ASERNIP/S
Australian Safety and Efficacy Register of New Interventional Procedures — Surgical

Rapid review

Treatments for varicose veins

ASERNIP-S REPORT NO. 66

Australian Government
Department of Health and Ageing

Australian Safety & Efficacy Register of New Interventional Procedures — Surgical

The Royal Australasian College of Surgeons
Disclaimer

This is a rapid systematic review in which the methodology has been limited in one or more areas to shorten the timeline for its completion. Thus, modifications have been made in at least one of the following areas: search strategy, inclusion criteria, assessment of study quality and data analysis. It is considered that these amendments would not significantly alter the overall findings of the rapid review when compared to a full systematic review.

The methodology used for the rapid review is described in detail, including the limits made for this particular topic. These limitations have been made possible mainly by restricting the specific clinical questions asked. These limits were applied following the requirements of the specific review topic, together with clinical guidance from a protocol surgeon.

Therefore, this rapid review is a limited evidence-based assessment that is based on a simple systematic search of studies published in the peer reviewed literature. As a result, this rapid review may be used to inform certain questions on the specific review topic.
Executive summary

Aim and scope
This rapid review aimed to assess the safety and effectiveness of current treatment options for varicose veins through a limited systematic review of the literature. The treatment options assessed include surgery, phlebectomy, sclerotherapy, endovenous laser therapy (ELT), radiofrequency ablation (RFA) and conservative therapies, including the use of compression hosiery.

Studies eligible for inclusion were those reporting on human patients with varicose veins of the legs, both superficial and complicated. Included studies were related to the use of one or more intervention for the treatment of varicose veins and compared at least one of the included interventions with another included treatment modality. Outcomes of interest included abolition of reflux, recurrence of varicose veins, reduction of symptoms, quality of life and the harms associated with each technique.

Studies were excluded if they were cost-effectiveness, in-vitro or laboratory studies, or studies comparing technologies or techniques within a particular treatment modality, including surgical technique, sclerosant type or concentration, ELT laser wavelengths, or post-treatment therapy.

Methods
The search strategy identified articles published between January 1988 and February 2008 in the English language. The following databases were searched: BMJ Clinical Evidence, The York (UK) Centre for Reviews and Dissemination (CRD), Cochrane Database of Systematic Reviews, PubMed and EMBASE. Extended searching of internet websites, conference abstracts, handsearching of journals, and contacting of authors for unpublished data was not undertaken. The search terms used included: varicose veins, venous insufficiency, vascular surgical procedures, ligation, sclerotherapy, laser surgery and catheter ablation.

Data was extracted from the included studies using tables created a priori, the methodological quality of the studies was assessed, results were examined and overall conclusions made.

Key results and conclusions
As searches identified several high-quality, recently published systematic reviews on the various treatments for varicose veins, these alone were included for assessment in the rapid review. One review compared ELT with surgery (MSAC 2003), one compared RFA with surgery (Adi et al 2004), one compared sclerotherapy with surgery (Rigby et al 2007), and one focused on foam sclerotherapy (Jia et al 2006). Conclusions based on the results of the reviews are summarised below:

- Ligation with stripping plus avulsion is generally regarded as the ‘gold standard’ treatment for primary long saphenous veins.
Compression stockings are often used as a first-line treatment for varicose veins; however, no evidence was found to support the effectiveness of this.

There appears to be a place for both surgery and sclerotherapy in the management of varicose veins. Sclerotherapy shows better immediate and early outcomes, but surgery produces more durable long-term (≥ 12 months) outcomes.

Sclerotherapy and phlebectomy may be best suited to patients with minor superficial varicose veins not related to reflux in the saphenous system, or as a post-treatment or adjunctive procedure to other treatments.

ELT appears to be as safe as conventional surgery with junction ligation and vein stripping, and is effective for occluding saphenous veins; however, it is unclear how ELT compares with other interventions.

Evidence suggests potential short-term clinical benefits from RFA compared with surgery involving junction ligation with or without vein stripping. Data suggest short-term safety of RFA is comparable to conventional surgery, with case-series evidence tentatively supporting its long-term safety.

The extent of varicose veins should govern the intervention of choice, with no single treatment universally employed.

A lack of high-quality comparative evidence made it difficult to make meaningful judgments regarding the relative safety and effectiveness of treatments for varicose veins. High-quality comparative studies (such as well-designed RCTs) are needed for definitive comparisons.
The ASERNIP-S review group

ASERNIP-S Surgical Director
Professor Guy Maddern
ASERNIP-S
Royal Australasian College of Surgeons
Stepney SA 5069

Protocol Surgeon
Associate Professor Robert Fitridge
Department of Surgery
Queen Elizabeth Hospital
Woodville SA 5011

Advisory Surgeon
Associate Professor Peter Woodruff
Vascular Surgery Unit
Princess Alexandra Hospital
Woolloongabba QLD 4102

ASERNIP-S Researcher
Ms Deanne Leopardi
ASERNIP-S
Royal Australasian College of Surgeons
Stepney SA 5069

ASERNIP-S Researcher
Mr Ben Hoggan
ASERNIP-S
Royal Australasian College of Surgeons
Stepney SA 5069
# Table of contents

**Introduction** ........................................................................................................ 1  
  Objective ............................................................................................................................. 1  
  Background .......................................................................................................................... 1  
    Condition ........................................................................................................................ 1  
    Clinical need ................................................................................................................... 1  
    Examination and investigation .................................................................................... 2  
    Treatment ....................................................................................................................... 3  

**Research questions** ............................................................................................. 7  

**Methodology** ........................................................................................................ 8  
  Inclusion criteria .................................................................................................................. 8  
  Exclusion criteria ................................................................................................................. 10  
  Literature search strategies .............................................................................................. 10  
    Databases searched .......................................................................................................... 10  
    Search terms .................................................................................................................. 11  
    Selection of studies ......................................................................................................... 11  
  Data extraction and appraisal of study methodology .................................................. 11  

**Results** ............................................................................................................... 14  
  Systematic review evidence ............................................................................................. 14  
  Summary of review findings ............................................................................................... 25  
    Overview ........................................................................................................................ 25  
    Sclerotherapy versus phlebectomy ............................................................................... 25  
    Sclerotherapy versus surgery ....................................................................................... 25  
    Surgery versus endovenous laser therapy ................................................................. 26  
    Surgery versus radiofrequency ablation ....................................................................... 27  

**Conclusions** ...................................................................................................... 28  

**References** ........................................................................................................ 30  

Appendix A: Search strategy .................................................................................. 34  
Appendix B: Excluded studies .................................................................................. 35  
Appendix C: Evidence tables .................................................................................. 40
Introduction

Objective
To assess the safety and effectiveness of current medical treatment options (not including medicinal interventions) for patients with varicose veins through a limited systematic review of the literature. The treatment options include surgery (junction ligation with or without stripping), phlebectomy, sclerotherapy, endovenous laser therapy (ELT), radiofrequency ablation (RFA) and conservative therapies, including the use of compression hosiery.

Background

Condition
Varicose veins are enlarged, tortuous, subcutaneous veins that commonly occur in the legs (Tisi 2007). The principal superficial leg veins are the great saphenous vein (GSV), which ascends the inner side of the leg from the inner arch of the foot up to the femoral vein, and the small saphenous vein (SSV), which runs from the outer arch of the foot up to the popliteal vein via the back of the leg (Gabella 1995). Veins carry deoxygenated blood from the body back to the heart to be oxygenated and recirculated around the body. Blood from the legs must travel against gravity to reach the heart. This movement is helped by contractions of the lower leg muscles and the elasticity of the vein walls, which act together to pump the blood upwards. Valves positioned along the length of the vein close as the blood is pumped through them to prevent blood flowing backwards during muscle relaxation.

Varicose veins are caused by faulty valves and decreased elasticity in the vein walls, which allow blood to backflow and pool. This is known as venous reflux (Tisi 2007). The affected veins enlarge and appear as green, dark blue or purple protrusions just below the skin’s surface (Tisi 2007). The severity of symptoms associated with varicose veins varies and may include pain, heaviness, pruritis, ulceration, skin discolouration and oedema (Beale and Gough 2005). Severe symptoms include thrombophlebitis, bleeding and venous dermatitis, which often require intervention (Wolf and Brittenden 2001). The exact cause of venous reflux is unknown; however, several risk factors for the condition have been identified, including increasing age, female sex, obesity, inactivity and pregnancy (Callam 1994).

Clinical need
Varicose veins are common in many populations. While a previous review of their prevalence found no data for the Australian population, the prevalence rates in countries with a similar ethnic composition to Australia generally ranged from 10.4% to 23.0% in men and 29.5% to 39.0% in women (Medical Services Advisory Committee 2003). Data from Medicare Australia suggest that the largest group of patients requiring varicose vein treatment are women between the ages of 35 and 64 years (Medicare Australia 2008). Due to the dynamic and recurrent nature of the varicosities, most varicose vein conditions are long term and often require multiple treatments. In 2001, the prevalence of self-reported “long-term” varicose...
veins in the Australian population was 2.3% — 1.1% in males and 3.5% in females (Australian Institute of Health and Welfare 2004). According to the Australian National Morbidity Database, 14,950 surgical junction ligation procedures (with or without vein stripping) were used to treat varicose veins in 2004–2005. In the same period, a further 2,654 ligation or stripping procedures were used to re-treat varicose veins (Australian Institute of Health and Welfare 2008).

**Examination and investigation**

A patient’s suitability for treatment is ascertained through clinical examination to determine the source of venous incompetency. Ideally, this examination is followed by a duplex Doppler ultrasonography scan to confirm the presence of reflux (Wolf and Brittenden 2001). Venous disease is defined using a number of classification systems, none of which is universally accepted. The CEAP classification is a consensus document endorsed by the joint councils of the Society for Vascular Surgery and the North American-International Society for Cardiovascular Surgery (Eklof et al 2004). Chronic venous disease is classified according to clinical signs (C), aetiology/cause (E), anatomic distribution (A), and pathophysiologic condition (P), and clinically rated as ranging in severity from C0 to C6 (Table 1).

**Table 1: CEAP classification**

<table>
<thead>
<tr>
<th>Classification</th>
<th>Clinical signs</th>
</tr>
</thead>
<tbody>
<tr>
<td>C0</td>
<td>No visible or palpable signs of venous disease</td>
</tr>
<tr>
<td>C1</td>
<td>Telangiectases or reticular veins</td>
</tr>
<tr>
<td>C2</td>
<td>Varicose veins; distinguished from reticular veins by a diameter of 3 mm or more</td>
</tr>
<tr>
<td>C3</td>
<td>Oedema</td>
</tr>
<tr>
<td>C4</td>
<td>Changes in skin and subcutaneous tissue secondary to venous disease, divided into two subclasses to better define differing severity of venous disease:</td>
</tr>
<tr>
<td></td>
<td>C4a: Pigmentation or eczema</td>
</tr>
<tr>
<td></td>
<td>C4b: Lipodermatosclerosis or atrophie blanche</td>
</tr>
<tr>
<td>C5</td>
<td>Healed venous ulcer</td>
</tr>
<tr>
<td>C6</td>
<td>Active venous ulcer</td>
</tr>
</tbody>
</table>

Source: Eklof et al 2004

Widmer’s classification of venous disease is still commonly used in German-speaking countries (Widmer et al 1981). This classification system differentiates clearly between uncomplicated varicose veins and chronic venous insufficiency (Table 2).

**Table 2: Widmer’s classification**

<table>
<thead>
<tr>
<th>Varicose veins</th>
</tr>
</thead>
<tbody>
<tr>
<td>Class 1</td>
</tr>
<tr>
<td>Class 2</td>
</tr>
<tr>
<td>Class 3</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Chronic venous insufficiency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade I</td>
</tr>
<tr>
<td>Grade II</td>
</tr>
<tr>
<td>Grade III</td>
</tr>
</tbody>
</table>

A similar classification system is Porter’s classification, published as part of a document on reporting standards of venous disease and shown in Table 3 (Porter and Moneta 1995).

