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CONTEXT AND POLICY ISSUES:

Varicose veins are characterized by tortuous and dilated superficial veins due to poorly functioning valves and decreased elasticity of the vein wall. This results in the reflux and pooling of blood within the veins, and their subsequent enlargement. In the United States, it has been estimated that approximately 25% of women and 15% of men have varicose veins. Risk factors include female gender, advancing age, family history, pregnancy, prolonged standing, obesity, vascular malformations, and hormone therapy. Symptoms include pain, swelling, heaviness, fatigue, burning, restlessness, and pruritus (itching) which interfere with activities of daily living and result in time lost from work. Varicose veins are associated with several complications including bleeding, superficial thrombophlebitis (chronic inflammation of the vein), deep venous thrombosis, and venous ulceration. Although the true incidence of these complications is unknown, they are estimated to occur in approximately 5% of patients with varicose veins.

Treatment options for varicose veins include conservative measures (lifestyle modification, diuretics, and compression therapy). If conservative treatment is unsuccessful, more invasive surgical interventions including saphenous vein stripping, ligation of the saphenofemoral junction, and ambulatory phlebectomy are used to reduce venous hypertension and prevent progression to chronic inflammation and ulcerations. Surgical procedures are usually performed under general or epidural anesthesia and may be outpatient or require hospitalization overnight. Surgical procedures may be associated with the development of scars, wound infection, post-operative pain, neurologic damage, and lymphatic complications. Furthermore, recurrence of varicose veins has been estimated to occur in approximately one third of cases five years following surgery.

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Minimally invasive techniques such as endovenous laser therapy (EVLT), radiofrequency ablation (RFA), and ultrasound-guided foam sclerotherapy (UGFS) have been introduced to improve effectiveness, treatment costs, post-operative pain, and complications associated with the management of varicose veins.\(^6\) EVLT works by delivering heat energy into the lumen of the saphenous vein via a laser-tipped probe, thereby occluding the varicose vein and abolishing venous reflux.\(^9\) EVLT is can be performed in an outpatient setting under local anesthesia which may potentially reduce hospital costs, complications, and recovery time.\(^5\)

As an emerging technology, a comparative assessment of EVLT with other treatment options for varicose veins is required to support implementation into clinical practice. This report will review the clinical-effectiveness, safety, and cost-effectiveness of EVLT compared to other treatments for relieving the symptoms and reducing the complications of varicose veins.

**RESEARCH QUESTIONS:**

1. What is the evidence for the clinical benefit and harm of endovenous laser therapy for patients with varicose veins, in the short and long-term?

2. What is the cost-effectiveness of endovenous laser therapy for patients with varicose veins?

**METHODS:**

A limited literature search was conducted on key health technology assessment (HTA) resources, including PubMed, the Cochrane Library (Issue 2, 2009), University of York Centre for Reviews and Dissemination (CRD) databases, ECRI, EuroScan, international health technology agencies, and a focused Internet search. The search was limited to English language articles published between 2004 and May 2009. No filters were applied to limit the retrieval by study type. This search was supplemented by hand searching the bibliographies of selected papers to include information from clinical trials and epidemiological studies not identified in the original search.

Studies comparing EVLT with other treatments for the management of varicose veins were selected for inclusion in the report. Studies assessing EVLT in combination with other treatment modalities such as surgery were excluded. Several HTAs, systematic reviews, randomized controlled trials (RCTs), and controlled clinical trials (CCTs) assessing the use of EVLT for the management of varicose veins were retrieved in the literature search. As a result, data from observational studies were excluded from this report. RCTs and CCTs not included in the identified HTAs or systematic reviews were appraised separately in this report.

HTIS reports are organized so that the higher quality evidence is presented first. Therefore, health technology assessment reports, systematic reviews, and meta-analyses are presented first. These are followed by randomized controlled trials, controlled clinical trials, and economic evaluations.

