

Clinical effectiveness and cost-effectiveness of minimally invasive techniques to manage varicose veins: a systematic review and economic evaluation

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Scientific summary

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Background

Varicose veins are enlarged, visibly lumpy knotted veins, usually in the legs. Uncomplicated varicose veins can cause pain, discomfort, aching, heaviness, itching, superficial thrombophlebitis, external bleeding, lipodermatosclerosis, eczema and ulceration. Varicose veins are part of chronic venous disease (CVD), which is reported to have a substantial negative impact on health-related quality of life (HRQoL).

Prevalence of varicose veins in the UK has been reported to be between 20% and 40% in adults. The NHS performed over 33,000 surgical procedures in 2010–11 to treat varicose veins. However, the number of procedures for this condition is declining and may be affected by economic considerations.

Traditional treatments for varicose veins involve surgical stripping and ligation, liquid sclerotherapy (LS) and the conservative management of symptoms. Surgical stripping is by far the most commonly performed procedure for varicose veins, but has been associated with nerve damage, scars, pain and long post-operative recovery. Conventional LS is considered faster but less effective than surgical stripping. Surgical procedures have been shown to produce a range of adverse effects such as wound infection, haematoma, lymph leaks, scarring, nerve injury and deep-vein thrombosis (DVT).

New minimally invasive treatments offer alternative methods of ablating the vein. These treatments typically involve use of laser, radiofrequency or foam sclerosant. They are endovenous laser ablation (EVLA), radiofrequency ablation/obliteration (RFA) and foam sclerotherapy. These techniques are increasingly widely used and offer potential benefits such as reduced complications, faster recovery, fewer physical limitations and increased HRQoL. They are also reported to have reduced costs and lower recurrence rates compared with surgical stripping or LS, while being equally effective.

Objectives

1. To evaluate the clinical effectiveness and cost-effectiveness of new minimally invasive techniques compared with other techniques, including traditional surgical techniques, LS and conservative management, in the management of varicose veins.
2. To evaluate the safety of new minimally invasive techniques compared with surgical techniques, LS and conservative management, in the management of varicose veins.
3. To identify any key areas for further research.

Methods

This report presents a systematic review of the clinical effectiveness and cost-effectiveness evidence, supplemented by an independent economic model. A search of 11 bibliographic databases, plus reference tracking of reviews and included studies, was conducted to identify randomised controlled trials (RCTs) comparing EVLA, RFA or FS with stripping or non-foam sclerotherapy, the principal surgical techniques. This search was conducted in July 2011. Study selection, data abstraction and risk of bias assessment were independently conducted by two reviewers. The following outcome data were extracted, where available: initial failure of the procedure and retreatment (within 1 month); technical and symptomatic recurrence (defined as the technical or symptomatic identification of retrograde flow anywhere in a treated vein, i.e. reflux, recanalisation or residual varicose veins after successful occlusion, ablation or stripping); retreatment following recurrence; Venous Clinical Severity Score (VCSS); pain; time to return to work or normal activity;

and adverse events. The quality of studies was assessed using an adapted version of the risk of bias tool for surgery studies.

Data were tabulated and included studies were combined in a formal network meta-analysis if the included trials were sufficiently similar in terms of population, intervention, comparator, and outcome and length of follow-up. The following outcomes were subjected to formal network meta-analyses: technical recurrence, VCSS and pain score. The model used accounted for the time element in the analysis for technical recurrence. Results of the network meta-analyses were reported in terms of the hazard ratios and 95% credible intervals (CrIs) relative to the baseline intervention (i.e. stripping) at 6 months, 1 year and 2 years. For the cost-effectiveness review and analysis, a search was performed of nine bibliographic databases for cost-effectiveness and utility literature in July 2011 and updated in September 2012. The model was developed as a discrete event simulation (DES) model in Simul8® (Simul8 Corporation, Boston, MA, USA) to simulate the experience of patients undergoing treatment for varicose veins. The baseline model has a time horizon of 10 years. The treatments for varicose veins considered in the model are for symptom relief and are assumed not to affect mortality.