<table>
<thead>
<tr>
<th>Classification</th>
<th>Clinical signs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Class 0</td>
<td>Asymptomatic</td>
</tr>
<tr>
<td>Class 1</td>
<td>Mild swelling and discomfort; superficial veins involved</td>
</tr>
<tr>
<td>Class 2</td>
<td>Hyperpigmentation in the gaiter area; subcutaneous fibrosis</td>
</tr>
<tr>
<td>Class 3</td>
<td>Ulcerative or preulcerative skin changes; eczema</td>
</tr>
</tbody>
</table>


**Treatment**

A variety of therapies are available for treating varicose veins, including conservative therapies and surgical interventions. Conservative therapy, which attempts to limit disease progression, is recommended in asymptomatic patients or those with mild to moderate symptoms. A clinician may advise lifestyle changes, including physical exercise and weight loss, to promote circulation. Patients may also be discouraged from prolonged sitting or standing and advised to elevate the affected limbs whenever possible to reduce pressure on impaired vein valves (National Health Service 2007). Compression stockings provide relief for varicose vein symptoms, such as pain and swelling, while improving venous haemodynamics (Beale and Gough 2005).

Surgical intervention generally becomes necessary when the symptoms of varicose veins significantly impinge on the patient’s quality of life. Provided the deep venous system of the legs is competent and free from obstruction, a patient can safely tolerate the surgical removal or occlusion of varicose veins. The SSV and GSV are part of the superficial venous system. Most of the blood from the legs is returned to the heart via the deep leg veins; therefore, blood that previously travelled through the saphenous vein can be redirected through deep leg veins if the GSV becomes distended and varicotic. Figure 1 shows the clinical decision-making process for diagnosing and treating patients with varicose veins.
Clinical examination (incl. history and Duplex scan)

Mild symptoms

Conservative therapy\(^a\)

Severe symptoms and/or large veins

Suitable for treatment

Great saphenous vein and/or small saphenous vein incompetence

Unsuitable for treatment

Contraindications:
- Pregnancy
- Immobility
- Venus outflow obstruction
- Deep vein thrombosis
- Phlebitis

Small or superficial veins (diameter <2.5 mm)
- Sclerotherapy or laser treatment

Large veins (diameter >2.5 mm)
- Phlebectomy
- Sclerotherapy (ultrasound guided)

Junction ligation/stripping
- Endovenous ablation (ELT\(^b\) or RFA\(^c\))
- Post-treatment sclerotherapy (if required)

Conservative therapy\(^a\)

\(^a\) Including reassurance, lifestyle advice (exercise and weight loss), compression therapy.

\(^b\) ELT: endovenous laser therapy.

\(^c\) RFA: radiofrequency ablation.

NOTE: dashed lines represent procedures not currently covered by MBS.

Figure 1: Clinical decision pathway for diagnosis and treatment of varicose veins
Sclerotherapy

Usually, sclerotherapy is an outpatient procedure and is done under local anaesthetic. Sclerotherapy involves injecting a liquid chemical (sclerosant) into the abnormal vein to initiate inflammation, occlusion and scarring (Beale and Gough 2005). The damaged vein collapses and eventually fades. Ultrasound-guided sclerotherapy allows the sclerosant to be injected directly into the GSV to treat larger and deeper varicosities (Beale and Gough 2005). Foam sclerotherapy mixes air or gas with the sclerosant to produce foam, allowing a small amount of sclerosant to cover a larger surface area by displacing blood within the vein (Beale and Gough 2005). Sclerosant can also be introduced to the vein by a catheter (known as endovascular sclerotherapy), allowing targeted and selective treatment (Belcaro et al 2000).

High recurrence rates are common in patients with larger veins or venous reflux (Jakobsen 1979), primarily because of recanalisation or neovascularisation. Recanalisation is the spontaneous restoration of the lumen of the saphenous vein after occlusion, while neovascularisation is the proliferation of blood vessels in tissue where the saphenous vein has previously been removed.

Although injection sclerotherapy is considered the ‘gold standard’ treatment for smaller veins, it has a number of drawbacks when used to remove large veins (those greater than 4 mm in diameter). Injection sclerotherapy is also associated with an increased risk of adverse events, such as intra-arterial injection, dyschromia, haematoma, ulceration and thrombophlebitis, and it also has inconsistent long-term effectiveness (Sadick 2005). In Australia, claims for sclerotherapy under the MBS are limited to the treatment of veins 2.5 mm or greater in diameter. Treatment of smaller reticular veins and telangiectases with sclerotherapy is common, but not covered on the MBS. The number of sclerotherapy claims (MBS item numbers 32500 and 32501) has increased by almost 10,000 over the past 4 years, with more than 55,000 claims made in the year 2006–2007 (Medicare Australia 2007).

Phlebectomy

Ambulatory phlebectomy involves removing abnormal veins below the saphenofemoral and saphenopopliteal junctions, not including the GSV and SSV. This procedure is best used on larger veins that do not have reflux. Under local anaesthetic, small incisions are made in the skin and large surface varicosities are extracted using a phlebotomy hook. This outpatient procedure is generally well tolerated and complications are rare. However, recurrence rates can be high if the source of the reflux is not treated (Sadick 2005). In Australia, the number of phlebectomy claims (MBS item number 32504) has increased by more than 1,100 over the past 4 years, with more than 2,500 claims made in the year 2006–2007 (Medicare Australia 2007).

Junction ligation, with or without vein stripping

Junction ligation with or without vein stripping is generally appropriate when the GSV or SSV have reflux or incompetence demonstrated on duplex scanning, and in the majority of cases is performed as an inpatient procedure under general anaesthetic. Junction ligation involves tying off the vessel at either the saphenopopliteal or the saphenofemoral junction (Wolf and Brittenden 2001). Ligation alone is usually associated with a high varicose vein recurrence
rate, and patients may need further treatment with sclerotherapy (Bergan et al 2001). In most cases, ligation is accompanied by GSV stripping and is regarded by many as the treatment of choice for varicose veins (Wolf and Brittenden 2001). Stripping the GSV involves making incisions in the patient’s groin and knee or ankle. After ligation of the GSV and tributary veins, a stripper is inserted into the vein and passed, either down from the groin to the knee or up from the ankle to the groin. The end of the GSV is tied onto the stripper, which is gently withdrawn from the point of exit, thereby removing the vein (Lofgren 1985; Bergan et al 2002). Perforate invagination (PIN) is a modification of conventional stripping that reduces the tissue trauma associated with conventional stripping.

While results are generally longer lasting than other treatments, surgical treatment is usually a day-case or inpatient operation with general anaesthesia. Surgery involving ligation, with or without stripping, may cause complications such as tissue trauma and nerve damage, and often requires a period of recuperation (Michaels et al 2006). Stripping below the knee is generally discouraged because it increases the risk of nerve damage (Winterborn et al 2004). In Australia, the combined number of ligation/stripping claims (MBS item numbers 32508, 32511, 32514 and 32517) has decreased by just over 1,000 procedures in the past 4 years, with approximately 10,000 claims being made in the year 2006–2007 (Medicare Australia 2007).

**Treatments not currently listed on the MBS**

Two endovenous treatments for varicose veins not currently available through the MBS are endovenous laser therapy (ELT) and radiofrequency ablation (RFA). Both treatments involve inserting a heat-generating laser fibre or catheter into the incompetent saphenous vein, positioned just below the saphenofemoral or saphenopopliteal junction. Heat is generated through laser (ELT) or radiofrequency (RFA) energy and the fibre or catheter is slowly withdrawn down the length of the vein causing endothelial and vein wall damage, contraction of the vein wall and, ultimately, destruction of the vessel (Manfrini et al 2000; Diomed Ltd 2001; Navarro et al 2001; Sybrandy and Wittens 2002; Myers et al 2006). Although these treatments are not listed on the MBS, they are included in this rapid review because they are used widely in Australia.
Research questions

This rapid review addressed the following specific research questions:

- What is the evidence regarding the effectiveness of current medical treatment options (not including medicinal interventions) for varicose veins—including surgery (junction ligation with or without stripping), phlebectomy, sclerotherapy, ELT, RFA and conservative therapies (including the use of compression hosiery)—compared with each other?
- What is the evidence regarding the safety of current medical treatment options for varicose veins compared with each other?
Methodology

Inclusion criteria
Studies were selected for inclusion in this rapid review on the basis of the criteria outlined below.

Population
Studies of human patients having treatment for varicose veins of the legs, both superficial and complicated, were included.

Intervention
Included studies were related to the use of one or more of the interventions for the treatment of varicose veins listed in Table 4.

Table 4: Interventions for study inclusion

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Conditions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sclerotherapy</td>
<td>Performed on veins greater than 2.5 mm in diameter</td>
</tr>
<tr>
<td></td>
<td>Performed using continuous compression techniques</td>
</tr>
<tr>
<td></td>
<td>Performed independently of other varicose vein interventions (excluding after-care)</td>
</tr>
<tr>
<td>Phlebectomy</td>
<td>Performed on tributary veins (includes ligation of perforator veins)</td>
</tr>
<tr>
<td></td>
<td>Performed independently of varicose vein surgery</td>
</tr>
<tr>
<td>Surgery</td>
<td>Ligation with or without stripping of saphenous vein</td>
</tr>
<tr>
<td></td>
<td>May also include phlebectomy or sclerotherapy of tributary and perforator veins as part of the same procedure</td>
</tr>
<tr>
<td>Radiofrequency ablation</td>
<td>Performed on saphenous vein only</td>
</tr>
<tr>
<td>(RFA)</td>
<td></td>
</tr>
<tr>
<td>Endovenous laser therapy</td>
<td>Performed on saphenous vein only</td>
</tr>
<tr>
<td>(ELT)</td>
<td></td>
</tr>
<tr>
<td>Conservative therapy</td>
<td>May include use of compression hosiery</td>
</tr>
</tbody>
</table>

Comparator interventions
Studies were considered for inclusion if they compared at least one of the included interventions with another included treatment modality.

Outcomes
Studies were included if they contained information on at least one of the following outcomes:

Effectiveness

- abolition of venous reflux
- recurrence of varicose veins
- recanalisation
- reduction of symptoms
• quality of life
• time taken to resume normal activities
• operating time.

Safety
• mortality
• thromboembolism
• nerve damage and paraesthesia
• postoperative infection
• bleeding
• pain
• haematoma
• ecchymosis
• bruising.

Study design
Recently published, well-conducted systematic reviews, rather than primary studies were selected preferentially for including in the review and critical appraisal. Systematic reviews were defined as those studies that met all the following criteria as defined by Cook et al (1997):

1. Focused clinical question
2. Explicit search strategy
3. Use of explicit, reproducible and uniformly applied criteria for article selection
4. Critical appraisal of the included studies
5. Qualitative or quantitative data synthesis.

Where there were two or more systematic reviews with the same inclusion and exclusion criteria, the latest and most complete study was included.

If no suitable systematic reviews on the topic were available, RCTs and pseudorandomised controlled trials were considered eligible for inclusion and critical appraisal. A study was deemed to be an RCT if the author(s) stated explicitly (usually by some variant of the term ‘random’ to describe the allocation procedure used) that the groups compared in the trial were established by random allocation (Higgins and Green 2005). Studies in which the method of allocation was known but was not considered strictly random (for example, alternation, date of birth and medical record number) were classified as pseudorandomised controlled trials.
(Higgins and Green 2005). Where no randomised or pseudorandomised controlled trials were identified, nonrandomised comparative studies were also included in the review.

When overlapping patient groups were reported in studies, only the paper quoting the most complete data set was used.

**Publication date**
Following an initial scoping search, several high-quality and recently published systematic reviews were identified on the topic. On the suggestion of an advisory surgeon with relevant knowledge and expertise on the treatment of varicose veins, literature considered eligible for inclusion and critical appraisal was restricted to studies published from January 1988 onwards.

**Language of publication**
Included studies were restricted to those published in English.

**Exclusion criteria**
The following types of studies were excluded from this rapid review:
- cost-effectiveness, in-vitro or laboratory studies
- studies comparing technologies or techniques within a particular treatment modality, including surgical technique (for example, conventional or inversion stripping, use of tourniquet, ligation with and without stripping), sclerosant type (for example, liquid or foam) or concentration, endovenous laser therapy (ELT) laser wavelengths, or post-treatment therapy

**Literature search strategies**

**Databases searched**
The following databases were searched from January 1988 to 12 February 2008:
- BMJ Clinical Evidence
- The York (UK) Centre for Reviews and Dissemination (CRD)
- The Cochrane Library
- PubMed
- EMBASE.