**SUMMARY OF FINDINGS:**

One HTA\(^{10}\) and four systematic reviews\(^{11-14}\) of EVLT treatment for varicose veins were identified. One RCT\(^{15}\) and one CCT\(^{16}\) published subsequent to the identified HTA and systematic reviews were included. Two cost-effectiveness studies\(^{17,18}\) and two costing studies\(^{10,19}\) were identified.
Health technology assessments

The Medical Services Advisory Committee (MSAC) completed a HTA (2008) examining the safety, effectiveness, and cost-effectiveness of EVLT for varicose veins to support public funding decisions in Australia. A systematic review of the literature published up to August 2007 was conducted to identify studies (including randomized, non-randomized comparative studies, and case series) that compared the clinical-effectiveness and safety of EVLT with surgical saphenous stripping or junction ligation of varicose veins. Case series were used for the assessment of safety outcomes only. Case reports were excluded. Clinical outcomes of interest were abolition of reflux, recurrence of varicose veins, recanalization rates, symptom reduction, changes in the quality of life, time taken to resume normal activities, and procedure operating time. Safety outcomes of interest were mortality rate and the rates of adverse effects including post-operative infection, laser-related adverse effects, thrombotic events, pain, bleeding complications, ecchymosis, paraesthesia, nerve damage, induration, phlebitis, and lymphedema. A total of 40 studies (two RCTs, three CCTs, and 35 case series) in 4,525 patients (6,575 limbs) were included in the review. The mean study follow-up was 10.1 (range, 0.25 to 36) months. Of the included studies, five directly compared EVLT to conventional junction ligation and stripping for the treatment of varicose veins.

Among the comparative studies, results showed no significant differences in the rates of reflux abolition between EVLT and surgery. Reflux was absent in 94.1% to 95.5% of limbs treated with EVLT and 94.4% to 100.0% of limbs treated with surgery at the conclusion of follow-up. The comparative trial (n=50, 58 limbs) with the longest follow-up (12 months) reported 95.5% of limbs treated with EVLT remained free of blood flow or reflux compared with 94.4% in patients treated with surgery. Patients receiving EVLT reported significant improvements in symptoms of varicose veins and quality of life compared with patients receiving surgery. However, many of these differences were statistically significant for only a short period of time (less than two months) following treatment. Patients treated with EVLT required less time to return to work than patients who had undergone surgery.

Across all included studies, minor self-limiting adverse effects such as ecchymosis (skin discoloration), bruising, induration (hardening of the skin), a sensation of tightness in the limb, and post-operative pain were commonly associated with EVLT. More serious complications such as pulmonary embolism, deep vein thrombosis, and nerve damage were uncommon. Pulmonary embolism was reported in one patient who experienced no long-term consequences. Twenty cases of deep vein thrombosis (0.4% of reported limbs) were identified across all patients treated with EVLT. The majority of deep vein thrombosis cases resolved spontaneously without further treatment. Seventy cases of nerve damage (0.8% of reported limbs) were reported after EVLT. The after-effects of two cases of neuritis persisted from four to eight months. One case of sural nerve palsy resolved after six months, while one case of saphenous nerve damage had not resolved after 12 months. Overall, the occurrence rates of more serious complications including deep vein thrombosis, nerve injury, paraesthesia, post-operative infection, and hematomas appeared to be higher after surgery compared with EVLT. In three comparative studies reporting adverse effects, EVLT was found to have lower occurrence rates of hematoma, bruising, edema, and post-procedural pain compared with surgery. The authors concluded that from the available evidence, EVLT is at least as safe and effective as saphenous junction ligation and vein stripping for the treatment of varicose veins.
Systematic reviews and meta-analyses

A recent meta-analysis (2009) assessed the clinical-effectiveness of endovenous therapies when compared with surgery for lower extremity varicosities.\(^{11}\) A systematic review was performed to identify studies assessing EVLT, RFA, and UGFS published up to February 2007. All studies (including RCTs, CCTs, and prospective or retrospective case series) that used ultrasound examination as an outcome measure were included. Definitions of treatment success by ultrasound examination varied considerably. Studies using definitions that assessed obliteration or complete removal of the varicose vein were selected and considered to be equally successful. For comparative studies, the arms of interest were included separately. English, German, French, and Dutch studies were included. Studies that examined combination therapies or non-truncal varicose veins were excluded. A random effects meta-analysis was performed and subgroup analysis and meta-regression were conducted to explore sources of between-study variation in terms of follow-up time and study design.