Results

The literature search for the clinical effectiveness review identified 1453 citations, 65 of which were relevant. Two further citations were identified from tracking references. Eleven citations were relevant ongoing trials (yet to report) and the data were not appropriate for any analyses in a further trial (two papers). The result was a total of 34 trials (54 papers) for assessment in the clinical effectiveness review. No studies were identified comparing any minimally invasive technique with conservative management. Approximately half of the included studies reported inadequate randomisation, allocation concealment, between-group comparability or intention-to-treat analyses. The results of individual studies and the review are therefore affected by uncertainty on account of the relatively high risk of bias present.

The reported proportion of initial failures was very small for all techniques. Where reported, retreatment consisted of stripping for RFA, or further sessions of sclerotherapy for FS or stripping. Where appropriate data were available, a network meta-analysis was performed for technical recurrence, VCSS and pain to compare each intervention (EVLA, RFA and FS) with the common comparator of conventional surgery (stripping). The relative likelihood of experiencing a technical recurrence of varicose veins over time was lower for EVLA (hazard ratios 0.70, 0.77 and 0.84) and RFA (hazard ratios 0.92, 0.93 and 0.94) than for ligation and stripping, at all time points (6 months, 1 year and 2 years, respectively). The relative likelihood of experiencing a technical recurrence of varicose veins over time was higher for FS (hazard ratios 1.12 and 1.02) than for ligation and stripping at 6 months and 1 year, respectively, but lower for FS (hazard ratio 0.92) than for ligation and stripping at 2 years.

Very few studies reported symptomatic recurrence, or reoperation rates beyond 1-month follow-up. Network meta-analysis found lower post-intervention VCSS for both FS and EVLA than for stripping (i.e. fewer clinical symptoms) whereas this score was slightly higher for RFA versus stripping. There was significantly lower post-operative pain for RFA than for stripping, as well as reduced pain for FS and a slightly increased level of pain for EVLA compared with stripping. Where the outcome was reported, significantly quicker return to work or normal activity was reported by all relevant studies for both FS and RFA than for stripping. Studies comparing EVLA and stripping reported either no difference or more rapid return to work for participants in the EVLA trial arm.

The analyses compared the minimally invasive treatments with the principal comparator currently provided in the NHS (i.e. stripping). No formal analysis was undertaken to compare these techniques with the less frequently performed comparators of LS and conservative management. This was because no head-to-head trials were identified comparing the minimally invasive techniques with conservative management, and only three trials that compared FS with LS, which does not represent a closed network.

A previous trial had also indicated that these comparators were less effective than surgery, both clinically and in terms of cost. The actual effectiveness of the minimally invasive techniques relative to these less frequently performed interventions is therefore uncertain.

There were no consistent or statistically significant differences between any of the interventions in terms of complications or adverse events. The FS treatment arms of trials were associated with a relatively higher incidence of DVT than any other intervention, but the number of such events was very small and not statistically significant.

Endovenous laser ablation and RFA are the most expensive procedures (more than £2000 for the total cost of treatment), and FS is the least expensive of the minimally invasive techniques at approximately £650 for the total cost of treatment. The total cost of stripping is approximately £1100. However, there was considerable variation in procedure costs between different studies.