The review did not include extended searching of internet websites and conference abstracts, handsearching of journals, contacting authors for unpublished data or pearling references from retrieved articles.
**Search terms**

Search terms used are listed below, while details of the full search strategy (based on a PubMed platform) are provided in Appendix A.

**BMJ Clinical Evidence**

Varicose veins

**York CRD and The Cochrane Library**


Text words: varicose near vein*, venous near (reflux or incomp* or insuff*), strip*, ligat*, phlebect*, sclerotherap*, laser*, radiofreq*

**PubMed and EMBASE**


Text words: varicose near vein*, venous near (reflux or incomp* or insuff*), strip*, ligat*, phlebect*, sclerotherap*, laser*, radiofreq

Note: * is a truncation character that retrieves all possible suffix variations of the root word; for example, surg* retrieves surgery, surgical, surgeon, etc. In databases accessed via the Ovid platform, the truncation character is $.

**Selection of studies**

The reviewer (BH) applied the inclusion criteria to identify those studies potentially eligible for selection and appraisal based on their abstracts; these studies were retrieved as full text. The selection criteria were then applied fully to the retrieved studies to identify those to be appraised and included in the review. Full publications subsequently found not to meet the inclusion criteria were excluded, and reasons for exclusion were documented.

**Data extraction and appraisal of study methodology**

Data from all included studies were extracted by one reviewer (DL) and checked by a second reviewer (BH) using standardised data extraction tables that were developed a priori. The studies included in the review were classified according to the National Health and Medical Research Council (NHMRC) hierarchy of evidence (NHMRC 2000) (Table 5).
Table 5: National Health and Medical Research Council hierarchy of evidence

<table>
<thead>
<tr>
<th>Level of evidence</th>
<th>Study design</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Evidence obtained from a systematic review of all relevant randomised controlled trials</td>
</tr>
<tr>
<td>II</td>
<td>Evidence obtained from at least one properly designed randomised controlled trial</td>
</tr>
<tr>
<td>III-1</td>
<td>Evidence obtained from well-designed pseudorandomised controlled trials (alternate allocation or some other method)</td>
</tr>
<tr>
<td>III-2</td>
<td>Evidence obtained from comparative studies (including systematic reviews of such studies) with concurrent controls and allocation not randomised, cohort studies, case–control studies, or interrupted time series with a control group</td>
</tr>
<tr>
<td>III-3</td>
<td>Evidence obtained from comparative studies with historical control, two or more single arm studies, or interrupted time series without a parallel control group</td>
</tr>
<tr>
<td>IV</td>
<td>Evidence obtained from case-series, either post-test or pre-test/post-test</td>
</tr>
</tbody>
</table>

Source: NHMRC 2000

Where systematic reviews were eligible for inclusion in the review, the methodology of these secondary studies was evaluated with respect to the following factors:

- Did the review ask a focused research question that incorporated the elements of the PICO?
- Were the inclusion and exclusion criteria of included studies clearly stated?
- Did the review use a clear and comprehensive search strategy?
- Did the review assess the validity of included studies, and if so which validity criteria were used?
- Was the analysis or synthesis of the results appropriate?
- Did the review include a summary of its main results, including a discussion of its strengths and limitations?

Where primary studies were eligible for inclusion in the review, the following criteria were used to appraise their methodology:

- Were the objectives of the study clearly defined?
- Were the inclusion and exclusion criteria clearly described?
- Was there a clear description of the interventions used?
- Were the characteristics of patients included in the study clearly described?
- Were patients randomly assigned to intervention groups, and if so was the method of randomisation described?
- Was the randomised assignment of patients to intervention groups concealed from both patients and staff administering the study until recruitment was complete?
- Was there an attempt made to blind both patients, and staff responsible for measuring outcomes of the intervention, to the interventions patients received?
• Were the number of patients who withdrew or dropped-out of the study reported, and the characteristics of these patients described?
• Were the main outcomes of interest adequately reported?
• Were point estimates and measures of variability presented for the primary outcome measures?

Non-randomised studies were also assessed for other features of study design or execution that may have introduced bias, such as comparability of patient groups at baseline, method of patient selection and comparability of timing of outcome assessment.

One reviewer (DL) appraised the studies, which were checked by the second reviewer (BH). Any differences were resolved through discussion.
Results

From the search strategy, 1860 potentially relevant articles were identified of which 54 (including one paper found separately through BMJ Clinical Evidence, and one independently found to be the primary report on which an identified paper was based) were retrieved. Retrieved papers included systematic reviews and primary studies. In total, 50 retrieved articles were excluded and these are listed in Appendix B.

As searches of relevant databases identified several recently published systematic reviews on the topic, literature considered eligible for critical appraisal was restricted to secondary studies. Four systematic reviews were considered eligible for appraisal and inclusion in this rapid review (Medical Services Advisory Committee 2003; Adi et al 2004; Rigby et al 2004; Jia et al 2006). A summary of included systematic reviews is shown in Table 6, and evidence tables of included papers are presented in Appendix C in date and then alphabetical order.

Systematic review evidence

Medical Services Advisory Committee (2003)

Appraisal of study methodology

The systematic review by the Medical Services Advisory Committee (2003) assessed the safety and effectiveness of ELT for treating varicose veins compared with vein stripping and junction ligation.

A comprehensive search was conducted in September 2003, involving searches of AustHealth, Australian Medical Index, Australian Public Affairs Information Service — Health, CINAHL, The Cochrane Library (including all incorporated databases), Current Contents, EMBASE, Pre-MEDLINE, MEDLINE, ProceedingsFirst, PsycInfo and the Web of Science — Science Citation Index Expanded. Three separate searches were carried out to identify ELT studies, stripping and/or junction ligation studies, and studies of the prevalence of varicose veins. An extensive list of search terms and the full search strategy were provided for each of these searches; no limitations were placed on publication date, while searches for stripping and/or junction ligation were limited to English-language studies. Relevant internet sites and citation lists were also searched to identify additional source material, and clinical expertise was sought where necessary. No handsearching of related journals or contact with authors was reported.
### Table 6: Summary of included systematic reviews

<table>
<thead>
<tr>
<th>Search details</th>
<th>Number and type of primary studies</th>
<th>Interventions (number of studies)</th>
<th>Number and type of patients</th>
<th>Outcome measures and follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medicare Services Advisory Committee (2003)</td>
<td></td>
<td></td>
<td></td>
<td>Outcomes measured: Effectiveness – abolition of reflux, re-treatment/recurrence, recanalisation/neovascularisation, reduction of symptoms, quality of life, time to resume normal activity, operating time Safety – infection, laser-related adverse events, thrombotic events, pain, bleeding complications, ecchymosis, paraesthesia, induration, phlebitis Follow-up: ELT 28 days to 36 months Surgery 1 week to 5 years</td>
</tr>
<tr>
<td><strong>Time span:</strong> 1966 to 2003</td>
<td>Level IV (n= 35)</td>
<td>ELT (17)</td>
<td>ELT Patients: n=1707 (range 20-423) Veins: n=2353 (range 20-504) Surgery Patients: n=317 (range 18-100) Veins: n=808 (range 13-100)</td>
<td>Varicose vein severity or type: Vein severity not reported; review criteria included patients with clinically documented primary venous reflux of the greater or lesser saphenous veins</td>
</tr>
<tr>
<td><strong>Limits:</strong> English language on searches for ligation/stripping studies</td>
<td></td>
<td>ELT</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>Ligation + stripping</strong> (10)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>Stripping</strong> (8)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>Surgery</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>Ligation + stripping</strong> (10)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>Stripping</strong> (8)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>Varicose vein severity or type:</strong> Vein severity not reported; review criteria included patients with clinically documented primary venous reflux of the greater or lesser saphenous veins</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>Outcomes measured:</strong> Effectiveness – abolition of reflux, re-treatment/recurrence, recanalisation/neovascularisation, reduction of symptoms, quality of life, time to resume normal activity, operating time Safety – infection, laser-related adverse events, thrombotic events, pain, bleeding complications, ecchymosis, paraesthesia, induration, phlebitis Follow-up: ELT 28 days to 36 months Surgery 1 week to 5 years</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>Follow-up:</strong> ELT 28 days to 36 months Surgery 1 week to 5 years</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adi et al (2004)</td>
<td>Level II (n = 2) Level IV (n= 17)</td>
<td>RFA (14)</td>
<td>RFA Patients: n=2082 (range 10-490) Limbs: n=2405 (range 18-450) Surgery Patients: n=53 (range 13-40)</td>
<td>Varicose vein severity or type: Vein severity not reported; review criteria included patients with complicated varicose veins (including venous incompetence, oedema, venous ulceration, varicose bleeding, changes in local skin colour, skin eczema and lipodermatosclerosis)</td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>RFA + phlebectomy or sclerotherapy</strong> (3)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>RFA + ligation + phlebectomy</strong> (2)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>Surgery</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>Ligation + stripping</strong> (1)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>Stripping</strong> (1)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>Varicose vein severity or type:</strong> Vein severity not reported; review criteria included patients with complicated varicose veins (including venous incompetence, oedema, venous ulceration, varicose bleeding, changes in local skin colour, skin eczema and lipodermatosclerosis)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>Outcomes measured:</strong> Effectiveness – quality of life, varicose vein or reflux recurrence, varicose vein re-operation, patient satisfaction, health care resource utilisation Safety – Pain, severe adverse events (e.g. mortality, deep vein thrombosis, pulmonary embolism) Follow-up: RFA versus surgery (Level II) 50 days to 4 months RFA (Level IV) 4.9 months to 3 years</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>Follow-up:</strong> RFA versus surgery (Level II) 50 days to 4 months RFA (Level IV) 4.9 months to 3 years</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Jia et al (2006)</td>
<td>Level II (n = 3) (n=1 of relevance to this review) Level IV (n= 64)</td>
<td>Sclerotherapy</td>
<td>Sclerotherapy Patients: n=9510 (range 1-808) Surgery Patients: n=309 Phlebectomy Patients: n=144</td>
<td>Varicose vein severity or type: From English language studies: ‘major’ vein incompetencies or varicosities n=4808; ‘minor’ vein venous disease n=443; both major and minor veins n=676; recurrent venous disease after treatment n=373; venous ulcers n=103; not reported n=453.</td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>Foam sclerosant</strong> (65)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>Liquid sclerosant</strong> (13)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>Surgery</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>Ligation</strong> (1)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>Phlebectomy</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>Avulsion</strong> (1)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>Varicose vein severity or type:</strong> From English language studies: ‘major’ vein incompetencies or varicosities n=4808; ‘minor’ vein venous disease n=443; both major and minor veins n=676; recurrent venous disease after treatment n=373; venous ulcers n=103; not reported n=453.</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>Outcomes measured:</strong> Effectiveness – Occlusion of veins, healing of venous ulcers, recurrence or development of new veins Safety – Anaphylaxis, arterial events, pulmonary embolism, deep vein thrombosis, necrosis, ulceration, intra-arterial injection, visual disturbance, transient confusion, headache, ‘minor’ vein thrombosis, thrombophlebitis, matting/skin staining/pigmentation, local neurological injury, pain at site of injection Follow-up: Sclerotherapy versus surgery versus phlebectomy (Level II) 10 years Sclerotherapy (Level IV) 20 days to 10 years</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>Follow-up:</strong> Sclerotherapy versus surgery versus phlebectomy (Level II) 10 years Sclerotherapy (Level IV) 20 days to 10 years</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Table 6 continued: Summary of included systematic reviews

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Time span:</strong> 1966 to 2004</td>
<td><strong>Level II (n = 9)</strong> (n=6 of relevance to this review)</td>
<td><strong>Sclerotherapy</strong></td>
<td><strong>Surgery</strong></td>
<td><strong>Phlebectomy</strong></td>
</tr>
<tr>
<td><strong>Limits:</strong> Methodological filters aimed at identifying guidelines, systematic reviews and clinical trials were applied in larger databases</td>
<td><strong>Foam sclerotherapy (1)</strong></td>
<td><strong>Ligation (2)</strong></td>
<td><strong>Patients: n=1134 (range 100-326)</strong></td>
<td></td>
</tr>
<tr>
<td></td>
<td><strong>Liquid sclerotherapy (6)</strong></td>
<td><strong>Ligation + stripping (5)</strong></td>
<td><strong>Patients: n=1138 (range 115-434)</strong></td>
<td></td>
</tr>
<tr>
<td></td>
<td><strong>Surgery</strong></td>
<td><strong>Avulsion (2)</strong></td>
<td><strong>Patients: n=144</strong></td>
<td></td>
</tr>
</tbody>
</table>

Varicose vein severity or type:
Vein severity not reported; review criteria included patients having treatment for primary varicose veins (including cosmesis and symptomatic veins). Trials including participants undergoing varicose vein re-treatment or treatment for complications of varicose veins, venous ulceration and chronic venous insufficiency excluded.