A total of 64 studies (with a total of 72 study arms) were selected that assessed 12,320 limbs. The average follow-up was 32.2 months (range, one day to 34 years). Of the included studies, 30 (27 prospective case series, three retrospective case series) evaluated EVLT, 13 (five RCTs, five prospective case series, three retrospective case series) evaluated surgery, 10 (two RCTs, five prospective case series, three retrospective case series) evaluated UGFS, and 19 (two RCTs, 12 prospective case series, five retrospective case series) evaluated RFA. After three years, the estimated pooled success rates were 78\% (95\% confidence interval [CI], 70\% to 84\%) for surgery, 77\% (95\% CI, 69\% to 84\%) for UGFS, 84\% (95\% CI, 75\% to 90\%) for RFA, and 94\% (95\% CI, 87\% to 98\%) for EVLT. After adjusting for follow-up, UGFS and RFA were as effective as surgery (adjusted odds ratio [AOR] 0.12 [95\% CI, -0.61 to 0.85; \(p=0.73\)] and AOR 0.43 [95\% CI, -0.19 to 1.04; \(p=0.16\)], respectively). EVLT was significantly more effective compared with surgery (AOR 1.13; 95\% CI, 0.40 to 1.87; \(p=0.006\)), UGFS (AOR 1.02; 95\% CI, 0.28 to 1.75; \(p=0.013\)), and RFA (AOR 0.71; 95\% CI, 0.15 to 1.27; \(p=0.016\)). Restricting the analysis to the 58 prospective studies supported results that EVLT was significantly more effective than surgery (\(p<0.001\)), UGFS (\(p<0.0001\)), and RFA (\(p=0.01\)). The authors concluded that in the absence of large comparative RCTs, these findings suggest that EVLT is more effective than surgery, UGFS, and RFA for the treatment of lower extremity varicose veins.

Hoggan et al. conducted a systematic review (2009) comparing the safety and efficacy of EVLT with surgery involving saphenous ligation and stripping for the treatment of varicose veins.\(^{12}\) A systematic search was used to identify studies published up to April 2008. Both randomized and non-randomized studies directly comparing outcomes for EVLT to surgery were included in the assessment of safety and effectiveness. Non-comparative studies were included for the assessment of safety. Foreign language articles were excluded unless the findings provided additional information to studies published in English. The primary outcome for assessing clinical effectiveness was abolition of reflux. Other outcomes of interest included rates of recanalization and neovascularization, reduction of varicose symptoms, changes in the quality of life, time required to return to normal activity, and procedure time. Safety outcomes of interest were the number of adverse events including thromboembolic events, neurological injuries, paraesthesia, infection, phlebitis, hematoma, bruising, hyperpigmentation, post-operative pain, bleeding complications, laser-related skin burns, and induration. A total of 59 studies (four RCTs, three CCTs, 37 case series, 15 comparative studies to modalities other surgery) were selected for inclusion. A total of 5,759 patients (6,702 limbs) were treated with EVLT and 6,395 patients (7727 limbs) were treated with surgery. Mean study population of studies describing EVLT was 66 (range, 11 to 1091) with a median follow-up of 6.8 (range, 0.25 to 36) months. Demographic and clinical characteristics appeared comparable across EVLT and surgery.
populations. Four RCTs\textsuperscript{19,21,23,24} and three CCTs\textsuperscript{18,20,22} directly compared ELT to surgery. These seven studies were used to assess both safety and effectiveness. The methodological quality of the four RCTs differed as concealment of treatment allocation was reported in two RCTs\textsuperscript{21,24} and two RCTs\textsuperscript{19,24} conducted analysis on an intention-to-treat basis. The median study size across the seven comparative studies was 95 (range, 20 to 164), while median follow-up was 9.0 (range, 3.0 to 26) months. Four of the seven comparative studies provided follow-up of six months or greater.\textsuperscript{18,21-23} The completeness of follow-up ranged from 53.5% to 100%.

