ultrasound guidance and local anaesthetic by vascular surgeons familiar with and approved in both ablative methods. Mechanochemical ablation was done using ClariVein (Vascular Insights LLC, USA) with 2% sodium tetradecyl sulphate. Radiofrequency ablation was done using the Covidien Venefit system (Covidien, USA), with tumescent anaesthesia. Stockings were worn for 2 weeks after the procedure and patients were advised to mobilise for at least 1 hour every day.
Follow-up	**1 month**
Conflict of interest/source of funding	Funded by a research grant from ClariVein manufacturer, Vascular Insights LLC and a research grant from the Graham-Dixon Charitable Trust. The research was also supported by the National Institute for Health Research Biomedical Research Centre and Imperial College London.

Analysis

Follow-up issues: 67% (78/117) of patients attended follow-up at 1 month.

Study design issues: Patients were randomised using an online computerised service. In patients receiving treatment to both lower limbs, the more symptomatic side was included in the study. The investigator at follow-up was blinded to the treatment group. The primary outcome was the degree of pain during the procedure. Immediately after the procedure, but before concurrent phlebectomy (if indicated), patients were asked to record their maximum and average pain score during the procedure using a visual analogue score (0–100 mm) and as a number on a scale from 0 to 10. The pain score in mechanochemical included the time from cannulation to vein ablation, while in radiofrequency ablation, it involved the time from cannulation (including infiltration of tumescence) to completion of ablation. The secondary outcomes were improvement in the Aberdeen Varicose Vein Questionnaire (AVVQ), EQ-5D-3 L, Venous Clinical Severity Score (VCSS), Venous Disability Score (VDS), and Clinical-Etiological-Anatomical and Pathophysiological (CEAP) classification at 1 month and 6 months and time taken to return to normal activities and work. The study sample size was calculated to be 94 patients (47 per group) at 90% power and 5% significance, assuming that a 20 mm difference in maximum pain score with a standard deviation of 20 mm was a significant difference.

Study population issues: There were no statistically significant differences in baseline characteristics between the treatment groups with regard to age, sex, length of vein treated and vein diameter. The baseline scores for the AVVQ, VCSS and CEAP were similar but the mean VDS score was higher in the mechanochemical group compared with the RFA group (1.44 versus 1.24 (p<0.05). The left leg was treated in 48% of patients and the great saphenous vein in 86% of procedures.

Other issues: Concurrent phlebectomies were done in 68% of patients in the mechanochemical ablation group and 77% of patients in the RFA group (p=0.30)

Key efficacy and safety findings

Efficacy

Number of patients analysed: **117 (119 legs; 60 versus 59)**

Clinical and quality of life scores at baseline and at 1-month follow-up

	Baseline			1-month follow-up		
	MOCA	RFA	p	MOCA	RFA	p
Clinical scores						
VCSS (SD)	6.5 (2.9)	5.6 (2.4)	0.086	2.12 (1.8)	2.96 (2.9)	0.220
VDS (SD)	1.44 (0.5)	1.24 (0.5)	0.046	0.53 (0.7)	0.69 (0.8)	0.451
Quality of life scores						
AVVQ (SD)	22.6 (9.9)	22.7 (12.8)	0.974	12.7 (10)	15.5 (13)	0.410
EQ-VAS (SD)	79.1 (17)	77.1 (16)	0.577	86.0 (9.3)	81.0 (14)	0.158
EQ-5D-3L (SD)	0.69 (0.22)	0.74 (0.22)	0.259	0.84 (0.15)	0.78 (0.22)	0.279

Mean maximum pain score during the procedure (visual analogue scale, 0–100)

- MOCA=19.3±19 mm
- RFA=34.5±23 mm, p<0.001

Average pain score during the procedure (visual analogue scale, 0–100)

- MOCA=13.4±16 mm
- RFA=24.4±18 mm, p=0.001

Mean maximum pain score during the procedure (number on scale 0–10)

- MOCA=2.6±2.2
- RFA=4.4±2.7 p=0.001

Average pain score during the procedure (number on scale, 0–10)

- MOCA=1.9±2.0
- RFA=3.2±2.2, p=0.002

Mean time to return to usual activities

- MOCA=3.5±3.1 days
- RFA=4.8±4.3 days, p=0.235

Mean time to return to work

- MOCA=5.3±8.7 days
- RFA=4.9±3.6 days, p=0.887

Occlusion rate at 1 month (n=78)

- MOCA=83% complete occlusion, 9% proximal occlusion (>5 cm)
- RFA=92% complete occlusion, p=0.790

1 patient in the RFA group had a completely patent saphenous vein at the 1-month follow-up.

Safety

Complications

Deep vein thrombosis

- MOCA=0% (0/60)
- RFA=1.7% (1/59) (non-occlusive popliteal vein deep vein thrombosis in a patient treated for great saphenous vein incompetence (with no concurrent phlebectomy) and was an extension along the gastrocnemius vein to the popliteal vein)

Thrombophlebitis

- MOCA=0% (0/60)
- RFA=3.4% (2/59)

Abbreviations used: AVVQ, Aberdeen Varicose Vein Questionnaire; EQ-VAS, EuroQol's visual analogue scale; MOCA, mechanochemical ablation; RFA, radiofrequency ablation; SD, standard deviation; VCSS, venous clinical severity score; VDS, venous disability score

Study 2 Van Eekeren (2013)

Details

Study type	**Non-randomised comparative study**
Country	The Netherlands
Recruitment period	January–December 2011
Study population and number	**n=68 (34 mechanochemical ablation versus 34 radiofrequency ablation)** Adult patients with unilateral symptomatic great saphenous vein incompetence.
Age and sex	Mean 58 years; 63% (43/68) female
Patient selection criteria	Age>18 years; C2 to C6 varicose veins and primary great saphenous vein incompetence. Exclusion criteria included pregnancy and lactation, the use of anticoagulants, previous surgical treatment of varicose veins or history of deep venous thrombosis. Allergy to polidocanol was a contraindication for mechanochemical ablation.
Technique	Mechanochemical ablation was done using the ClariVein system (Vascular Insights, USA). The proximal 10–15 cm of the vein was treated with 2 ml of 2% polidocanol and the remaining vein with 1.5% polidocanol. Radiofrequency ablation was done using the VNUS ClosureFAST catheter (VNUS Medical Technologies, USA), with tumescent anaesthesia.
Follow-up	**6 weeks**
Conflict of interest/source of funding	None

Analysis

Follow-up issues: There were no losses to follow-up.

Study design issues: Prospective observational study with consecutive patients. Patients who did not want to be treated by mechanochemical ablation were routinely offered radiofrequency ablation treatment. The primary endpoint of the study was postoperative pain. The sample size was calculated as 34 patients in each group to detect a 50% difference in postoperative pain during the first 3 days. At the end of the procedure, patients marked the amount of pain they experienced during the procedure on a 100-mm visual analogue scale. At the 6-week follow-up, quality of life was assessed using the Dutch version of the RAND-36-Item Short-Form Health Survey (RAND-36) and the Aberdeen Varicose Vein Questionnaire (AVVQ). A vascular surgeon assessed the Venous Clinical Severity Score (VCSS).

Study population issues: There were no significant differences between the groups with regard to demographic data, CEAP classification, preoperative VCSS and AVVQ. The treated vein was significantly wider at the saphenofemoral junction in the radiofrequency ablation group than in the mechanochemical group (p=0.03).