Outcomes measured:
Effectiveness – subjective improvement of symptoms or appearance, patient satisfaction, objective testing, quality of life
Safety – adverse events such as nerve damage, skin pigmentation, infection, haemorrhage, thrombophlebitis, deep venous thrombosis
Follow-up:
12 months to 10 years

ELT: endovenous laser therapy; RFA: radiofrequency ablation

Inclusion criteria limited the patient sample to adults (≥18 years of age) with clinically documented primary venous reflux of the GSV or SSV where sclerotherapy was unlikely to be successful. The endovenous laser assessed was the EVLT® laser treatment by Diomed, Inc. (Andover, MA, USA) (2001). For stripping and junction ligation studies, only RCTs and meta-analyses involving humans, and written in English, were suitable for including, due to the wealth of literature available. Outcomes of interest were not reported in the methodology, and no specific exclusion criteria for studies were described. Studies were retrieved and appraised for inclusion, and one reviewer extracted data using extraction tables developed a priori.

Seventeen studies, including eight abstracts from conference proceedings, met inclusion criteria for ELT, while the junction ligation and stripping arm of 18 RCTs were included. It should be noted here that two of these RCTs were also included in the systematic review by Adi et al (2004) for the assessment of surgery compared to RFA (Rautio et al 2002; Lurie et al 2003). Thorough critical appraisal methodology was used. Studies were assessed and classified using the dimensions of evidence defined by the National Health and Medical Research Council (NHMRC 2000), with expert clinical input where necessary. Included studies for ELT and stripping and ligation were appraised using a checklist developed by Young and colleagues (Young et al 1999) for case-series, because the literature for both treatments did not use controls. No literature directly compared ELT with other surgical treatments; Level IV (case-series) evidence only was available for assessing ELT. As a result, indirect comparisons of treatments were required and no meta-analysis could be performed.

**Safety**

Minor adverse events such as postoperative pain, ecchymosis, induration, bruising, haematoma and phlebitis were commonly associated with ELT. Ecchymosis was the most
common adverse event after ELT, reported in seven studies involving 662 limbs at a median rate of 100% (range: 23.0% to 100%). Induration was reported in five studies involving 300 limbs at a median rate of 100% (range: 34.1% to 100%), while bruising and haematoma were found in four studies involving 926 limbs at a median rate of 24.0% (range: 4.8% to 100%). The researchers noted these complications were usually self-limiting or required mild medication, and the vast majority resolved within a month of treatment. Some events persisted, with a small number of cases extending past six months duration; however it should be noted that almost all of these cases occurred in one study that surgically ligated the saphenous vein before performing ELT (Chang and Chua 2002).

Infection, bruising, haematoma and paraesthesia were commonly associated with surgical ligation and stripping of the saphenous vein. Paraesthesia, or damage to the saphenous nerve, was the most common and serious adverse event associated with ligation and stripping, and was reported in 10 studies involving 517 limbs at a median rate of 11.7% (range: 4.1% to 30.3%). Bruising and haematoma were reported in five studies involving 143 limbs at a median rate of 30.8% (range: 4.0% to 52.9%). A small number of adverse events persisted past four months, and some cases of paraesthesia were still present after 3 years of follow-up.

Serious adverse events were rare. After treatment with ELT, deep vein thrombosis was reported in one limb (one study of 41 limbs) and incorrect laser placement occurred in two patients (two studies of 61 limbs); after stripping and ligation, one study of 36 limbs reported two incidents of superficial venous thrombosis and another study of 74 limbs reported one patient who experienced a pulmonary embolism. While good-quality data were not available to assess the relative safety of the two procedures, the researchers concluded that the ELT procedure was relatively safe compared with conventional surgery of ligation and stripping.

**Effectiveness**

No studies were found that compared the effectiveness of ELT directly with vein stripping and/or junction ligation; this was further complicated by the fact that the main effectiveness outcome (abolition of reflux) was assessed differently between the two treatments. From the low-level evidence available, ELT appeared to be beneficial for most patients over the short term. ELT resulted in a median reflux abolition rate of 96.3% (range: 90% to 100%) across nine studies involving 750 limbs (follow-up ranged from 28 days to 17 months), while stripping and ligation resulted in a median reflux abolition rate of 87.1% (range: 57.1% to 100%) across four studies involving 166 limbs (follow-up ranged from 3 months to 5 years). Re-treatment and recurrence of varicose veins occurred at a higher rate for stripping and ligation (median occurrence rate of 21.6% [range: 15.7% to 33.3%] across six studies involving 344 limbs with follow-up of 21 months to 5 years) than ELT (median occurrence rate of 2.6% [range: 1.8% to 3.3%] across two studies involving 594 limbs with follow-up of 6 to 17 months). However, this measure of treatment effectiveness was highly biased as there was no clear distinction between true recurrent veins and residual incompetencies.

**Authors’ conclusions**

The authors concluded that ELT appears to be as safe as the current practice of vein stripping and/or junction ligation, and is effective for occluding the saphenous veins. It is unknown
how ELT compares with conventional stripping. Indirect comparisons made between ELT and stripping and junction ligation only provide a simple representation of their safety and effectiveness outcome rates, and should not be used to compare the effectiveness of the two procedures. The authors note that high-quality RCTs are needed before the two procedures can be compared.

Furthermore, MSAC (2003) recommended that public funding for ELT as a treatment of varicose veins should not be supported at that time, due to the lack of evidence on the relative effectiveness and cost-effectiveness of the procedure.


Appraisal of study methodology


A rigorous search of MEDLINE, EMBASE, CINAHL, the Cochrane Library, specialist economic databases, and registers of ongoing research took place in January 2004. Website searches of health technology assessment (HTA) agencies were also carried out. The full search strategy was provided for each database searched, with no limitation placed on publication date or language. Additional hand searches of citation lists and communication with the manufacturer of the RFA device (VNUS Medical Technologies Inc., San Jose, CA, USA) were carried out to obtain further studies. Two authors were contacted regarding ongoing trials.

Inclusion criteria incorporated RCTs, pseudorandomised clinical trials, observational comparative studies (including cohort studies) and case-series. The study population was patients with ‘complicated’ varicose veins. This included presence of venous incompetence or insufficiency as an aetiological mechanism, but also encompassed oedema, venous ulceration, varicosity bleeding, skin discolouration, eczema and lipodermatosclerosis. The intervention was RFA as a single or adjunctive therapy, with conventional surgical procedures as a comparator (including stripping and/or ligation). Outcomes of interest included quality of life, adverse events and varicose vein or reflux recurrence. Individual case reports, duplicate publications in editorials, animal studies, conference abstracts, patients with uncomplicated varicose veins and nonsurgical comparators (including sclerotherapy and compression therapy) were excluded. Data were extracted by one author and checked by a second using extraction forms created a priori.

Overall, 19 studies (two RCTs comparing RFA with stripping, with or without ligation, and 17 case-series) were included in the review. It should be noted here that the junction ligation and stripping arms of two included RCTs were also included in the systematic review from MSAC (2003) for the assessment of surgery compared to ELT (Rautio et al 2002; Lurie et al 2003). Study quality was assessed by the first author using predefined appraisal criteria. RCTs were assessed for quality (that is, randomisation method, allocation concealment, blinding outcome assessment, losses to follow-up) using the Jadad scale (Jadad et al 1998), while case-series were assessed for bias using an amended version of a checklist suggested by the
Cochrane Collaboration (Clarke and Oxman 2001). The RCT evidence was not of high quality, with short follow-up, no details of randomisation procedures, no blinding of assessors, and highly selective patient populations. Both RCTs recorded Jadad scores of less than 3. Meta-analyses were not performed due to data heterogeneity between studies. Case-series data was also poor, with only one study reported to have consecutive patients and only one being a prospective case series. None of the studies stated that a different assessor than the operating surgeon carried out assessment. Validity of measures was not discussed in any of the studies, and there was a large loss to follow-up in over half of the studies.

**Safety**

Regarding occurrence of adverse events, one RCT found no significant difference between treatments, while the second RCT found significantly fewer cases of ecchymosis, haematoma and tenderness for RFA compared with stripping with ligation at 72 hours after the procedure, and at 1- and 3-week follow-up.

Case-series reporting on the adverse events associated with RFA found serious adverse events were rare. Deep vein thrombosis occurred at a rate of 1% across three studies involving 694 patients, while pulmonary embolism occurred in 0.3% of patients in one study of 323 patients. Mild adverse events occurred at a rate of 1% to 15% for paraesthesia (across six studies involving 1153 patients), 1.4% to 4.2% for burns (across five studies involving 998 patients), and 2.0% to 6.7% for clinical thrombophlebitis (across four studies involving 1170 patients).

**Effectiveness**

Regarding clinical benefits, RCT evidence was statistically significant in favour of RFA over stripping, with or without ligation, for a number of outcomes. Improvement of post-procedural pain, quality of life in the first week following surgery, and days required to return to work and normal activity were each found to be significantly better among RFA patients. Neither RCT found a significant difference in absence of reflux at follow-up between RFA versus stripping (7-8 weeks post-treatment) and RFA versus stripping with ligation (4 months post-treatment). In the case-series, the proportion of patients reporting relief from pain after RFA ranged from 69% to 100% across six studies involving 1141 patients. The rate of varicose vein recurrence ranged from 0% to 27% across 10 studies involving 994 patients (follow-up ranged from 6 months to 2 years), while rate of reflux recurrence ranged from 0% to 27% across 17 studies involving 2022 patients (follow-up ranged from postoperatively to 2 years).

**Authors’ conclusions**

Adi et al (2004) concluded that evidence from two poor-quality RCTs suggested short-term benefits of RFA in terms of improvement in pain, quality of life and work stoppage compared with conventional surgery; however, the long-term clinical outcomes of RFA have not been well established by comparative studies. The long-term safety of RFA was supported by case-series evidence of up to 2 years’ follow-up; however, evidence from this type of study is prone to substantial bias. The authors also mention the potential for bias because RFA is not funded by the National Health Service (NHS); therefore, patients who choose to have the procedure...
were likely to be of a higher economic status, which may have explained their willingness to return to work. Further unbiased estimates of the relative long-term effects of RFA compared with conventional surgery are needed before sound conclusions can be made.

Jia et al (2006)

Appraisal of study methodology


A comprehensive search was conducted in May 2006 and encompassed searches of MEDLINE, EMBASE, MEDLINE In-Process, Biosis, Science Citation Index, ISI Proceedings, the Cochrane Controlled Trials Register, Conference Papers Index, ZETOC Conference, Database of Abstracts of Reviews of Effectiveness, HTA Database, National Research Register, Clinical Trials and Current Controlled Trials. Complete search strategies used for each major database were provided, with no limitation placed on publication date. Publication language was restricted to English, French, German, Italian, Spanish, Dutch and Portuguese. Relevant professional and commercial websites and citation lists of included studies were also searched. Additional studies were sourced through electronic and hand-searching of recent conference proceedings of prominent phlebology and vascular organisations. Hand-searching of the contents of two phlebology journals, known to be inadequately indexed by the major databases, was also done to ascertain if all relevant material had been procured. The only commercial manufacturer of foam sclerosant identified (Provensis) was contacted for additional data from two unpublished studies, and authors of included studies were contacted for clarification where necessary.