No comparative studies reported significant differences between EVLT and surgery in rates of reflux-free limbs, recanalization, or neovascularization, although long-term follow-up was lacking. Saphenous vein occlusion with abolition of reflux was achieved in 87.8% to 100% of limbs after EVLT and in 91.7% to 100% of limbs after surgery. Statistical comparison of reflux abolition was performed in three of the seven comparative studies, and no significant differences between treatments were found. The majority of studies found no significant improvements from baseline in varicose vein symptoms (measured using the Aberdeen Varicose Vein Questionnaire [AVVQ] and the Venous Clinical Severity Score [VCSS]) and quality of life (measured using the Short-Form-36 [SF-36] health survey or the Chronic Venous Insufficiency Quality of Life Questionnaire [CVIQ]). One CCT\textsuperscript{20} reported significantly better (p<0.001) AVVQ scores at the 6-week and 12-week follow-up in EVLT patients compared with surgery after adjustment for baseline differences between treatment groups. Two CCTs reported significantly better quality of life SF-36 (p<0.010)\textsuperscript{20} and CVIQ (p<0.002)\textsuperscript{18} scores less than two months after treatment. One\textsuperscript{23} of three RCTs\textsuperscript{19,23,24} that reported on time required for patients to return to work found a significant difference (p=0.005) between EVLT and surgery. Of note, the RCT that favored EVLT for improved recovery performed EVLT under local anesthesia while the other two RCTs performed EVLT under general anesthesia. Serious adverse events, such as deep vein thrombosis after EVLT or surgery were rare. Of the 20 cases of deep vein thrombosis reported in one case series of 187 patients (210 limbs) following EVLT, 12 were non-occlusive thrombi. No other cases of deep vein thrombosis were reported in the other studies included in the systematic review. Paraesthesia occurred more frequently following surgery than EVLT. Results from comparative studies showed statistically significant improvements for EVLT in the occurrence of hematomas, edema, post-operative pain, and bruising when compared to surgery.\textsuperscript{18,19,21,22,24} Laser skin burns and induration were reported only after EVLT while bleeding complications and lymphorrhrea or seroma where reported only following surgery. The authors concluded that EVLT appears to be at least as effective as surgery up to 12 months after treatment.

Luebke et al. conducted a systematic review (2008) to assess the safety and effectiveness of EVLT in comparison to conventional ligation and vein stripping.\textsuperscript{13} A literature search using several databases was used to identify studies published between 1970 and 2007. The primary outcomes for assessing safety were mortality and morbidity due to laser-related adverse events, post-operative infection, thrombotic events, pain, bleeding complications, ecchymosis, and paraesthesia, induration, and phlebitis. Clinical effectiveness was assessed as the abolition of reflux, rate of re-treatment, recanalization or neovascularization, reduction of symptoms, and quality of life. A total of 29 case series, assessing 13,045 patients treated with EVLT were selected for inclusion. Follow-up data were reported for a mean of 30 days to 48 months. Overall, rates of deep vein thrombosis (odds ratio [OR] 0.00; 95% CI, 0.00 to 0.01), paraesthesias (OR 0.04; 95% CI, 0.01 to 0.08), phlebitis (OR 0.04; 95% CI, 0.02 to 0.07) were low following EVLT. The occurrence of induration (OR 0.87; 95% CI, 0.63 to 0.99) and ecchymosis (OR 0.78; 95% CI, 0.55 to 0.94) was common following EVLT. Results showed that 10,812 patients of 11,277 patients receiving EVLT (OR 0.96; 95%, 0.94 to 0.97) had successfully occluded great saphenous veins at the end of follow-up. Eleven of the 29 studies indicate that recanalization occurred in 52 of 1,161 patients after receiving EVLT (OR 0.04; 95%
The authors selected two RCTs\textsuperscript{19,25} and one CCT\textsuperscript{26} comparing EVLT with conventional surgery (junction ligation with stripping) for a meta-analysis. The three studies examined a total of 305 patients (157 treated with EVLT and 148 treated with surgery). Follow-up ranged from 12 weeks to 18 months. Results showed no significant difference between treatments for complete occlusion at the end of follow-up (OR 1.03; 95% CI, 0.23 to 4.70; \(p=0.97\)). There was no significant difference between EVLT and surgery in the incidence of paraesthesia at 6 months (OR 0.32; 95% CI, 0.03 to 3.12; \(p=0.32\)). There was a significant difference in bruising at 12 days in favor of EVLT (OR 0.3; 95% CI=0.14 to 0.67; \(p=0.003\)). There was a significant difference in favor of EVLT in terms of various quality of life measures (AVVQ and SF-36 scores) after the procedure and at follow-up. There was no significant difference between the groups in terms of disease severity at end of follow-up using VCSS (OR 0.01; 95% CI, -0.08 to 0.09; \(p<0.90\)). The authors concluded that both EVLT and surgery were at least equally effective in terms of complete occlusion of the treated vein with a general improvement in quality of life for patients treated with EVLT when compared to surgery.