Key efficacy and safety findings

Efficacy

Number of patients analysed: **68 (34 versus 34)**

Treatment time was significantly shorter in the mechanochemical group (p=0.02)

Mean pain scores (mm, measured on a 0–100 mm visual analogue scale)

Follow-up	MOCA	RFA	p value
During the procedure	22±16	27±15	0.16
3 days	6.2±9.2	20.5±25.5	0.004
14 days (mean postoperative pain per day)	4.8±9.7	18.6±17.0	<0.001

Median Venous Clinical Severity Score (IQR)

Follow-up	MOCA	RFA	p value
Baseline	3.0 (2.75 to 5.25)	4.0 (3.0 to 7.0)	0.09
6 weeks	1.0 (1.0 to 2.0)	3.0 (1.25 to 3.75)	0.21
p value	<0.001	<0.001	

Quality of life – Aberdeen Varicose Vein Questionnaire score (IQR)

Follow-up	MOCA	RFA	p value
Baseline	7.1 (5.3 to 9.2)	9.5 (4.5 to 16.4)	0.17
6 weeks	5.0 (3.0 to 8.5)	4.5 (1.5 to 11.2)	0.17*
p value	0.006	0.002	

* difference in change between the groups

The RAND-36 scores showed that health status significantly improved in 2 dimensions for MOCA (physical functioning and role limitations physical) at 6 weeks after treatment. In the RFA group, there was an improvement in bodily pain after 6 weeks. Patients in both groups perceived an improved change in health status.

Time to return to usual activities

- MOCA=1.0 day (IQR, 0–1.0)
- RFA=1.0 day (IQR, 1.0–3.0), p=0.01

Time to return to work

- MOCA=1.0 day (IQR, 0–3.75)
- RFA=2.0 days (IQR, 2.0–7.0), p=0.02

Safety

No major complications (including deep vein thrombosis, pulmonary embolism, skin burn) occurred in either group and there was no statistically significant difference in the incidence of minor complications between the groups.

Minor complications

Haematoma

- MOCA=6% (2/34)
- RFA=12% (4/34), p=0.67

Paraesthesia

- MOCA=0% (0/34)
- RFA=0% (0/34)

Thrombophlebitis

- MOCA=0% (0/34)
- RFA=6% (2/34), p=0.49

Induration

- MOCA=12% (4/34)
- RFA=24% (8/34), p=0.20

Hyperpigmentation

- MOCA=9% (3/34)
- RFA=9% (3/34), p=1.00

Abbreviations used: IQR, interquartile range; MOCA, mechanochemical ablation; RFA, radiofrequency ablation

Study 3 Deijen CL (2015)

Details

Study type	**Case series**
Country	The Netherlands (2 centres)
Recruitment period	2011–12
Study population and number	**n=449 (570 incompetent veins)** Adult patients with symptomatic incompetent great or small saphenous veins
Age and sex	Mean 53 years; 63% (284/449) female
Patient selection criteria	Age>18 years; symptomatic incompetent great saphenous vein of more than 30 cm or incompetent small saphenous vein of more than 10 cm of the vein, with or without saphenofemoral or saphenopopliteal junction incompetence. Exclusion criteria: asymptomatic incompetent great or small saphenous vein; diameter of the vein <3 or >12 mm; pregnancy.
Technique	The ClariVein system (Vascular Insights, USA) was used, with 2% polidocanol in the proximal 10 cm of the vein and 1.5% polidocanol in the distal part of the vein (maximum 2 mg/kg).
Follow-up	**Median 54 days (range 12–266)**
Conflict of interest/source of funding	None

Analysis

Follow-up issues: 35 (8%) patients were lost to follow-up and an additional 17 (4%) patients had no duplex ultrasonography done at follow-up. The 17 patients were unwilling to have the postoperative duplex ultrasonography because they were satisfied and free of complaints; the procedure was deemed to be successful based on physical examination. Follow-up was at 6 weeks in 1 study centre and at 3 months in the other.

Study design issues: Consecutive patients were included. Retrospective data analysis. Primary outcome was occlusion of the treated vein at follow-up. Occlusion was defined as 80% or more obliteration of the total length of the treated segment of the vein. The vein had to be incompressible and without flow; if treated areas were patent but not refluxing, this was considered as failure. Secondary outcomes were peri- and postoperative complications.

Study population issues: 64% of patients with incompetent great saphenous vein also had saphenofemoral junction incompetence.

Key efficacy and safety findings

Efficacy	Safety
Number of patients analysed: **449 (570 incompetent veins)** The procedure could not be done in 12 patients because the vein was too small to be punctured (n=7), the vein could not be canalised because of kinking (n=2), the vein was already obliterated (n=2), or no incompetent veins could be identified with duplex ultrasonography (n=1). There were, therefore, 558 treated limbs. **Occlusion of treated vein at follow-up=90% (457/506)** Occlusion rate for great saphenous vein=92% Occlusion rate for small saphenous vein=84% Occlusion rate for great saphenous vein at 6 weeks=94.5% Occlusion rate for great saphenous vein at 3 months=89% (p=0.047) Occlusion rate for small saphenous vein at 6 weeks=85% Occlusion rate for small saphenous vein at 3 months=80.5% (p=0.52) With regard to great saphenous vein, in univariate analysis treatment failure was only associated with saphenofemoral junction incompetence (p=0.04) and diameter of the vein (p=0.10) In multivariate analysis, treatment failure was only associated with saphenofemoral junction incompetence (Odds ratio 4; 95% CI 1.0 to 17.1, p=0.049). With regard to the small saphenous vein, univariate analysis showed a relationship between treatment failure and cigarette consumption (p=0.09) and hypertension (p=0.12), but these risk factors were not statistically significant in multivariate analysis.	There were no perioperative complications. **Postoperative complications=4.5% (25/558)** • Thrombophlebitis of the treated limb=2.2% (12/558) of limbs • Painful and erythematous extremity=1.1% (6/558) of limbs • Pulmonary emboli=0.5% (2/437) of patients (1 patient had dyspnoea 1 week after the procedure and pulmonary emboli were seen in the right lung on CT; he was admitted overnight and treated with coumarins. The other patient presented with a painful swollen limb and dyspnoea 1 month after treatment; pulmonary emboli were found in both lungs on CT and duplex ultrasonography showed deep vein thrombosis in the popliteal and femoral vein of the treated limb. The patient was admitted overnight and treated with coumarins. Neither patient had any sequelae). • Deep vein thrombosis=0.2% (1/437) (diagnosed in the popliteal vein 3 weeks after treatment. The patient was treated with coumarins for 3 months and at 6-month follow-up, the popliteal vein was no longer occluded. The patient had no sequelae.) • Sural nerve injury resulting in transient hyperaesthesia=0.2% (1/437) (the patient already had sensory sural neuropathy after previous saphenopopliteal junction ligation, which was aggravated by the mechanochemical ablation). • Blister=0.2% (1/437) • Abscess at puncture site=0.2% (1/437) • Haematoma at puncture site=0.2% (1/437)
Abbreviations used: CI, confidence interval	

Study 4 Van Eekeren R (2014)

Details

Study type	**Case series**
Country	The Netherlands (2 centres)
Recruitment period	December 2010–November 2011
Study population and number	**n=92 (106 legs)** Adult patients with great saphenous vein insufficiency.
Age and sex	Mean 52 years; 67% (62/92) female
Patient selection criteria	Age>18 years; C2 to C6 varicose veins; great saphenous vein diameter 3–12 mm; primary great saphenous vein incompetence. Exclusion criteria: pregnancy and lactation; use of coagulants; previous surgical treatment of the target vein; history of deep vein thrombosis; coagulation disorders; severe renal or liver insufficiency; allergy to polidocanol.
Technique	The ClariVein system (Vascular Insights, USA) was used, with 2% polidocanol in the proximal 10 cm of the vein and 1.5% polidocanol in the remaining vein. After the procedure, patients were discharged with a compression stocking continuously for the first 24 hours and during the daytime for the next 2 weeks. No concomitant phlebectomy or sclerotherapy was done. Patients were instructed to use analgesics after the procedure only when pain was experienced.
Follow-up	**1 year**
Conflict of interest/source of funding	None

Analysis

Follow-up issues: At 6 months and 1 year, respectively, 2 (2%) and 3 (3%) patients were lost to follow-up. The patients were contacted and stated that they did not attend follow-up because they had no complaints.