Included studies were either published or unpublished RCTs, nonrandomised comparative studies, case-series, case reports or population-based registry reports that prospectively collected audit data on foam sclerotherapy. The criteria restricted the patient sample to adults (≥ 16 years of age) undergoing foam sclerotherapy for the treatment of venous disease in the lower limbs. It should be noted here that sclerotherapy was performed on smaller veins and telangiectases in a number of studies; however, the majority of procedures were performed on larger tributaries and truncal (saphenous) veins. There were no inclusion restrictions for foam-producing technique, sclerosant type, strength or volume. For the comparative studies, there was no limitation on comparator treatment type. Outcomes of interest included adverse events (e.g. arterial events, thromboembolism, central nervous system disturbance or local effects) and effectiveness outcomes (e.g. occlusion of veins, varicose vein recurrence, quality of life). Studies were excluded if they were a duplicate of an earlier study or if patient(s) had cutaneous venous malformations. One reviewer searched the literature and assessed studies for full-text retrieval. Reports were assessed for inclusion by different reviewers, depending on the language of publication; uncertainty was resolved by a second reviewer where necessary. Two reviewers independently extracted data from English studies, one reviewer extracted from conference abstracts and two from German and French reports.

Overall, 67 studies were included in the review, which incorporated 10 RCTs and eight non-randomised comparative studies; of these, three RCTs compared surgery to sclerotherapy.
Only one RCT provided a suitable comparison between surgery (ligation without stripping) and sclerotherapy for inclusion in the current review (Belcaro et al 2003); it should be noted here that this RCT was also included in the systematic review of sclerotherapy versus surgery by Rigby et al (2004). The results of two RCTs were not included in the current review; the sclerotherapy arm of one RCT included surgery (ligation) as an adjunct to treatment (Bountouroglou et al 2006), while the surgical arm of one RCT treated patients with two separate interventions (ligation with stripping, phlebectomy) but did not present outcomes separately for each treatment (Wright et al 2006). The remainder of the included studies either compared variations in sclerotherapy treatment such as liquid versus foam sclerotherapy or concentration of sclerosant, or were sclerotherapy case series and case reports.

Two reviewers assessed the quality of included studies. RCTs were assessed using a checklist adapted from Verhagen et al (1998). Nonrandomised comparative studies and case-series were assessed with a checklist derived from the NHS Centre of Reviews and Dissemination (2001), Verhagen et al (1998), Downs and Black (1998), and the Generic Appraisal Tool for Epidemiology (Jackson et al 2006); however, evidence from non-English language studies and conference abstracts were not quality assessed. Meta-analyses were conducted where homogeneity was established between the studies; however, the results of these were not applicable to the current review.

**Safety**

A substantial amount of case series evidence on adverse events and safety was available for sclerotherapy. For ease of interpretation, the review authors did not include studies that did not report patient numbers in the calculation of medians and ranges; these studies were reported to have results similar to studies reporting patient-level data. Serious adverse events were uncommon among patients receiving sclerotherapy to treat varicose veins. One event of pulmonary embolism was reported among seven studies involving 2293 patients, one case of ulceration was reported in three studies involving 218 patients, and nine cases of necrosis were reported across 10 studies involving 1655 patients. Arterial events occurred after sclerotherapy at a median rate of 1.4% (range: 0% to 2.8%) across three studies involving 1061 patients. Deep vein thrombosis was reported in 22 studies involving 5193 patients at a median occurrence rate of 0.6% (range: 0% to 5.7%). Mild adverse events were generally uncommon, with the exception of matting, skin staining and pigmentation (median occurrence 15.8% [range: 0% to 66.7%] across 12 studies involving 1486 patients) and pain at the injection site (median occurrence 16.2% [range: 0.6% to 34.1%] across six studies involving 1025 patients). Other mild adverse events associated with sclerotherapy occurred at median rates of 5% or less.

**Effectiveness**

Clinical effectiveness was measured using occlusion rates in treated veins. Occlusion occurred at a median rate of 88% (range: 41.6% to 98.2%) after sclerotherapy (across 22 studies involving 4120 patients), compared with rates of 89.4% of 132 patients following ligation without stripping and 69.7% of 122 patients after avulsion phlebectomy. After sclerotherapy, healing of venous ulcers occurred at a median rate of 80.4% (range: 60.0% to 100%) across
four studies involving 256 patients, while recurrence or development of new varicose veins occurred at a median rate of 8.1% (range: 0.3% to 52.2%) across 11 studies involving 2099 patients. The one included RCT comparing sclerotherapy to surgery (also included in the review by Rigby et al (2004)) found foam sclerotherapy to have a significantly better rate of vein occlusion at 10-year follow-up than ambulatory phlebectomy, but also have a significantly higher rate of new varicose vein development compared to surgery (ligation without stripping).

**Authors’ conclusions**

Jia et al (2006) concluded that serious adverse events associated with foam sclerotherapy were rare and not significantly varied from liquid sclerotherapy or surgery involving ligation without stripping. Foam sclerotherapy was effective for occluding incompetent veins, both major and minor; however, its longer-term efficacy (in terms of recurrence or new varicosities) is uncertain. More high-quality RCTs are needed before meaningful comparisons can be made of the relative effectiveness of foam sclerotherapy and other minimally invasive treatments or surgery (including ligation, stripping and phlebectomy).


**Appraisal of study methodology**

The systematic review by Rigby et al (2004) assessed whether sclerotherapy or surgery should be recommended for the management of primary varicose veins.

The comprehensive search strategy included searches of AMED, Best Evidence, Biological Abstracts, the Cochrane Peripheral Vascular Diseases Review Group’s Specialised Register, the Cochrane Central Register of Controlled Trials, the Cochrane Database of Systematic Reviews, EMBASE, HIMC, MEDLINE, NHS Databases, PubMed and Science Citation Index. These searches were initially carried out in April 2000, and were rerun in October 2000, March 2001, November 2002 and June 2004. Full search strategies were described for the major databases used, with no limitation of publication date or language. In larger databases, searches were limited to guidelines, systematic reviews and clinical trials. In smaller databases, searches were not restricted by publication type or study design. Hand-searching of relevant journals, citation lists, public health websites (including HTA organisations and trial registers) were carried out and authors were contacted for additional information where trial data were missing.

Inclusion criteria restricted studies to prospective RCTs for the treatment of varicose veins, where any comparison was made between surgery and sclerotherapy. This included any combination of these techniques and new techniques. All patients with clinical and/or cosmetic symptoms of primary varicose veins were included. Outcomes of interest included improvement of symptoms, objective testing, quality of life and adverse events, both immediate and long-term. Studies were excluded if they treated patients with complicated varicosities, venous ulceration, chronic venous insufficiency and recurrent varicose veins. Two authors independently assessed studies for inclusion and exclusion based on explicit criteria. Discrepancies were clarified by a third author where necessary.
Nine RCTs were included in the review, of which six were of interest to the current review. The surgery arm of one RCT treated patients with two separate interventions (ligation with stripping, phlebectomy) but did not present outcomes separately for each treatment (Einarsson et al 1993). The sclerotherapy arm of one RCT included ligation as part of the procedure (Rutgers et al 1994). In one RCT sclerotherapy was not performed in line with MBS guidelines (Belcaro et al 2000). None of these three RCTs were included in the current review or used to compare the relative safety or effectiveness of sclerotherapy and surgery. It should be noted here that one RCT relevant to the current review was also included in the systematic review of foam sclerotherapy by Jia et al (2006).

Quality assessment of the studies was based on key determinants of trial quality identified by the NHS Centre for Reviews and Dissemination (2001) (that is, comparability of subgroups at baseline, analysis of results on intention to treat, completeness to follow-up, blinding, objectiveness of outcome assessment, and appropriateness and completeness of statistical analysis results), with a Jadad score (Jadad et al 1998) allocated to each study. Although the review aimed to assess the homogeneity of the studies and perform meta-analyses, this was not possible due to poorly-documented statistical results and adverse event rates.

**Safety**

Among studies that compared sclerotherapy to surgery, one RCT found no significant difference in complication rates between sclerotherapy and surgery (ligation with stripping), while another RCT found no significant difference in complication rates between sclerotherapy and surgery (ligation without stripping). After surgery that involved ligation with stripping, pulmonary embolism rates ranged from 0.48% to 0.62% across two studies involving 1171 patients (follow-up ranged from 1 to 3 years). One study of 688 patients (follow-up of 1 year) reported deep vein thrombosis at a rate of 0.96% and wound infection at a rate of 7.25%. The same study reported saphenous nerve injury in 10% of patients after stripping to the knee and an overall complication rate of 6.6% after sclerotherapy.

**Effectiveness**

Definitions of treatment failure differed across included studies, and included patients requiring further treatment, or the leg being cosmetically the same or worse than before treatment. Across all studies that compared sclerotherapy to surgery involving ligation with stripping, two RCTs reported sclerotherapy to be significantly better than surgery 1 year after treatment. However, the effectiveness of sclerotherapy rapidly declined so that by 2 years’ follow-up, there was no significant difference between treatments. At 3 years’ follow-up, one RCT reported that surgery was significantly better than sclerotherapy, while two other RCTs reported no significant difference in effectiveness at this point. By 5 years’ follow-up, two RCTs found that surgery had significantly better outcomes than sclerotherapy. One RCT found differences between sclerotherapy and surgery in rates of re-treatment increased with age, with sclerotherapy re-treatment rates significantly higher than surgery in patients 35 years and older. It also found in patients with ankle oedema and flares, need for re-treatment was significantly higher following sclerotherapy, regardless of age. One RCT found surgery
required significantly more time off work post-procedure. All studies concluded that the outcomes of sclerotherapy were worse than those of surgery (ligation with stripping).

In studies comparing sclerotherapy to surgery involving ligation without stripping, one RCT found both subjective and objective evaluations of surgery to be significantly better than sclerotherapy at 3-year follow-up. Another RCT (also included in the review by Jia et al (2006)) reported recurrence of varicose veins after 5 years varied from 34% for surgery to 48% for sclerotherapy, increasing to 38% and 56% respectively at 10 years; however, the significance of these results was not reported. This study also included a parallel group consisting of non-randomised participants, who underwent ligation with stripping, but no patient numbers or details on recruitment method were given; the study stated that the combined proportion of lost patients plus treatment failures in this parallel group was 54%, significantly higher than the 25% reported after sclerotherapy.

One RCT reporting on the treatment of lateral accessory veins found ambulatory phlebectomy to have lower vein recurrence rates than sclerotherapy at 1 and 2 years' follow-up; however, occurrence of teleangiectatic matting was significantly higher after phlebectomy at 2 years. This study concluded that phlebectomy was the treatment of choice for lateral accessory varicose veins. An RCT treating incompetent great saphenous veins (also included in the review by Jia et al (2006)) found varicose vein recurrence rate following stab avulsion was significantly higher than after surgery (ligation without stripping) or sclerotherapy after 10 years.

**Authors’ conclusions**

Rigby et al (2004) concluded that there was insufficient evidence to preferentially recommend the use of sclerotherapy or surgery. Until clearer evidence becomes available, it appears there is a place for both procedures in the management of varicose veins. There appears to be a trade-off between the costs and complications associated with either treatment, with sclerotherapy showing better early outcomes and less postoperative pain, but surgery showing better long-term results. The extent of a patient’s varicose veins governs the choice of intervention, with no single treatment universally used. The authors suggested that sclerotherapy may be best suited to patients with minor, superficial varicose veins not related to reflux in the saphenous system.
Summary of review findings

Overview
This rapid review identified four eligible secondary research publications, one published in 2003, two in 2004 and one in 2006. The methodological quality of these reviews was generally high, with all using comprehensive search strategies and appraisal methodology.

All four systematic reviews reported safety and effectiveness data on various varicose vein treatments. Reviews generally identified similar adverse events associated with varicose vein treatments, including infection, bleeding, bruising, ecchymosis, skin discolouration, thrombotic events and paraesthesia. The most commonly reported measures of effectiveness included abolition of reflux, recurrence of varicose veins, symptom reduction, quality of life and time required to return to work or normal activity.