The cost-effectiveness model shows that any differences in benefits (quality-adjusted life-years; QALYs) between the different procedures are negligible, but marginally favour the novel treatments relative to stripping. The time to treatment failure curves are all very similar. Disutility associated with post-operative pain, although not severe and limited to a few days' duration, affects the results in the short term (2 years), demonstrating the limited effects of time to failure on differential QALYs. There are differences in treatment costs, however, and with little differences in QALYs incremental net benefits are primarily driven by costs. Treatment costs are primarily composed of the initial treatment cost. Differences between treatments are negligible in terms of clinical outcomes, so the treatment with the lowest cost appears to be most cost-effective. Our central estimate is that total FS costs are the lowest and it is marginally more effective than stripping (+0.0015 QALYs), with a probability of being the most cost-effective treatment above 90% for willingness-to-pay thresholds in the range £20,000–50,000. This result is, however, sensitive to the model time horizon (i.e. cost-effectiveness is reduced in the shorter term because of the early failure rates for this technique). EVLA and RFA both cost more than surgery, and with very little difference in QALYs they cannot be considered cost-effective at the usual threshold of £20,000–30,000, a result that is robust to parameter variation and model time horizon. There is considerable uncertainty in the cost differences between treatments arising from different reported costs of the procedures, and in fact these are likely to vary with setting, and may also vary over time. Threshold analysis shows that the additional costs of EVLA and RFA would have to be no more than £50 and £24, respectively, to be considered cost-effective at a threshold of £20,000.

Discussion

The clinical effectiveness review identified almost three times the number of relevant RCTs of any previously published review. The network meta-analysis calculated the probability of an individual experiencing an event at any time, rather than their relative likelihood of experiencing the event at a set time point, which is a limitation of existing published analyses. However, there was substantial heterogeneity between included studies in terms of the outcome measures used. This dictated that some data from included studies could not be pooled in the analyses. The analyses did not control for within-or between-study differences in terms of the impact of risk of bias criteria such as the performance of intention-to-treat analyses.

All of the effectiveness analyses presented here used only technical rather than symptomatic recurrence data, so the true proportion of treated individuals who are likely to present with symptoms of recurrence requiring retreatment is not certain. The rates of technical recurrence reported here are therefore higher than those encountered in clinical practice. The findings on initial failure and retreatment, symptomatic recurrence and retreatment for recurrence are affected by a high degree of uncertainty due to the relative infrequency with which such data were reported, as well as the limitations of the primary studies' reporting of these data.

The findings of this report need to be verified by data from future trials with longer follow-up and using more standardised outcome measures. For the purposes of a more meaningful comparison of effectiveness and costs, trial arms should have equally experienced surgeons, comparable groups in terms of clinical status, aetiology, anatomy, pathophysiology score and after care, and report all details of 'top-up' treatments, reoperations and symptomatic as well as technical recurrence. The relative efficacy of the interventions compared with stripping might be underestimated if surgeons are insufficiently experienced in performing the more recent minimally invasive techniques.

The vast majority of the trials were conducted in Western Europe in populations who would typically present in the UK with varicose veins and be treated with one of the modalities assessed. The relative costs of the alternative techniques evaluated in the model are based on NHS tariffs. However, the relative clinical effectiveness and cost-effectiveness of the techniques are principally based on rates of post-operative technical recurrence rather than symptomatic recurrence. A figure reflecting the likely proportion of treated individuals who would experience symptomatic recurrence, requiring retreatment (with its associated costs), therefore, had to be calculated by the authors based on a small number of studies.

Conclusions

This assessment of the currently available evidence suggests there is little to choose between the minimally invasive techniques in terms of efficacy, and each offers a viable, clinically effective alternative to stripping. Foam sclerotherapy might offer the most cost-effective alternative to stripping, within certain time parameters. Training and experience in the minimally invasive techniques might be required before relative benefits are apparent.

Future trials should aim to measure and report outcomes in a standardised manner, which would permit more efficient pooling of their results [e.g. mean and standard deviation (SD)] of all validated and commonly used measures, such as VCSS and European Quality of Life-5 Dimensions (EQ-5D). Trial authors should also report both technical and symptomatic recurrence, to permit assessment of likely retreatment rates and costs, and utilise surgeons with adequate experience of the minimally invasive techniques, if the comparison with stripping (currently the most common procedure performed by all surgeons) is to be internally valid.

Study registration

This study is registered as PROSPERO number CRD42011001355.

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