Study design issues: Consecutive patients were included. Patients who did not want to participate in the study were routinely offered radiofrequency ablation. The primary outcome measures were anatomic success, defined as occlusion of the treated vein; clinical success, defined as an improvement in Venous Clinical Severity Score; technical success, defined as the ability to do the procedure as planned without any technical problems. Failure of treatment was defined as a recanalised segment of >10 cm of the treated great saphenous vein. Secondary outcome measures included postprocedural pain, complications, general and disease-specific quality of life, and time to return to work.

Other issues: The procedures were done by 3 experienced surgeons who had done more than 50 mechanochemical ablation procedures.

Key efficacy and safety findings

<table>
<tr><th>Efficacy</th><th>Safety</th></tr>
<tr><td>
Number of patients analysed: 92 (106 legs)
Mean treatment time=11 minutes

Technical success rate=99% (105/106) (1 procedure was stopped because of leakage of sclerosant through the device handle; the procedure was converted to radiofrequency ablation).

Procedural pain, postprocedural pain and return to usual activities
• Median pain score during the procedure (0–100 mm visual analogue scale)=20 mm (IQR, 10–30 mm)
• Median pain score during the first 14 days after treatment=7.5 mm (IQR, 0.0–10.0 mm)
• Median time to return to usual activities=1.0 day (IQR, 0.0–1.0 day)
• Median time to return to work=1.0 day (IQR, 1.0–4.0 days)

Anatomic success
• At 6 months, 93.2% (96/103) of treated veins were obliterated.
• At 1 year, 88.2% (90/102) of treated veins were obliterated.
There was complete recanalisation of the treated vein in 12 patients and partial recanalisation in 8 patients.

One patient with an open great saphenous vein was diagnosed with autoimmune thrombocytopaenia 1 year after treatment and was retreated with radiofrequency ablation.

Clinical outcome (VCSS, lower scores indicate less severe disease)
<table>
<tr><td>Follow-up</td><td>Median VCSS (IQR)</td><td>p value</td></tr>
<tr><td>Baseline</td><td>4 (3 to 5)</td><td></td></tr>
<tr><td>6 months</td><td>1.0 (0 to 2.0)</td><td><0.001</td></tr>
<tr><td>1 year</td><td>1.0 (0 to 1.0)</td><td><0.001</td></tr>
</table>
The VCSS deteriorated in 2 patients, 1 of whom had a recanalised vein.

22% (23/105) of legs were treated by adjunctive therapy (sclerotherapy or ultrasound foam sclerosis).

Quality of life (lower scores indicate improved quality of life)
<table>
<tr><td>Follow-up</td><td>Median AVVQ (IQR)</td><td>p value</td></tr>
<tr><td>Baseline</td><td>11.1 (8.0 to 19.2)</td><td></td></tr>
<tr><td>6 months</td><td>6.6 (4.0 to 11.0)</td><td><0.001</td></tr>
<tr><td>1 year</td><td>2.4 (0.5 to 6.2)</td><td><0.001</td></tr>
</table>
There was a significant improvement in almost all physical domains of RAND-36 at 1-year follow-up, compared with baseline. The greatest improvement was seen in the domain of bodily pain. There was also improvement in perceived change of health.
</td><td>
There were no major complications (specifically, there were no reports of deep vein thrombosis, saphenous nerve neuralgia or skin necrosis).

Complications
• Superficial thrombophlebitis=3%
• Induration along the course of the treated vein=12%
• Localised haematoma=9%
• Mild hyperpigmentation at the puncture site=5%

All complications were described as minor.
No permanent hyperpigmentation was seen at 1-year follow-up.
</td></tr>
<tr><td colspan="2">Abbreviations used: IQR, interquartile range; VCSS, Venous Clinical Severity Score</td></tr>
</table>

Study 5 Boersma D (2013)

Details

Study type	**Case series (prospective)**
Country	The Netherlands
Recruitment period	June 2010–April 2011
Study population and number	**n=50** Adult patients with small saphenous vein insufficiency.
Age and sex	Mean 53 years; 64% (32/50) female
Patient selection criteria	Age>18 years; duplex-confirmed small saphenous vein incompetence at sapheno-popliteal junction; long-segment small saphenous vein insufficiency (>10 cm); vein diameter 2.5–11 mm; C2–6. Exclusion criteria: previous surgical treatment of the small saphenous vein; history of ipsilateral deep vein thrombosis; ipsilateral great saphenous vein or deep venous insufficiency; peripheral arterial occlusive disease; use of anticoagulants. Patients with allergy, pregnancy or lactation or other contraindications for the use of polidocanol were excluded.
Technique	The ClariVein system (Vascular Insights, USA) was used. The entire length of the first 15 small saphenous veins was treated with 1.5% polidocanol. In the later 35 procedures, the proximal vein (10–15 cm) was treated with 2% polidocanol and the remainder with 1.5% polidocanol. No concomitant phlebectomies were done. Patients wore compression stockings continuously for the first 24 hours and during the daytime for the next 2 weeks. Patients were allowed to perform their daily activities immediately.
Follow-up	**1 year**
Conflict of interest/source of funding	None

Analysis

Follow-up issues: All patients were scheduled for follow-up at 6 weeks and 1 year. At 1 year, 6% (3/50) of patients were lost to follow-up: 1 patient was free of complaints and refused follow-up, the other 2 patients did not respond to repeated invitations for the follow-up assessment.

Study design issues: Consecutive patients were recruited. The primary outcome measures were technical success, defined as the ability to perform the procedure as planned and achieve immediate occlusion after the procedure, and anatomic success, defined as occlusion of treated vein. A recanalised vein or treatment failure was defined as an open segment of >10 cm. Secondary outcomes included complications, treatment time, patient satisfaction, and procedural pain. Pain was recorded on a visual analogue scale, from 0 cm (no pain) to 10 cm (worst imaginable pain). Patients who were lost to follow-up were censored at 6 weeks after treatment.

Study population issues: The median small saphenous vein diameter was 4.8 mm (interquartile range, 3.5–7 mm).

Key efficacy and safety findings

<table>
<tr><th>Efficacy</th><th>Safety</th></tr>
<tr><td>
Number of patients analysed: 50
Technical success=100% (50/50)
Occlusion of treated vein at 6 weeks=100% (50/50)
In 18% (9/50) patients, residual varicosities were treated by sclerotherapy to optimise cosmetic outcome.

Anatomic success at 1 year=94% (44/47) (95% CI 0.87 to 1.00)
Recanalisation occurred in 2 of the 15 patients treated with low-dose polidocanol (anatomic success 87% [13/15]; 95% CI 0.71 to 1.00).

Recanalisation occurred in 1 of the 32 patients treated with the elevated dose of polidocanol (anatomic success 97% [31/32]; 95% CI 0.91 to 1.00).

Median pain score during treatment (VAS, 0–10 cm)=2 cm (IQR, 2 to 4).
Median duration of treatment=20 minutes (IQR, 15 to 24)
Median patient satisfaction at 6-week follow-up (score 0–10)=8 (IQR, 8 to 9).

Median Venous clinical severity score (VCSS)
<table>
<tr><th>Follow-up</th><th>VCSS</th><th>p value</th></tr>
<tr><td>Baseline</td><td>3 (IQR 2–5)</td><td></td></tr>
<tr><td>6 weeks</td><td>1 (IQR 1–3)</td><td><0.001</td></tr>
<tr><td>1 year</td><td>1 (IQR 1–2)</td><td><0.001</td></tr>
</table>
</td><td>
There were no major complications: there were no signs of any nerve injury, no deep vein thrombosis, skin necrosis, infection or hyperpigmentation.

Minor complications

Localised ecchymosis=12%
Induration around the access site=12%
Transient superficial thrombophlebitis of the treated vein=14%

Pain lasted longer than 1 week in 10% (5/50) of patients, all caused by superficial thrombophlebitis.