Due to the lack of evidence comparing ELT with ligation and stripping, the MSAC (2003) review was used to make indirect comparisons, which significantly decreased the validity of its findings. Those reviews that used level IV evidence or poor-quality RCTs as the basis of their findings were less reliable, because these types of studies are generally prone to substantial bias (MSAC 2003; Adi et al 2004; Jia et al 2006).

Although it was the intention of many of the reviews to pool trial data to produce quantitative results, this was often not possible due to the heterogeneity of trials in each review. Only Jia et al (2006) found sufficient homogeneity for meta-analyses; however, the results of these were not applicable to the current review.

Sclerotherapy versus phlebectomy
One systematic review, reporting results from two RCTs, found no significant difference between sclerotherapy and phlebectomy in complication rates (Rigby et al 2004). The relative effectiveness of avulsion phlebectomy and sclerotherapy appeared to depend on the veins treated. The RCT examining treatment of lateral accessory varicose veins found varicose vein recurrence rates for phlebectomy to be significantly better than sclerotherapy at both 1- and 2-year follow-up. The second RCT reported on treatment of larger, main trunk (saphenous) varicose veins, and found stab avulsion phlebectomy to have a significantly higher rate of vein recurrence than sclerotherapy alone at 10-year follow-up.

Sclerotherapy versus surgery
Safety
Jia et al (2006) found side effects following foam sclerotherapy to be rare, with only skin matting, staining or pigmentation and localised pain at the injection site occurring at a median rate of greater than 5% of patients. Few direct comparisons were made between sclerotherapy and surgery (ligation with or without stripping); the one study that did make such a comparison found no significant difference in the occurrence of adverse events between sclerotherapy and surgery (ligation with stripping), reported in Rigby et al (2004).
Effectiveness

Sclerotherapy generally entailed higher rates of varicose vein recurrence and re-treatment than surgical interventions (Rigby et al 2004; Jia et al 2006). The review by Jia et al (2006) reported on one RCT with long-term (10 years) follow-up that found foam sclerotherapy had significantly higher rates of recurrence of new veins compared with surgery (ligation without stripping). The authors concluded foam sclerotherapy appears efficacious in treating all types of superficial venous disease, despite insufficient evidence to reliably compare the relative effectiveness of sclerotherapy and surgery (ligation with or without stripping).

The review by Rigby et al (2004) cast doubts over the durability of sclerotherapy as a treatment for varicose veins compared to surgery (ligation with or without stripping). Sclerotherapy showed superior short-term clinical and cosmetic results ($\leq 12$ months), but this effectiveness declined rapidly; surgery (ligation with or without stripping) was consistently found to be more durable and require fewer re-treatments over the long-term ($\geq 2$ years). One RCT also found differences in re-treatment rates between the interventions increased with patient age. Where reported, patients who underwent sclerotherapy required significantly less time on average to return to work than those who underwent conventional surgery (ligation with stripping). The authors concluded that it appears there is a place for both procedures in the management of varicose veins, with a trade-off between initial results and long-term benefits. The authors suggested that on the basis of the evidence available, the extent of a patient’s varicose veins should govern the choice of intervention; sclerotherapy may be best suited to patients with minor, superficial varicose veins not related to reflux in the saphenous system.

Surgery versus endovenous laser therapy

As there was no available literature directly comparing ELT to surgery, the review by MSAC (2003) was forced to make indirect comparisons, which provide a simple presentation of the safety and effectiveness profile of ELT but may be misleading and are prone to bias.

Safety

The review by MSAC (2003) found that common adverse events after ELT included pain, ecchymosis, induration and phlebitis. The majority of events were mild and self-limiting, generally resolving within a month of treatment; in a small number of cases adverse events persisted past 6 months, but this primarily occurred when surgical ligation of the saphenous vein was performed before ELT. Serious adverse events after ELT were rare. Common adverse events after surgery (ligation with stripping) included paraesthesia, infection, bruising and haematoma, with more serious thrombotic events uncommon. The majority of events resolved soon after treatment; in a small number of cases adverse events had not resolved within 4 months, and some cases of paraesthesia persisted for over 3 years. The authors concluded that ELT was as safe as surgery (ligation and stripping).

Effectiveness

The review by MSAC (2003) summarised studies that suggested superior rates of reflux abolition, recurrence, re-treatment and recanalisation/neovascularisation after ELT than
surgery (ligation and stripping); however, this could not be confirmed due to a lack of direct comparative evidence, differences in the way reflux is assessed after the two interventions and the fact that the majority of ELT studies provided short-term follow-up ($\leq 6$ months) data on the treated limbs. Regarding improvement of varicose vein symptoms, the review reported clinically relevant reductions in symptoms such as pain and oedema after ELT, and reductions in symptoms as measured on venous severity scoring scales after surgery (ligation with stripping). The review reported no work stoppage amongst a large cohort of its patient sample following ELT, whereas a considerable number of days to return to normal activities and work were generally required after surgery (ligation with stripping). The authors concluded that from the available literature, ELT appears to be effective in occluding the saphenous vein in the short-term ($\leq 6$ months); however, it could not be determined whether ELT was as effective, or more effective, as surgery (ligation with stripping).

**Surgery versus radiofrequency ablation**

**Safety**

One review reported on adverse events in studies comparing surgery to RFA (Adi et al 2004). Serious adverse events associated with RFA were rare. Adi et al (2004) included one RCT that reported no significant difference in occurrence of adverse events between treatments, while a second RCT found significantly fewer cases of ecchymosis, haematoma and tenderness for RFA compared to surgery (ligation with stripping) up to 3 weeks after treatment. The long-term safety of RFA was supported by case-series evidence of up to 2 years’ follow-up; however, evidence from this type of study is prone to substantial bias.

**Effectiveness**

Adi et al (2004) included two RCTs that reported no significant difference in the reflux free status of patients following RFA and vein stripping with and without ligation. Some short-term benefits were seen for RFA, with RCT evidence significantly favouring RFA over saphenous stripping, with or without ligation, with regards to post-procedural pain and analgesic usage ($\leq 2$ weeks), quality of life ($\leq 1$ week), and days required to return to work and normal activity. The authors concluded that long-term clinical outcomes of RFA had not been well established by comparative studies.
Conclusions

Four reviews, all published between 2003 and 2006, were identified as eligible for inclusion in this rapid review. All were systematic reviews of the existing literature regarding various treatments for varicose veins. One review compared ELT with surgery (MSAC 2003), one compared RFA with surgery (Adi et al 2004), one compared sclerotherapy with surgery (Rigby et al 2004) and one focused on foam sclerotherapy (Jia et al 2006). Conclusions based on the results of the review are summarised below:

1. Ligation with stripping plus avulsion is generally regarded as the ‘gold standard’ treatment for primary long saphenous veins, with good long-term effectiveness ($\geq$ 12 months) at the cost of short-term inconvenience and discomfort compared to less invasive procedures.

2. Compression stockings are often used as a first-line treatment for varicose veins; however, no evidence was found to support the effectiveness of this.

3. There appears to be a place for both surgery and sclerotherapy in the management of varicose veins. There also appears to be a trade-off between initial results and long-term benefits, with sclerotherapy showing better immediate and early outcomes, but surgery producing more durable long-term outcomes ($\geq$ 12 months).

4. There is little evidence for the use of sclerotherapy to treat symptomatic varicose veins in patients with demonstrated saphenous reflux. Sclerotherapy and phlebectomy may be best suited to patients with minor superficial varicose veins not related to reflux in the saphenous system, or as a post-treatment or adjunctive procedure to other treatments.

5. ELT appears to be as safe as conventional surgery with junction ligation and vein stripping, and is effective for occluding saphenous veins in the short-term ($\leq$ 6 months); however, it is unclear how ELT compares with other interventions, especially the ‘gold standard’ of surgery (ligation with stripping).

6. Evidence suggests some potential quality of life benefits for patients undergoing RFA compared with surgery (vein stripping with or without junction ligation) in the immediate postoperative period ($\leq$ 2 weeks); however, there is not enough evidence to assess long-term effectiveness. Data suggests short-term safety ($\leq$ 3 weeks) of RFA is comparable to conventional surgery, with case-series evidence tentatively supporting its long-term safety ($\leq$ 2 years).

A lack of high-quality comparative evidence means it is difficult to make meaningful judgments regarding the relative safety and effectiveness of treatments for varicose veins. It is also unclear from the evidence retrieved whether some treatments are more or less effective in particular patient subgroups, dependent on the aetiology of the varicose veins. High-quality comparative studies (such as well-designed RCTs) are needed before newer varicose vein treatments and surgery (ligation plus stripping) can be definitively compared. The extent of varicose veins should govern the intervention of choice, with no single treatment universally employed.
Acknowledgements

The authors wish to acknowledge Dr Ann Scott for her assistance during the preparation of this review.
References


REFERENCES


Appendix A: Search strategy

#1  Search venous insufficiency Field: MeSH Terms [no explode]
#2  Search varicose veins Field: MeSH Terms [no explode]
#3  Search #1 OR #2
#4  Search varicose near vein* Field: Text Word
#5  Search venous near (reflux or incomp* or insuff*) Field: Text Word
#6  Search #4 OR #5
#7  Search #3 OR #6
#8  Search vascular surgical procedures Field: MeSH Terms [no explode]
#9  Search ligation Field: MeSH Terms [no explode]
#10 Search sclerotherapy Field: MeSH Terms [no explode]
#11 Search laser surgery Field: MeSH Terms [no explode]
#12 Search catheter ablation Field: MeSH Terms [no explode]
#13 Search #8 OR #9 OR #10 OR #11 OR #12
#14 Search strip* Field: Text Word
#15 Search ligat* Field: Text Word
#16 Search phlebect* Field: Text Word
#17 Search sclerothreap* Field: Text Word
#18 Search laser* Field: Text Word
#19 Search radiofreq* Field: Text Word
#20 Search #14 OR #15 OR #16 OR #17 OR #18 OR #19
#21 Search #13 OR #20
#22 Search #7 AND #21 Limits: Human, English language, Published 1988 onwards
Appendix B: Excluded studies

Duplication of results reported in included reviews


Non-systematic reviews


**Primary studies**


**Ineligible comparator procedures**


**Non-randomised comparative studies**


**Not published in English**


Appendix C: Evidence tables

Table C1: Evidence table of appraised secondary studies relating to varicose veins treatment methods