No additional complications were seen at follow-up.
</td></tr>
<tr><td colspan="2">Abbreviations used: CI, confidence interval; IQR, interquartile range; VCSS, venous clinical severity score</td></tr>
</table>

Study 6 Bishawi M (2014)

Details

Study type	**Case series (prospective)**
Country	USA (6 centres)
Recruitment period	Not reported
Study population and number	**n=126** Symptomatic patients with CEAP Class 2 or higher needing treatment of the great saphenous vein.
Age and sex	Mean 65.5 years; 81% (102/126) female
Patient selection criteria	Symptomatic patients with CEAP Class 2 or higher disease of the great saphenous vein, vein diameter between 4 mm and 12 mm (measured at 2 cm below the saphenofemoral junction, mid-thigh and distal thigh in the standing position). Patients with small saphenous and accessory vein reflux, non-saphenous vein reflux, acute deep or superficial vein thrombosis, deep vein obstruction, previous venous intervention, significant peripheral arterial disease, and limb infection were excluded.
Technique	The ClariVein system (Vascular Insights, USA) was used. The sclerosant used was sodium tetradecyl sulphate in 84% of the patients and polidocanol in 16% of the patients. Adjunctive treatment was done in 11% of patients at the time of the procedure (mini-phlebectomy in 7% and sclerotherapy in 4%).
Follow-up	**6 months**
Conflict of interest/source of funding	The corresponding author has no conflict of interest; the remaining 6 authors received a grant from Vascular Insights for survey expenses.

Analysis

Follow-up issues: Complete follow-up data were available for 79% (100/126) of patients at 3 months and 71% (89/126) of patients at 6 months. The reasons for patients being lost to follow-up were not described.

Study design issues: Multicentre, prospective observational study.

Study population issues: 43% of the patients had hypertension and 21% had hyperlipidaemia. The mean diameter of the treated vein was 7.3 mm.

Key efficacy and safety findings

<table>
<tr><th>Efficacy</th><th>Safety</th></tr>
<tr><td>Number of patients analysed: 126
Technical success=100% (126/126)
Closure rates
• 1 week=100%
• 3 months=98%
• 6 months=94%
There were 5 recanalisations, 2 of which were complete and 3 segmental, which were asymptomatic.

At 1 week, 49% of treated patients had residual varicose veins.

Mean pain score during the procedure (VAS, 0–10)=2
Mean pain score at 1 week <1

CEAP and VCSS (numbers are approximate – estimated from graphical representation)
<table>
<tr><th>Follow-up</th><th>CEAP</th><th>p value</th><th>VCSS</th><th>p value</th></tr>
<tr><td>Baseline</td><td>3.5</td><td></td><td>9</td><td></td></tr>
<tr><td>1 week</td><td>3.0</td><td><0.01</td><td>6</td><td><0.01</td></tr>
<tr><td>3 months</td><td>2.25</td><td><0.01</td><td>4</td><td><0.01</td></tr>
<tr><td>6 months</td><td>1.75</td><td><0.01</td><td>3</td><td><0.01</td></tr>
</table>
</td><td>Complications
• Thrombophlebitis=10%
• Ecchymosis=9%
• Haematoma=1%

There were no reports of venous thromboembolism.</td></tr>
<tr><td colspan="2">Abbreviations used: CEAP, clinical, etiological, anatomic and pathophysiologic; VAS, visual analogue score; VCSS, venous clinical severity score</td></tr>
</table>

Study 7 Vun SV (2014)

Details

Study type	**Non-randomised comparative study**
Country	Australia
Recruitment period	2011–12
Study population and number	**n=55 (57 veins) mechanochemical ablation; 50 radiofrequency ablation (RFA) procedures; 40 endovenous laser treatment (EVLT) procedures.** Patients with symptomatic saphenous vein incompetence (51 great saphenous veins and 6 small saphenous veins were treated by mechanochemical ablation)
Age and sex	Median 50 years; 66% (33/50) female (patient demographic data only given for patients treated by mechanochemical ablation and sex breakdown only includes 50 of the 55 patients).
Patient selection criteria	Duplex criteria for incompetence of the saphenofemoral, saphenopopliteal, great saphenous vein and small saphenous vein were defined as >1.0 second reflux with pulsed wave Doppler. Those patients with non-tortuous veins between 3 mm and 10 mm who opted for endovenous ablation were offered a choice of mechanochemical ablation, RFA or EVLT.
Technique	The ClariVein system (Vascular Insights, USA) was used, with 1.5% sodium tetradecyl sulphate, for mechanochemical ablation. VNUS Closure RFG2 (VNUS Medical Technologies, USA) was used for RFA. Ceralas E (Biolitec AG, Germany) was used for EVLT. All patients had compression bandaging for 24 hours, followed by compression stockings for 6 weeks. Patients treated by RFA or EVLT were given 2 days of routine non-steroidal anti-inflammatory agents for analgesia. No routine postoperative analgesia was given to patients treated by mechanochemical ablation. No concomitant procedures were done.
Follow-up	**6 weeks**
Conflict of interest/source of funding	None

Analysis

Follow-up issues: An additional 9 patients were treated by mechanochemical ablation but they did not attend for a follow-up duplex and were excluded from all analyses. There is no description of why the patients did not attend follow-up.

Study design issues: Patients were offered the option of conventional surgery or compression hosiery and endovenous ablation was additionally offered if suitable. There was no attempt at randomisation. The aim of the study was to assess the safety and efficacy of mechanochemical ablation. A vein was considered to be occluded if it was incompressible and free from blood flow on colour Doppler.

Study population issues: No patient demographics were reported for the comparator groups.

Key efficacy and safety findings

Efficacy	Safety
Number of patients analysed: **147 (57 mechanochemical ablation versus 50 RFA versus 40 EVLT)** **Technical success of mechanochemical ablation**=91% (52/57) Duplex showed patency of 3 treated veins and 2 more veins had only a short length of occlusion. Technical success rate of RFA and EVLT=93% (historical comparison, actual numbers not reported in the study paper). **Procedure times (minutes)** • Mechanochemical ablation=23.0±8.3 • RFA=37.9±8.3 • EVLT=44.1±11.4 Mechanochemical ablation versus RFA, p<0.05 Mechanochemical ablation versus EVLT, p<0.05 RFA versus EVLT, p=not significant **Median pain scores (visual analogue scale)** • Mechanochemical ablation=1 • RFA=5 • EVLT=6 p<0.01	Complications • Superficial wound infection, n=1
Abbreviations used: EVLT, endovenous laser treatment; RFA, radiofrequency ablation.	

Study 8 Ozen (2014)

Details

Study type	**Case series**
Country	Turkey
Recruitment period	2012–14
Study population and number	**n=63 patients (73 legs)** Patients with great saphenous vein insufficiency
Age and sex	Mean 45 years (range 26–72); 68% (43/63) female
Patient selection criteria	Great saphenous vein diameter >4.5 mm and grade 4 reflux. Exclusion criteria: history of allergy, history of deep venous thrombosis or deep venous thrombosis on Doppler ultrasonography, peripheral artery disease.
Technique	The ClariVein system (Vascular Insights, USA) was used, with polidocanol. Phlebectomy was done in 29% (21/73) of legs.
Follow-up	**2 years**
Conflict of interest/source of funding	None

Analysis

Follow-up issues: Patients were called for follow-up with coloured Doppler ultrasonography after 6 months, 1 year, and 2 years. Data were available for 88% (64/63) of legs at 1-year follow-up and for 58% (42/73) of legs at 2-year follow-up. The authors do not discuss losses to follow-up.

Study design issues: The baseline values for the venous clinical severity score were not reported.

Key efficacy and safety findings

Efficacy	Safety
Number of patients analysed: 63 (73 legs) Technical success=98% (72/73) **Closure rate:** • 6 months=94% (68/72) • 12 months=95% (61/64) • 24 months=95% (40/42) **Venous clinical severity score at follow-up (baseline score not reported):** • 6 months=3.2 (IQR 2–6) (the report states that this is less than the preoperative value) • 12 months=1.2 (IQR 1–3, p<0.001 compared with preoperative value) • 24 months=1.1 (IQR 1–2, p<0.001 compared with preoperative value)	No major complications such as nerve damage, deep venous thrombosis or infection were observed. • Local ecchymosis=8% (6/73) • Hardening and pain at injection site=18% (13/73) • Superficial thrombophlebitis=13% (10/73)

Study 9 Lane T (2015)

Details

Study type	**Case report**
Country	UK
Recruitment period	Not reported
Study population and number	**n=1** Patient with incompetent and refluxing small saphenous vein and an incompetent and refluxing great saphenous vein
Age and sex	70 years; male
Patient selection criteria	Not applicable
Technique	The ClariVein system (Vascular Insights, USA) was used, with 2% sodium tetradecyl sulphate.
Follow-up	**6 months**
Conflict of interest/source of funding	Not reported

Key efficacy and safety findings

Efficacy	Safety
Case report: retrograde inversion stripping A short time into the procedure to treat the small saphenous vein, the catheter would no longer withdraw and the motor slowed. The motor was shut off and a short jerking pull was given to the catheter in an attempt to free it of the obstruction, but no further movement was possible. No obvious obstruction or misalignment was seen on ultrasound. A further pull was used to free the catheter and no sclerosant was injected. On retrieval through the original cannulation site, the entire small saphenous vein was extracted, having been inversion stripped. The entry site wound was closed with a suture and the patient was turned over for treatment of the great saphenous vein. Treatment of the great saphenous vein was uneventful. The vein and device combination was dissected, and the tip was found to be fixed to a small calcified tributary. At the 6-week and 6-month follow-up visits, the patient was asymptomatic and pain free with no abnormal neurology and no cutaneous numbness. There was no recurrence or revascularisation.	

Efficacy

Pain

A randomised controlled trial of 117 patients with great or small saphenous vein incompetence treated by mechanochemical ablation or radiofrequency ablation reported mean pain scores (measured on a visual analogue scale, 0–100) during the procedure of 13.4±16 mm and 24.4±18 mm, respectively (p=0.001)[1]. A non-randomised comparative study of 68 patients with great saphenous vein incompetence treated by mechanochemical ablation or radiofrequency ablation reported pain scores (measured on a visual analogue scale, 0–100) of 22±16 mm and 27±15 mm during the procedure (p=0.16)[2]. At 3 days after the procedure, pain scores were 6.2±9.2 mm and 20.5±25.5 mm respectively (p=0.004) and the mean postoperative pain scores per day over the first 14 postoperative days were 4.8±9.7 and 18.6±17.0 mm respectively (p<0.001). A case series of 92 patients (106 legs) with great saphenous vein insufficiency reported a median pain score (measured on a visual analogue scale, 0–100) during the procedure of 20 mm[4]. The median pain score during the first 14 days after treatment was 7.5 mm. A case series of 126 patients with great saphenous vein insufficiency reported a mean pain score (measured on a visual analogue scale, 0–10) during the procedure of 2[6]. The mean pain score at 1-week follow-up was <1. A case series of 50 patients with small saphenous vein insufficiency reported a median pain score (measured on a visual analogue scale, 0–10) during treatment of 2 cm[5]. A non-randomised comparative study of 147 patients treated by mechanochemical ablation, radiofrequency ablation or endovenous laser therapy reported median pain scores during the procedure of 1, 5 and 6 respectively (p<0.01)[7].

Occlusion rates

The randomised controlled trial of 117 patients with great or small saphenous vein incompetence treated by mechanochemical ablation or radiofrequency ablation reported complete occlusion rates of 83% and 92% respectively at 1-month follow-up (p=0.79)[1]. A case series of 449 patients (570 veins) reported occlusion rates of 89% for the great saphenous vein and 81% for the small saphenous vein at 3-month follow-up[3]. The case series of 92 patients (106 legs) with great saphenous vein insufficiency reported that 88% (90/102) of treated veins were obliterated at 1-year follow-up[4]. The case series of 126 patients with great saphenous vein insufficiency reported a closure rate of 94% at 6-month follow-up[6]. A case series of 63 patients (73 treated legs) reported occlusion rates of 94% (68/72), 95% (61/64) and 95% (40/42) at 6-, 12- and 24-month follow-up respectively[8]. The case series of 50 patients with small saphenous vein insufficiency reported an occlusion rate of 94% (44/47) at 1-year follow-up[5].

Clinical scores

The randomised controlled trial of 117 patients treated by mechanochemical ablation or radiofrequency ablation reported similar venous clinical severity scores (VCSS) in the 2 groups at 1-month follow-up (2.12 and 2.96 respectively, p=0.22, compared with 6.5 and 5.6 respectively at baseline, p=0.086)[1]. The non-randomised comparative study of 68 patients with great saphenous vein incompetence treated by mechanochemical ablation or radiofrequency ablation reported statistically significant improvements in VCSS from baseline in both treatment groups at 6-week follow-up (from 3.0 to 1.0, p<0.001 and from 4.0 to 3.0, p<0.001 respectively)[2]. The case series of 92 patients (106 legs) with great saphenous vein insufficiency reported that the median VCSS improved from 4 at baseline to 1.0 at 1-year follow-up (p<0.001)[4].

Quality of life and patient satisfaction

The randomised controlled trial of 117 patients treated by mechanochemical ablation or radiofrequency ablation reported improvements in the Aberdeen Varicose Vein Questionnaire (AVVQ) in both groups at 1-month follow-up (12.7 and 15.5 respectively, p=0.41, compared with 22.6 and 22.7, respectively at baseline, p=0.97)[1]. The non-randomised comparative study of 68 patients with great saphenous vein incompetence treated by mechanochemical ablation or radiofrequency ablation reported statistically significant improvements in AVVQ scores from baseline in both treatment groups at 6-week follow-up (from 7.1 to 5.0, p=0.006 and from 9.5 to 4.5, p=0.002 respectively)[2]. The case series of 92 patients (106 legs) with great saphenous vein insufficiency reported that the median AVVQ improved from 11.1 at baseline to 2.4 at 1-year follow-up (p<0.001)[4]. The case series of 50 patients reported the median patient satisfaction score (scale 0–10) was 8 (interquartile range [IQR], 8–9) at 6-week follow-up[5].

Time to return to usual activities

The randomised controlled trial of 117 patients treated by mechanochemical ablation or radiofrequency ablation reported the mean time to return to usual activities as 3.5 and 4.8 days respectively (p=0.235)[1]. The case series of 92 patients (106 legs) reported that the median time to return to usual activities was 1.0 day (IQR, 0–1.0)[4].

Time to return to work

The randomised controlled trial of 117 patients treated by mechanochemical ablation or radiofrequency ablation reported the mean time to return to work as 5.3 and 4.9 days respectively (p=0.887)[1]. The non-randomised comparative study of 68 patients treated by mechanochemical ablation or radiofrequency ablation reported that the median time to work resumption was 1.0 day (IQR, 0–3.75) and 2.0 days (IQR, 2.0–7.0) respectively (p=0.02)[2]. The case series of 92 patients (106 legs) reported that the median time to return to work was 1.0 day (IQR, 1.0–4.0)[4].

Safety

Deep vein thrombosis or pulmonary emboli

A randomised controlled trial of 117 patients reported that no patients treated by mechanochemical ablation and 1 patient treated by radiofrequency ablation had deep vein thrombosis[1]. A case series of 449 patients reported that 1 patient had deep vein thrombosis, diagnosed in the popliteal vein 3 weeks after treatment. The patient was treated with coumarins for 3 months and at 6-month follow-up, the popliteal vein was no longer occluded[3]. In the same study, pulmonary embolism was reported in 0.5% (2/437) of patients (at 1 week and 1 month postoperatively respectively); 1 of these patients also had a deep vein thrombosis in the popliteal and femoral vein of the treated limb. Both patients were admitted overnight and treated with coumarins. Neither patient had any sequelae.

Nerve injury

Sural nerve injury resulting in transient hyperaesthesia was reported in 1 patient in the case series of 449 patients[3]. The patient already had sensory sural neuropathy after previous saphenopopliteal junction ligation, which was aggravated by the mechanochemical ablation.