<table>
<thead>
<tr>
<th>Review details</th>
<th>Aim and search method</th>
<th>Study design and inclusion/ exclusion criteria</th>
<th>Results and author(s) conclusions</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medical Services Advisory Committee (MSAC), 2003</td>
<td>Aim: To systematically review the safety, effectiveness and cost-effectiveness of Endovenous Laser Treatment (EVLT™) for varicose veins.</td>
<td>Exclusion criteria: Studies were to treat adult patients (&gt;18 years) with clinically documented primary venous reflux of great or small saphenous veins where sclerotherapy was not likely to be beneficial. Treatment to be endovenous laser treatment (as described by Diomed Ltd (2001)) or surgical stripping and/or ligation. Human studies only. For studies of stripping and/or ligation: stripping and/or junction ligation arm of meta-analysis of RCT evidence or RCTs only.</td>
<td>17 studies included for ELT (nine case-series, eight case-series in abstract form); 18 studies included for conventional stripping and/or junction ligation (all RCTs).</td>
<td>Extensive search strategy</td>
</tr>
<tr>
<td></td>
<td>Search period: 1966 to Sept 2003.</td>
<td></td>
<td>Safety: Studies; n/N median occurrence rate (%) (range)</td>
<td>Extensive inclusion criteria</td>
</tr>
<tr>
<td></td>
<td>Databases searched: AustHealth, Australian Medical Index, Australian Public Affairs Information Service — Health, CINAHL, Cochrane Library (including: Cochrane Database of Systematic Reviews, Database of Abstracts of Reviews of Effects, the Cochrane Central Register of Controlled Trials (CENTRAL), the Health Technology Assessment Database, the NHS Economic Evaluation Database); Current Contents, Embase, Pre-MEDLINE, MEDLINE, ProceedingsFirstSearch, PsycInfo, Web of Science — Science Citation Index Expanded.</td>
<td></td>
<td>▪ Infection — Stripping/ligation: Seven studies; 18/335; 5.4 (2.0–8.0)</td>
<td>No exclusion criteria provided</td>
</tr>
<tr>
<td></td>
<td>Full list of terms provided (based on PubMed platform).</td>
<td></td>
<td>▪ Laser-related adverse events (including burns, incorrect placement) — ELT: Three studies; 14/313; 4.8 (3.0–5.0)</td>
<td>No date restrictions</td>
</tr>
<tr>
<td></td>
<td>Restricted to English only for stripping/junction ligation searches. No language restriction on ELT searches.</td>
<td></td>
<td>▪ Thrombotic events — ELT: One study; 1/41; 2.4; Stripping/ligation: One study; 2/36; 5.6</td>
<td>No language restriction (excluding stripping studies due to quantity)</td>
</tr>
<tr>
<td></td>
<td>Additional information: Search of relevant internet databases and health technology agency websites. All reference lists of included studies were searched for additional source material. Clinical expertise was sought where necessary.</td>
<td></td>
<td>▪ One stripping/ligation study (74 limbs) reported one patient suffered a pulmonary embolism</td>
<td>Handsearching of reference lists of all included studies</td>
</tr>
<tr>
<td></td>
<td>Evidence assessed for quality and classified using NHMRC dimensions of evidence and a previously developed checklist.</td>
<td></td>
<td>▪ One stripping/ligation study (14 patients) reported one patient suffering bleeding from wound in groin at six weeks.</td>
<td>No hand searches of relevant journals</td>
</tr>
<tr>
<td></td>
<td>Operation time — Two ELT studies reported mean operation times of 122 (ELT combined with ligation) and 60 minutes. Four stripping/ligation studies reported operating times between a median of 25 minutes and a mean of 89 minutes.</td>
<td></td>
<td>▪ Infection — Stripping/ligation study (37 limbs) reported two cases of cellulitis (5.4%)</td>
<td>Consultation of relevant online health services</td>
</tr>
<tr>
<td></td>
<td>Conclusion: As there was no available literature directly comparing ELT with other surgical procedures, indirect comparisons were made, which provides a simple presentation of the safety and effectiveness profile of ELT; however, comparison results may be misleading. From the literature, ELT is as safe as conventional stripping and is effective in occluding the saphenous vein; however it is unknown whether ELT is as effective as or more effective than conventional stripping.</td>
<td></td>
<td>▪ Hyperpigmentation — ELT: Three studies; 4/373; 1.1 (0.8–3.8)</td>
<td>Data extraction and appraisal methodology described</td>
</tr>
<tr>
<td></td>
<td>▪ Pain/tightness — ELT: Six studies; 590/744; 91.0 (6.0–100); Stripping/ligation: Two studies; 24/136; 20.9 (14.0–27.8)</td>
<td></td>
<td>▪ Erythema — Stripping/ligation: One study; 3/36; 8.3</td>
<td>One reviewer responsible for data extractions</td>
</tr>
<tr>
<td></td>
<td>▪ Phlebitis — ELT: Seven studies; 37/1187; 3.2 (1.0–7.7)</td>
<td></td>
<td>▪ Paraesthesia — ELT: Four studies; 98/472; 5.5 (1.1–36.5); Stripping/ligation: 10 studies; 76/517; 11.7 (4.1–30.3)</td>
<td>Data extraction tables created a priori</td>
</tr>
<tr>
<td></td>
<td>▪ Quality of life (QoL) — Three stripping/ligation studies reported on QoL; all three reported a worsening of QoL shortly after treatment; however, two studies reported QoL had improved to pretreatment levels or better at later follow-up.</td>
<td></td>
<td>▪ Recanalisation/neovascularisation — ELT: Four studies; 64/69; 0 (0–4.8); stripping/ligation: One study; 2/28; 40.6</td>
<td>Extensive description of included studies</td>
</tr>
<tr>
<td></td>
<td>▪ Time taken to return to normal activities — One ELT study reported no work stoppage required for the 14 treated patients with occupational activities. One stripping/ligation study reported a mean of 3.89 days was required to resume normal activities, while four stripping/ligation studies reported that between a median of seven days and a mean of 20 days were required to return to work.</td>
<td></td>
<td>▪ Reduction of symptoms — One ELT study found increased number of patients with no symptoms for oedema, pain or pruritus and ≥20% decrease in number of patients with severe symptoms. Another study reported a statistically significant improvement in CEAP score after ELT (P&lt;0.05). One stripping study used three adaptations of CEAP scoring system, and found an improvement in all three scores after treatment.</td>
<td>Explanation for excluded studies</td>
</tr>
<tr>
<td></td>
<td>▪ Operation time — Two ELT studies reported mean operation times of 122 (ELT combined with ligation) and 60 minutes. Four stripping/ligation studies reported operating times between a median of 25 minutes and a mean of 89 minutes.</td>
<td></td>
<td>▪ Quality of life (QoL) — Three stripping/ligation studies reported on QoL; all three reported a worsening of QoL shortly after treatment; however, two studies reported QoL had improved to pretreatment levels or better at later follow-up.</td>
<td>Extensive background</td>
</tr>
<tr>
<td></td>
<td>▪ Extensive background</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>▪ Search terms clearly provided</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>▪ Clinical decision pathway for EVLT for varicose veins</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>▪ Extensive tabular data, including result summaries and profiles of included studies</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>▪ Clinical expertise sort where necessary</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>▪ Noted that results liable to bias and may be misleading due to indirect comparisons</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>▪ Possible duplications of results in numerous cases</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Table C1 continued: Evidence table of appraised secondary studies relating to varicose veins treatment methods

<table>
<thead>
<tr>
<th>Review details</th>
<th>Aim and search method</th>
<th>Study design and inclusion/ exclusion criteria</th>
<th>Results and author(s) conclusions</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adi Y, Bayliss S &amp; Taylor R, 2004</td>
<td>Extensive search strategy</td>
<td>No language restrictions</td>
<td>No handsearching</td>
<td>Extensive search strategy</td>
</tr>
<tr>
<td></td>
<td>No handsearching of 19 studies included: two RCTs and 17 case-series</td>
<td>Relevant journals</td>
<td>Handsearching of reference lists of included studies</td>
<td>No handsearching of relevant journals</td>
</tr>
<tr>
<td></td>
<td>Post-treatment pain (as reported on visual analogue scale) significantly lower for RFA at rest (P=0.017), standing (P=0.026) and walking (P=0.036).</td>
<td>Significantly less analgesics required by RFA group (P=0.004).</td>
<td>Authors contacted where necessary</td>
<td>No handsearching of relevant journals</td>
</tr>
<tr>
<td></td>
<td>RCT evidence: RFA versus conventional stripping</td>
<td>No significant difference in freedom from reflux at follow-up; RFA (100%), stripping (92%).</td>
<td>Website searches of relevant healthcare agencies</td>
<td>Handsearching of reference lists of included studies</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Significantly fewer sick days needed following RFA: 6.5 days versus 15.6 days (P&lt;0.001).</td>
<td>Manufacturer of RFA device contacted for further studies</td>
<td>No handsearching of relevant journals</td>
</tr>
<tr>
<td></td>
<td></td>
<td>RFA versus stripping + ligation</td>
<td>Significantly more stripping patients were not satisfied with their cosmetic outcome (31% not satisfied) compared with RFA patients (7% not satisfied).</td>
<td>Extensive inclusion/exclusion criteria described</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>No significant difference in occurrence of adverse events (RFA versus stripping); paraesthesia (13% versus 23%), thrombophlebitis (20% versus 0%), haematoma (7% versus 31%), skin injury (7% versus 0%).</td>
<td>Search terms specified for each database</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Few complications; annoying rather than serious.</td>
<td>Search strategy carried out by two authors independently</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Data extraction and appraisal methodology described</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Extensive background, including prevalence, risk factors, etc.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Total number of included/excluded studies specified and described in flow diagram (with reasons for exclusions)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Description of included and excluded studies</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Meta-analysis not done due to clinical heterogeneity</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Extensive tabular data, including exclusion tables</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Studies susceptible to bias, thus review provides low-quality evidence</td>
</tr>
</tbody>
</table>

### Study C1

**Aim:** To systematically review the clinical effectiveness and the cost-effectiveness of studies of radiofrequency ablation (RFA) for treating varicose veins.

**Review question:** In patients with varicose veins, does RFA compared with conventional surgical methods improve outcomes or cost effectiveness?

**Search period:** 1996 to 2004.

**Databases searched:** MEDLINE, EMBASE, CINAHL, Cochrane Library (Issue 3, 2004); specialist economic databases (for example, NHS Centre for Reviews and Dissemination Economic Evaluation Database — NHS EED and Office of Health Economics, Economic Evaluations Database — HEED); registers of ongoing research (for example, National Research Register, metaRegister of Controlled Trials, MRC Clinical Trials Register, and ClinicalTrials.gov); and websites of health technology assessment agencies (HSTAT, DIHTA, SINTEF, AETMIS, NZHTA, CCQHTA, INAHTA, York CRD, NICE, NCCHTA, Alberta Heritage Foundation).

**Full list of search terms provided for each database.**

**No language restrictions on search.**

**Additional information:** Handsearching of reference lists of included studies, manufacturer of RFA device (VNUS Medical Technology) contacted for further studies and two authors contacted for further information regarding their ongoing trials.

**Inclusion criteria:** Studies were to treat patients with complicated varicose veins (complications included venous incompetence, oedema, venous ulceration, varicose bleeding, skin discoloration, eczema and lipodermatosclerosis) and perform RFA as a single or combined therapy with conventional surgical therapies (including stripping and/or ligation) as a comparator. Study design included RCTs, pseudorandomised clinical trials, observational comparative studies (including cohort studies) and case-series.

**Exclusion criteria:** Individual case reports, duplicate publications in editorials, and animal studies. Studies treating patients with uncomplicated varicose veins, using nonsurgical comparators (for example, drugs, sclerotherapy, compression), or reporting no clinical outcomes.

**Study selection and appraisal methods:** Data were extracted by one reviewer and checked by another using proforma created a priori. Inclusion/exclusion criteria carried out by two reviewers. Study characteristics and methodological quality assessed by first reviewer; controlled studies using the Jadad scale, and case-series using a Cochrane Collaboration checklist.

**Results:** 19 studies included: two RCTs and 17 case-series.

**RCT evidence:**

- Post-treatment pain (as reported on visual analogue scale) significantly lower for RFA at rest (P=0.017), standing (P=0.026) and walking (P=0.036).
- Significantly less analgesics required by RFA group (P=0.004).
- No significant difference in freedom from reflux at follow-up; RFA (100%), stripping (92%).
- Significantly fewer sick days needed following RFA: 6.5 days versus 15.6 days (P<0.001).
- Significantly more stripping patients were not satisfied with their cosmetic outcome (31% not satisfied) compared with RFA patients (7% not satisfied).
- No significant difference in occurrence of adverse events (RFA versus stripping); paraesthesia (13% versus 23%), thrombophlebitis (20% versus 0%), haematoma (7% versus 31%), skin injury (7% versus 0%).
- Few complications; annoying rather than serious.

**RFA versus stripping + ligation**

- Postoperative pain significantly lower for RFA at 72 hours (P<0.0001) and one week (P<0.0001).
- No significant difference in freedom from reflux at follow-up; RFA (95%), stripping + ligation (100%).
- Significantly fewer sick days needed following RFA: 4.7 days versus 12.4 days (P<0.01).
- Significantly less ecchymosis, haematoma and tenderness after RFA at 72 hours, one and three weeks (tenderness at 72 hours only).

**Case-series evidence after RFA:**

- Pain: Proportion of patients reporting relief from pain ranged from 69% to 100% across six studies.
- Recurrence/recanalisation: Varicose vein recurrence/recanalisation rate ranged from 0% to 27% across 10 studies (follow-up six months to two years).
- Reflux recurrence: Reflux recurrence ranged from 0% to 27% across 17 studies (follow-up immediately postoperative to two years).
- Satisfaction: Proportion of patients who would recommend the procedure to a friend ranged from 94% to 100% across five studies.
- Occurrence rates of mild adverse events: Paraesthesia (1% to 15% across six studies), burns (1.4% to 4.2% across five studies) and clinical thrombophlebitis (2.0% to 6.7% across four studies).
- Occurrence rates of severe adverse events: Deep vein thrombosis (1% across three studies) and pulmonary embolism (0.3% in one study).

**Conclusions:** Evidence from two poor-quality RCTs suggests short-term benefit in terms of improvement in pain and quality of life, and shorter sick leave relative to conventional surgery. Long-term outcomes of RFA have not been well established by comparative studies. Long-term safety of RFA supported by evidence from noncomparative studies (up to two years follow-up) prone to substantial attrition bias. There is a potential for bias as RFA not covered by NHS; therefore people opting for the treatment were likely to be of a higher economic status, which could explain their willingness to return to work quickly following treatment.
### Table C1 continued: Evidence table of appraised secondary studies relating to varicose veins treatment methods

<table>
<thead>
<tr>
<th>Review details</th>
<th>Aim and search method</th>
<th>Study design and inclusion/ exclusion criteria</th>
<th>Results and author(s) conclusions</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Jia X, Mowatt G, Ho V, Cook J, Fraser C &amp; Burr J, 2006</td>
<td>Aim: To systematically review the evidence for the safety and efficacy of foam sclerotherapy for venous disease of the lower limbs.</td>
<td>Inclusion criteria: Studies with adults (≥16 years) undergoing foam sclerotherapy for the treatment of venous disease in the lower limbs; no restrictions on foam-producing technique, type, strength or volume of sclerosant or comparator. Published/unpublished RCTs, nonrandomised comparative studies, case-series, case reports, and population-based registry reports that prospectively collect audit data on foam sclerotherapy.</td>
<td>67 studies (104 papers) included: nine RCTs, one registry, eight nonrandomised comparative studies, 43 case-series, six case reports. Note: Sclerotherapy arm of RCT by Bountouroglou et al (2006) included ligation. ‘Surgery’ arm of RCT by Wright et al (2006) did not stratify outcomes for ligation/stripping and phlebectomy patients. These RCTs were not included within the current review.</td>
<td>Extensive search strategy</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Exclusion criteria: Earlier reports with data duplicated in newer studies, and studies reporting treatment of cutaneous venous malformations.</td>
<td>Safety (combined results of foam and liquid sclerotherapy):</td>
<td>Moderate inclusion/exclusion criteria</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Study selection and appraisal methods: One reviewer screened retrieved abstracts for full-text retrieval. One reviewer assessed English, Italian and Dutch reports for inclusion, two reviewers French and German, and one reviewer Portuguese. Uncertainty was resolved through a second reviewer. Two reviewers independently extracted study data from English studies, one reviewer conference abstracts, and two reviewers German and French reports. Two reviewers independently assessed study quality using one of two separate checklists. Disagreement resolved by consensus or a third party.</td>
<td>Serious adverse events: Studies; n/N Median occurrence rate (%) (range)</td>
<td>No data restrictions</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Anaphylaxis: Two studies; 0/823; 0 (0–0)</td>
<td>No language restrictions</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Arterial events (e.g. stroke, cerebrovascular accident, myocardial infarction): Three studies; 6/1061; 1.4 (0–2.8)</td>
<td>Handsearching of relevant journals and conference proceedings</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Pulmonary embolism: Seven studies; 1/2293; 0 (0–0.3)</td>
<td>Double checked (handsearching) contents table of two journals known to be inadequately indexed by major databases</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Deep vein thrombosis: 22 studies; 28/5193; 0.6 (0–5.7)</td>
<td>Searched reference lists of included studies for further relevant trials</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Necrosis: 10 studies; 9/1655; 0.1 (0–2.6)</td>
<td>Searched relevant professional and commercial websites</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Ulceration: Three studies; 1/218; 0 (0–3.6)</td>
<td>Foam sclerosant manufacturers contacted</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Intra-arterial injection: One study; 0/108; 0</td>
<td>Authors contacted</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Adverse events: Studies; n/N Median occurrence rate (%) (range)</td>
<td>Two reviewers independently assessed retrieved studies, disagreements arbitrated by third reviewer</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Visual disturbance: 14 studies; 38/3953; 1.1 (0–2.6)</td>
<td>Data extraction and appraisal methodology extensively described</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Transient confusion: Four studies; 4/611; 0.5 (0–1.2)</td>
<td>Screening process (re: number of studies) well described in flow diagram</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Headache: Two studies; 16/632; 2.4 (0.7–4.1)</td>
<td>Search terms described for each database</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Other systemic symptoms (e.g. coughing, chest tightness/heaviness, panic attack): Six studies; 12/1091; 0.5 (0–2.8)</td>
<td>Description of included/excluded studies</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Local effect: ‘minor’ vein thrombosis: Seven studies; 38/1862; 1.2 (0–15.0)</td>
<td>Brief background</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Local effect: thrombophlebitis: 19 studies; 157/2195; 5.0 (0–45.8)</td>
<td>Meta-analyses performed, but invalid for inclusion in current review</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Local effect: matting/skin staining/pigmentation: 12 studies; 147/1486; 15.8 (0–66.7)</td>
<td>Extensive tabular data</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Local neurological injury: Six studies; 2/2040; 0 (0–0.7)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Pain at the site of injection: Six studies; 154/1025; 15.6 (0.6–34.1)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Other adverse events (e.g. local allergic reaction, haematoma, extravasations): Five studies; 4/1008; 0.5 (0–1.1)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Effectiveness (combined results of foam and liquid sclerotherapy): Studies; n/N Median occurrence rate (%) (range)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Complete occlusion of veins: 22 studies; 3538/4120; 88.0 (41.6–98.2)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• After surgery (ligation without stripping): One study; 118/132; 89.4</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• After avulsion phlebectomy: One study; 85/122; 69.7</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Healing of venous ulcers: Four studies; 205/256; 80.4 (40.0–100.0)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Recurrence or development of new veins: 11 studies; 289/2099; 8.1 (0.3–52.2)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• After surgery (ligation without stripping): One study; 50/132; 37.9</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• After avulsion phlebectomy: One study; 50/122; 41.0</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• One RCT found foam sclerotherapy had a (marginally) significantly higher rate of recurrence/new veins compared with surgery (ligation without stripping).</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Conclusions: Serious adverse events associated with foam sclerotherapy are rare and the safety profile of foam sclerotherapy and liquid sclerotherapy appear to be similar. Insufficient evidence is available to make a meaningful comparison of the effectiveness of foam sclerotherapy and other minimally invasive treatments (liquid sclerotherapy) or surgery (including stripping, ligation, phlebectomy).</td>
<td></td>
</tr>
</tbody>
</table>
### Table C1 continued: Evidence table of appraised secondary studies relating to varicose veins treatment methods

<table>
<thead>
<tr>
<th>Review details</th>
<th>Aim and search method</th>
<th>Study design and inclusion/ exclusion criteria</th>
<th>Results and author(s) conclusions</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rigby KA, Palfreyman SJ, Beverley C &amp; Michaels JA, 2004</td>
<td><strong>Aim:</strong> To identify whether the use of surgery or sclerotherapy should be recommended for the management of primary varicose veins.</td>
<td>Inclusion criteria: All prospective RCTs for the treatment of primary varicose veins (incorporating treatment for cosmetic and/or symptomatic varicose veins) where any comparison was made between surgery and sclerotherapy. In larger databases, searches were limited to guidelines, systematic reviews and clinical trials. In smaller databases, searches were not restricted by publication type or study design. Exclusion criteria: Trials including participants with complications of varicose veins, venous ulceration, chronic venous insufficiency and recurrent varicose veins. Study selection and appraisal methods: All studies that were randomised or described as randomised were retrieved and assessed for inclusion; two reviewers independently implemented inclusion/exclusion criteria. Discrepancies clarified by third author. Methodological quality assessed on basis of key determinants identified by NHS Centre for Reviews and Dissemination and Jadad scale.</td>
<td>Nine RCTs were included. Note: ‘Surgery’ arm of RCT by Einarsson et al (1993) did not stratify outcomes for ligation/stripping and phlebectomy patients. Sclerotherapy arm of RCT by Rutgers et al (1994) included ligation. In Belcaro et al (2000) sclerotherapy was not performed in line with MBS guidelines. These RCTs were not included within the current review. Sclerotherapy versus surgery (ligation with stripping): Treatment success or failure • After one year, two studies stated sclerotherapy was significantly better than surgery. After one year, the effectiveness of sclerotherapy rapidly declined so that by two years, no significant differences were seen. At three years, one study reported that surgery was significantly better than sclerotherapy subjectively and objectively, but two other studies still found no significant difference at this point. By five years, two trials reported that surgery had a significantly better outcome than sclerotherapy. • One RCT found surgery (ligation with stripping) required significantly more time off work post-procedure. • All studies showed sclerotherapy results to be worse than surgery. One study showed difference in re-treatment rates increased with age (that is, age 15–34 years showed no significant difference; age 35–44 years significantly more re-treatment after sclerotherapy [P&lt;0.001]; 45–64 years showed significantly more re-treatment after sclerotherapy [P&lt;0.01]). • Showed no difference in re-treatment rates in participants without signs of venous insufficiency (ankle oedema and flares). In those with ankle oedema or flares, need for re-treatment was significantly higher after sclerotherapy (P&lt;0.01). Complication rates: • One RCT reported no significant difference between surgery (ligation with stripping) and sclerotherapy. • After surgery (ligation with stripping): pulmonary embolism rate ranged from 0.48% to 0.62% (two studies); deep vein thrombosis was reported at 0.96% (one study); wound infection was 7.25% (one study); saphenous nerve injury was 10% after stripping to the knee (one study). • One study reported a 6.6% complication rate after sclerotherapy. Sclerotherapy versus surgery (ligation without stripping): • One study reported recurrence of varicose veins ranged from 34% for surgery to 48% for sclerotherapy at 5 years; at 10 years this increased to 38% and 56% respectively (significance not reported). • This study also found recurrence in a parallel, non-randomised surgery group (ligation with stripping) to be significantly higher (54%). • One study reported subjective/objective evaluation following surgery (ligation without stripping) to be significantly better compared with sclerotherapy alone at three years (P&lt;0.0005). • This study found no significant difference in complication rates between surgery (ligation without stripping) and sclerotherapy. Sclerotherapy versus phlebectomy: • One study stated that ambulatory phlebectomy was clinically better than sclerotherapy at both one and two-year follow-up; ambulatory phlebectomy is the treatment of choice for lateral accessory varicose veins. • Significantly more telangiectatic matting after phlebectomy at two years (P&lt;0.039); no significant difference in rate of phlebitis or haematoma. • One study showed varicose vein recurrence rate after stab avulsion was significantly higher than surgery + sclerotherapy and sclerotherapy alone (P&lt;0.02). Conclusions: Until clearer evidence is produced, there still appears to be a place for the use of both surgery and sclerotherapy for managing varicose veins. There appears to be a trade-off between costs and complications, with sclerotherapy showing better early outcomes but surgery more durable long-term outcomes. Extent of varicose veins governs intervention of choice, with no single treatment used universally. Suggest that sclerotherapy may be best suited to those patients with minor superficial varicose veins not related to reflux in the saphenous system.</td>
<td>Extensive search strategy described • Moderate inclusion/exclusion criteria • No date restrictions • No language restrictions • Searches of relevant articles reference list carried out • Handsearching of relevant journals • Consultation of relevant online health services • Two authors assessed trials independently • Discrepancies between authors for study inclusion arbitrated by third author • Contacted authors re: missing data and additional information where possible • Extensive description of included studies • Search terms clearly defined • Brief background • Meta-analysis precluded • Data extraction and appraisal methodology outlined (Jadad score given) • Analysis on ITT • Extensive tabular data, including characteristics of included/excluded/ ongoing trials and individual studies results • Number of included/excluded/ ongoing studies described</td>
</tr>
</tbody>
</table>