Thrombophlebitis

Thrombophlebitis of the treated limb was reported in 2% (12/558) of limbs in the case series of 449 patients[3]. Thrombophlebitis was reported in no patients treated by mechanochemical ablation and in 6% (2/34) of patients treated by radiofrequency ablation in a non-randomised comparative study of 68 patients[2]. Thrombophlebitis was reported in no patients treated by mechanochemical ablation and in 3% (2/59) of patients treated by radiofrequency ablation in the randomised controlled trial of 117 patients[1]. Superficial thrombophlebitis was reported in 3% of patients and 13% (10/73) of legs in 2 case series of 92 and 63 patients respectively[4,8]. Transient superficial thrombophlebitis of the treated vein was reported in 14% of patients in a case series of 50 patients[5]. Thrombophlebitis was reported in 10% of patients in a case series of 126 patients[6].

Pain and erythema

Pain and erythema were reported in 1% (6/558) of limbs in the case series of 449 patients[3]. Hardening and pain at the injection site was reported in 18% (13/73) of legs in the case series of 63 patients[8].

Abscess at puncture site

Abscess at the puncture site was reported in 1 patient in the case series of 449 patients[3].

Haematoma at the puncture site

Haematoma at the puncture site was reported in 1 patient in the case series of 449 patients[3]. Haematoma was reported in 6% (2/34) of patients treated by mechanochemical ablation and in 12% (4/34) of patients treated by radiofrequency ablation in the non-randomised comparative study of 68 patients (p=0.67)[2]. Localised haematoma was reported in 9% of patients in the case series of 92 patients[4]. Localised ecchymosis was reported in 12% of patients and 8% (6/73) of legs in the 2 case series of 50 and 63 patients respectively[5,8]. Ecchymosis was reported in 9% of patients and haematoma in 1% of patients in the case series of 126 patients[6].

Wound infection

A superficial wound infection was reported in 1 patient treated by mechanochemical ablation in a non-randomised comparative study of 147 patients[7].

Hyperpigmentation

Hyperpigmentation was reported in 9% (3/34) of patients treated by mechanochemical ablation and in 9% (3/34) of patients treated by radiofrequency ablation in the non-randomised comparative study of 68 patients[2]. Mild hyperpigmentation at the puncture site was reported in 5% of patients in the case series of 92 patients[4].

Induration

Induration was reported in 12% (4/34) of patients treated by mechanochemical ablation and in 24% (8/34) of patients treated by radiofrequency ablation in the non-randomised comparative study of 68 patients (p=0.20)[2]. Induration along the course of the treated vein was reported in 12% of patients in the case series of 92 patients[4]. Induration around the access site was reported in 12% of patients in the case series of 50 patients[5].

Retrograde inversion stripping

Retrograde inversion stripping of a small saphenous vein was reported in 1 patient in a case report[8]. During the ablation procedure, the catheter got stuck and the motor was shut off. The catheter was pulled out and the entire small saphenous vein was also extracted, having been inversion stripped. The tip of the catheter was found to be affixed to a small calcified tributary. The patient was asymptomatic and pain free at the 6-week and 6-month follow-up. There was no recurrence, no sign of revascularisation and no neurological compromise.

Validity and generalisability of the studies

- The studies include treatment of both great saphenous veins and small saphenous veins.
- There is 1 UK-based randomised controlled trial.
- The longest reported follow-up is 2 years.
- Different sclerosants and different strengths of sclerosant were used within and between studies. This may have an effect on the efficacy of the procedure.
- Some studies reported that patients had concomitant procedures.

Existing assessments of this procedure

There were no published assessments from other organisations identified at the time of the literature search.

Related NICE guidance

Below is a list of NICE guidance related to this procedure. Appendix B gives details of the recommendations made in each piece of guidance listed.

Interventional procedures

- Ultrasound-guided foam sclerotherapy for varicose veins. NICE interventional procedure guidance 440 (2013). Available from http://guidance.nice.org.uk/IPG440
- Endovenous laser treatment of the long saphenous vein. NICE interventional procedure guidance 52 (2004). Available from http://guidance.nice.org.uk/IPG52
- Transilluminated powered phlebectomy for varicose veins. NICE interventional procedure guidance 37 (2004). Available from http://guidance.nice.org.uk/IPG37
- Radiofrequency ablation of varicose veins. NICE interventional procedure guidance 8 (2003). Available from http://guidance.nice.org.uk/IPG8

NICE guidelines

- Varicose veins in the legs: the diagnosis and management of varicose veins. NICE clinical guideline 168 (2013). Available from http://guidance.nice.org.uk/CG168

Specialist advisers' opinions

Specialist advice was sought from consultants who have been nominated or ratified by their Specialist Society or Royal College. The advice received is their individual opinion and is not intended to represent the view of the society. The advice provided by Specialist Advisers, in the form of the completed questionnaires, is normally published in full on the NICE website during public consultation, except in circumstances but not limited to, where comments are considered voluminous, or publication would be unlawful or inappropriate. Four Specialist Adviser Questionnaires for 'Endovenous mechanochemical ablation for varicose veins were submitted' and can be found on the NICE website.

Patient commentators' opinions

NICE's Public Involvement Programme sent 65 questionnaires to 2 NHS trusts for distribution to patients who had the procedure (or their carers). NICE received 30 completed questionnaires.

The patient commentators' views on the procedure were consistent with the published evidence and the opinions of the specialist advisers.

Issues for consideration by IPAC

Ongoing trials:

- Mechanochemical Endovenous Ablation (MOCA) Versus RADiofrequeNcy Ablation (RFA) in the Treatment of Primary Great Saphenous Varicose Veins: a Multicentre Randomized Trial (NCT01936168); randomised controlled trial; the Netherlands; estimated enrolment: 460; estimated study completion date: December 2020.

- Registry of the Treatment of Primary Insufficiency of the Great Saphenous Vein With a Diameter >/= 12 mm, Antero-lateral Branches, or Great Saphenous Vein Insufficiency Below the Knee With Mechano-chemical Endovenous Ablation (MOCA) (NCT02345018); prospective cohort study; the Netherlands; estimated enrolment: 90; estimated study completion date: December 2017.

- Mechanochemical Endovenous Ablation of Great Saphenous Vein Incompetence Using the ClariVein Device: a Prospective Study (NCT01459263); prospective case series; the Netherlands; estimated enrolment: 100; estimated study completion date: December 2017.

References

1. Bootun R, Lane T, Dharmarajah B et al. (2014) Intra-procedural pain score in a randomised controlled trial comparing mechanochemical ablation to radiofrequency ablation: The Multicentre Venefit™ versus ClariVein® for varicose veins trial. Phlebology doi: 10.1177/0268355514551085
2. van Eekeren RR, Boersma D, Konijn V et al. (2013) Postoperative pain and early quality of life after radiofrequency ablation and mechanochemical endovenous ablation of incompetent great saphenous veins. Journal of Vascular Surgery 57: 445–50
3. Deijen C, Schreve MA, Bosma J et al. (2015) Clarivein mechanochemical ablation of the great and small saphenous vein: early treatment outcomes of two hospitals. Phlebology doi: 10.1177/0268355515600573
4. van Eekeren RRJP, Boersma D, Holewijn S et al. (2014) Mechanochemical endovenous ablation for the treatment of great saphenous vein insufficiency. Journal of Vascular Surgery: Venous and Lymphatic Disorders 2: 282–8
5. Boersma D, van Eekeren RR, Werson DA et al. (2013) Mechanochemical endovenous ablation of small saphenous vein insufficiency using the ClariVein® device: one-year results of a prospective series. European Journal of Vascular & Endovascular Surgery 45: 299–303
6. Bishawi M, Bernstein R, Boter M et al. (2014) Mechanochemical ablation in patients with chronic venous disease: a prospective multicenter report. Phlebology 29: 397–400
7. Vun S, Rashid S, Blest N et al. (2015) Lower pain and faster treatment with mechanico-chemical endovenous ablation using ClariVein®. Phlebology 30: 688–92
8. Ozen Y, Cekmecelioglu D, Sarikaya S et al. (2014) Mechano-chemical endovenous ablation of great saphenous vein insufficiency: two-year results. Turkish Journal of Vascular Surgery 23: 176–9
9. Lane TRA, Moore HM, Franklin IJ et al. (2015) Retrograde inversion stripping as a complication of the ClariVein® mechanochemical venous ablation procedure. Annals of the Royal College of Surgeons 97: e18–20

Appendix A: Additional papers on endovenous mechanochemical ablation for varicose veins

The following table outlines the studies that are considered potentially relevant to the IP overview but were not included in the main data extraction table (table 2). It is by no means an exhaustive list of potentially relevant studies.

Article	Number of patients/ follow-up	Direction of conclusions	Reasons for non-inclusion in table 2
Elias S, Raines JK (2012) Mechanochemical tumescentless endovenous ablation: final results of the initial clinical trial. Phlebology 27: 67–72	n=29 patients (30 veins) Mean FU=9 months	Mean treatment time=14 minutes. Primary closure rate at mean follow-up of 260 days (based on ultrasound)=97% (29/30) One vein recanalised between the 1-week and 1-month visits (recanalisation was seen on ultrasound but the treated vein was not refluxing).	Larger studies are included. (Study was included in table 2 of the 2012 overview)
Bootun R, Lane TR, Davies AH (2015) The advent of non-thermal, non-tumescent techniques for treatment of varicose veins. Phlebology doi: 10.1177/0268355515593186	Review	So far, mechanochemical ablation and cyanoacrylate glue have been shown to be at least equivalent to endothermal techniques and probably superior to ultrasound-guided foam sclerotherapy with respect to occlusion rates. They also appear to offer better comfort and earlier return to normal activities. Further randomised controlled trials with longer follow-up will hopefully be able to provide more robust evidence of their respective merits.	Review without a meta-analysis.
Boersma D, Kornmann VN, van Eekeren RR et al. (2016) Treatment Modalities for Small Saphenous Vein Insufficiency: Systematic Review and Meta-analysis. Journal of Endovascular Therapy 23: 199-211	Systematic review n=49 articles (1 on mechano-chemical ablation)	The pooled anatomical success rate was 58% (95% CI 41% to 75%) for surgery in 798 SSVs, 98.5% (95% CI 98% to 99%) for EVLA in 2950 SSVs, 97% (95% CI 94% to 100%) for RFA in 386 SSVs, and 64% (95% CI 47% to 80%) for UGFS in 494 SSVs. One study reported results of MOCA, with an anatomical success rate of 94%. Neurologic complications were most frequently reported after surgery (mean 20%) and thermal ablation (EVLA: mean 5%; RFA: mean 10%). Deep venous thrombosis was a rare complication (0% to 1%).	The review only includes 1 study on mechanochemical ablation.

Article	Number of patients/ follow-up	Direction of conclusions	Reasons for non-inclusion in table 2
Kendler M, Kratzsch J, Schmidt R et al. (2015) Serum endothelin 1 levels before, during and after mechanochemical endovenous ablation with foam and surgical correction of incompetent great saphenous veins. Journal of the European Academy of Dermatology and Venereology, doi: 10.1111/jdv.12944	n=12 (6 mechano-chemical versus 6 surgery)	Neither mechanochemical ablation or high ligation and stripping increase Endothelin 1 (ET-1) levels during or after treatment. This suggests that ET-1 related complications, such as neurological and visual disturbances, may be rare when using these methods for varicose vein treatment.	Study focuses on serum endothelin 1 levels with a small sample size – reported as a letter to the editor.
Moore HM, Lane TR, Franklin IJ et al. (2014) Retrograde mechanochemical ablation of the small saphenous vein for the treatment of a venous ulcer. Vascular 22: 375–7	n=1 FU=3 months	A patient with complicated varicose veins of the leg and a non-healing venous ulcer was treated successfully with retrograde Mechanochemical ablation. The patient's symptoms improved and the ulcer size reduced after the procedure.	Case report.
Mueller RL, Raines JK (2013) ClariVein mechanochemical ablation: background and procedural details. Vascular & Endovascular Surgery 47: 195-206	Review	This procedure is an exciting addition to the phlebologist's toolbox and has the potential to become a first-line treatment.	Review without a meta-analysis.
Pavlovic MD, Schuller-Petrovic S (2014) Endovascular techniques for the treatment of chronic insufficiency of the lower limb's superficial venous system. Reviews in Vascular Medicine 2: 107–17	Review	The efficacy and safety of novel treatments for varicose veins should approach those of radiofrequency segmental ablation and endovenous laser ablation and/or time-sparing effects and higher comfort for the patients, along with possible cost reductions must be decisive factors to position these new methods in the phlebological toolbox. All of that requires several years of carefully designed clinical studies.	Review without a meta-analysis.
Sadek M, Kabnick LS (2014) Are Non-Tumescent Ablation Procedures Ready to Take Over? Phlebology 29: 55-60	Review	Tumescentless procedures have demonstrated some promising, although conflicting, initial safety and efficacy data. They should continue to be evaluated and used in a trial setting.	Review without a meta-analysis.

Article	Number of patients/ follow-up	Direction of conclusions	Reasons for non-inclusion in table 2
van Eekeren RR, Hillebrands JL, van der Sloot K et al. (2014) Histological observations one year after mechanochemical endovenous ablation of the great saphenous vein. Journal of Endovascular Therapy 21: 429–33	n=1	Microscopic evaluation of a Mechanochemical ablation treated vein showed a circumferential disappearance of the endothelial layer and fibrosis of the vein. The media was considerably damaged, with changes in collagen structure, supporting the therapeutic effect of the procedure.	Case report, describing histological observations.
van Eekeren RRJP, Boersma D, Elias S et al. (2011) Endovenous mechanochemical ablation of great saphenous vein incompetence using the ClariVein device: a safety study. Journal of Endovascular Therapy 18: 328–34	n=25 patients (30 veins) Mean FU=6 weeks	Complete occlusion at 6 weeks=87% (26/30) Median venous clinical severity score (scale 0–30, lower scores indicating less severe disease) • Baseline=3.0 (IQR 2.0–4.75) • 6 weeks after the procedure=1.0 (IQR 0.25–3.0), p<0.001 After 6 weeks, median patient satisfaction=8.5 (IQR 8–9, on a scale of 0–10)	Larger studies are included. (Study was included in table 2 of the 2012 overview)
Witte ME, Reijnen MM, de Vries JP et al. (2015) Mechanochemical Endovenous Occlusion of Varicose Veins Using the ClariVein Device. Surgical Technology International 26: 219-225	Review	Mechanochemical occlusion using ClariVein has proven to be safe and effective and has several advantages compared to endothermal techniques. The possibility of retrograde ablation of distal SSV insufficiency in C6 ulceration is considered a significant advantage. Randomised comparative studies with long-term follow up will continue to define the definite place of mechanochemical occlusion.	Review without a meta-analysis.

Appendix B: Related NICE guidance for endovenous mechanochemical ablation for varicose veins

Guidance	Recommendations
Interventional procedures	**Cyanoacrylate glue occlusion for varicose veins. NICE interventional procedure guidance 526 (2015).** 1.1 Current evidence on the safety and efficacy of cyanoacrylate glue occlusion for varicose veins is limited in quantity and quality. Therefore, this procedure should only be used with special arrangements for clinical governance, consent and audit or research. 1.2 Clinicians wishing to use cyanoacrylate glue occlusion for varicose veins should: • Inform the clinical governance leads in their NHS trusts. • Ensure that patients understand the uncertainty about the procedure's safety and efficacy and provide them with clear written information. In addition, the use of NICE's information for the public is recommended. • Audit and review clinical outcomes of all patients having cyanoacrylate glue occlusion for varicose veins (a national register is currently under development). 1.3 Patient selection should be done by clinicians who can offer a range of treatment options in addition to cyanoacrylate glue occlusion. 1.4 This procedure should only be done by clinicians with specific training in this technique. 1.5 NICE may update the guidance on publication of further evidence. **Ultrasound-guided foam sclerotherapy for varicose veins. NICE interventional procedure guidance 440 (2013).** 1.1 Current evidence on the efficacy of ultrasound-guided foam sclerotherapy for varicose veins is adequate. The evidence on safety is adequate, and provided that patients are warned of the small but significant risks of foam embolisation (see section 1.2), this procedure may be used with normal arrangements for clinical governance, consent and audit. 1.2 During the consent process, clinicians should inform patients that there are reports of temporary chest tightness, dry cough, headaches and visual disturbance, and rare but significant complications including myocardial infarction, seizures, transient ischaemic attacks and stroke.

	Endovenous laser treatment of the long saphenous vein. NICE interventional procedure guidance 52 (2004). 1.1 Current evidence on the safety and efficacy of endovenous laser treatment of the long saphenous vein appears adequate to support the use of this procedure provided that the normal arrangements are in place for consent, audit and clinical governance. Current evidence on the efficacy of this procedure is limited to case series with up to 3-years follow-up. Clinicians are encouraged to collect longer-term follow-up data. **Transilluminated powered phlebectomy for varicose veins. NICE Interventional procedure guidance 37 (2004).** 1.1 Current evidence on the safety and efficacy of transilluminated powered phlebectomy for varicose veins includes small numbers of patients and is of limited quality. It does not appear adequate to support the use of this procedure without special arrangements for consent and for audit or research. Clinicians wishing to undertake transilluminated powered phlebectomy for varicose veins should inform the clinical governance leads in their Trusts. They should ensure that patients offered it understand the uncertainty about the procedure's safety and efficacy and should provide them with clear written information. Use of the Institute's information for the public is recommended. Clinicians should ensure that appropriate arrangements are in place for audit or research. Publication of safety and efficacy outcomes will be useful in reducing the current uncertainty. NICE is not undertaking further investigation at present. **Radiofrequency ablation of varicose veins. NICE interventional procedure guidance 8 (2003).** 1.1 Current evidence on the safety and efficacy of radiofrequency ablation of varicose veins appears adequate to support the use of this procedure as an alternative to saphenofemoral ligation and stripping, provided that the normal arrangements are in place for consent, audit and clinical governance.
NICE guidelines	**Varicose veins in the legs: The diagnosis and management of varicose veins. NICE guideline CG168 (2013).** **1.1 Information for people with varicose veins** 1.1.1 Give people who present with varicose veins information that includes: • An explanation of what varicose veins are. • Possible causes of varicose veins. • The likelihood of progression and possible complications, including deep vein thrombosis, skin changes, leg ulcers, bleeding and thrombophlebitis. Address any misconceptions the person may have about the risks of developing complications. • Treatment options, including symptom relief, an overview of

interventional treatments and the role of compression.

- Advice on:
  - weight loss (for guidance on weight management see Obesity [NICE guideline CG43])
  - light to moderate physical activity
  - avoiding factors that are known to make their symptoms worse, if possible
  - when and where to seek further medical help.

1.1.2 When discussing treatment for varicose veins at the vascular service tell the person:

- What treatment options are available.
- The expected benefits and risks of each treatment option.
- That new varicose veins may develop after treatment.
- That they may need more than 1 session of treatment.
- That the chance of recurrence after treatment for recurrent varicose veins is higher than for primary varicose veins.

1.2 Referral to a vascular service

1.2.1 Refer people with bleeding varicose veins to a vascular service immediately.

1.2.2 Refer people to a vascular service if they have any of the following.

- Symptomatic* primary or symptomatic recurrent varicose veins.
- Lower-limb skin changes, such as pigmentation or eczema, thought to be caused by chronic venous insufficiency.
- Superficial vein thrombosis (characterised by the appearance of hard, painful veins) and suspected venous incompetence.
- A venous leg ulcer (a break in the skin below the knee that has not healed within 2 weeks).
- A healed venous leg ulcer.

* Veins found in association with troublesome lower limb symptoms (typically pain, aching, discomfort, swelling, heaviness and itching).

1.3 Assessment and treatment in a vascular service

Assessment

1.3.1 Use duplex ultrasound to confirm the diagnosis of varicose veins and the extent of truncal reflux, and to plan treatment for people with suspected primary or recurrent varicose veins.

Interventional treatment

1.3.2 For people with confirmed varicose veins and truncal reflux:

- Offer endothermal ablation (see Radiofrequency ablation of varicose veins [NICE interventional procedure guidance 8] and

	Endovenous laser treatment of the long saphenous vein [NICE interventional procedure guidance 52]). • If endothermal ablation is unsuitable, offer ultrasound‑guided foam sclerotherapy (see Ultrasound-guided foam sclerotherapy for varicose veins [NICE interventional procedure guidance 440]). • If ultrasound-guided foam sclerotherapy is unsuitable, offer surgery. If incompetent varicose tributaries are to be treated, consider treating them at the same time. 1.3.3 If offering compression bandaging or hosiery for use after interventional treatment, do not use for more than 7 days. **Non-interventional treatment** 1.3.4 Do not offer compression hosiery to treat varicose veins unless interventional treatment is unsuitable.

Appendix C: Literature search for endovenous mechanochemical ablation for varicose veins

Databases	Date searched	Version/files
Cochrane Database of Systematic Reviews – CDSR (Cochrane Library)	01/02/2016	Issue 2, 2016
Cochrane Central Database of Controlled Trials – CENTRAL (Cochrane Library)	01/02/2016	Issue 2, 2016
HTA database (Cochrane Library)	01/02/2016	
MEDLINE (Ovid)	01/02/2016	1946 to January Week 3 2016
MEDLINE In-Process (Ovid)	01/02/2016	January 29, 2016
EMBASE (Ovid)	01/02/2016	1974 to 2016 Week 05
PubMed	01/02/2016	-
JournalTOCS	01/02/2016	-

Trial sources searched on 16/07/2015

- Clinicaltrials.gov
- ISRCTN
- WHO International Clinical Trials Registry

Websites searched on 16/07/2015

- National Institute for Health and Care Excellence (NICE)
- NHS England
- Food and Drug Administration (FDA) - MAUDE database
- Australian Safety and Efficacy Register of New Interventional Procedures – Surgical (ASERNIP – S)
- Australia and New Zealand Horizon Scanning Network (ANZHSN)
- EuroScan
- General internet search

The following search strategy was used to identify papers in MEDLINE. A similar strategy was used to identify papers in other databases.

1	exp Venous Insufficiency/
2	((venous or vein*) adj4 (incomp* or insuffic*)).tw.
3	((venous or vein*) adj4 ulcer*).tw.
4	telangiectasis/
5	telangiect*.tw.
6	((reticular or thread or spider) adj4 (vein* or venous)).tw.

7	or/1-6
8	exp lower extremity/
9	(lower limb* or lower extremit* or leg* or calf or valves or thigh* or membrum inferius).tw.
10	or/8-9
11	7 and 10
12	exp varicose veins/
13	(varicos* adj4 vein*).tw.
14	(varix or varices or microvaricosity or phlebarteriectasia or phlebectas* or prevaricos* or vein ectasia or venectasia).tw.
15	Saphenous Vein/
16	((saphenous or perforator) adj4 (vein* or vena or incomp* or insuffic*)).tw.
17	GSV.tw.
18	or/11-17
19	clarivein.tw.
20	MOCA.tw.
21	((mechanochemical or mechano-chemical or mechanical) adj4 ablat*).tw.
22	((non-thermal or nonthermal or "non thermal") adj4 ablat*).tw.
23	(infus* adj4 catheter*).tw.
24	((damag* or disrupt* or disturb* or destroy* or break* or destruct*) adj4 (endothelium or endothelial or lining)).tw.
25	(rotat* adj4 (wire* or tip*)).tw.
26	tumescentless.tw.
27	((spasm* adj2 vein*) or venospasm).tw.
28	or/19-27
29	18 and 28
30	animals/ not humans/
31	29 not 30