Mundy et al. published a systematic review (2005) of studies published from January 1966 to September 2004 evaluating the safety and effectiveness of EVLT for varicose veins.\textsuperscript{14} The primary outcomes for assessing safety were mortality and morbidity due to laser-related adverse events, post-operative infection, thrombotic events, pain, bleeding complications, ecchymosis, paraesthesia, and phlebitis. Clinical effectiveness was assessed by abolition of reflux, rates of re-treatment, recanalization, or neovascularization, reduction of symptoms, and quality of life. At the time, no controlled studies were available to assess the effectiveness of EVLT in comparison to surgery. A total of 13 case series studies (n=1,289, 1,631 limbs) were selected for inclusion. Mean follow-up ranged from one month to 19 months. Seven studies provided follow-up of more than six months for all treated limbs. Results showed that venous occlusion rates ranged from 87.9% to 100%. The four largest series, ranging from 121 patients to 252 patients, reported occlusion rates from 93% to 96.8%. Self-limiting adverse effects such as pain, ecchymosis, induration, and phlebitis were commonly observed after treatment with EVLT. Deep vein thrombosis and incorrect placement of the laser in vessels were uncommon adverse events occurring in one patient and two patients, respectively. The authors concluded that based on available low-level evidence, EVLT may benefit most patients short-term, but rates of recanalization, re-treatment, occlusion and reflux may alter with longer follow-up.

**Randomized controlled trials**

Disselhoff et al. conducted a single-center RCT to compare the effectiveness of EVLT with surgical cryoablation for varicose veins.\textsuperscript{15} A total of 120 patients with uncomplicated great saphenous varicose veins were randomly assigned to two treatment groups using numbered and sealed envelopes. Interventions were either performed as a day-case procedure under general anesthetic (38 EVLT, 49 surgery) or as an outpatient procedure under local anesthetic (22 EVLT, 11 surgery) according to patient preference. A single surgeon equally experienced in EVLT and surgery performed all procedures. Principle outcome measures were freedom from recurrent varicose veins on duplex ultrasound imaging, and improvement in VCSS and AVVQ scores at six, 12, and 24 months after treatment. An intention-to-treat analysis was used. Participants were balanced in terms of clinical and demographic characteristics prior to receiving treatment. At 10 days, there were no significant differences between the groups in terms of bruising, superficial thrombophlebitis or saphenous neuralgia. No severe complications, including deep vein thrombosis or pulmonary embolism, were noted in either group. Significantly more patients in the EVLT group experienced tightness (\(p<0.001\)) when compared with surgery. At ten days, EVLT was statistically significantly superior to surgery regarding post-procedural pain scores (\(p=0.003\)), induration (\(p<0.001\)), and resumption of normal physical activity.
(p=0.001). After two years, overall freedom from recurrent reflux was achieved in 77% (95% CI, 72% to 78%) of patients after EVLT and 66 (95% CI, 60% to 67%) after surgery. The difference between the two groups was not statistically significantly different (p=0.253). VCSS and AVVQ values improved significantly after treatment which persisted for the two-year study period in both treatment groups. However, the differences between the two groups at two years were not statistically significant. The authors concluded that EVLT and surgical cryostripping were similarly effective but patients favored EVLT because of less pain and post-operative morbidity, and quicker return to normal activity. Limitations of this study include a sample size of 120 patients. Studies of small sample size are underpowered to detect differences in serious adverse events such as cases of deep vein thrombosis and pulmonary embolism that typically have low event rates. Furthermore, neither the patients nor the personnel in the study could be blinded to the treatment given.

**Controlled clinical trials**

Gonzalez-Zeh et al. conducted a non-randomized, prospective controlled study to compare the clinical-effectiveness and complications of EVLT with UGFS in patients with great saphenous vein reflux. Selected patients were allowed to choose between UGFS (n=53) or EVLT (n=45). EVLT was carried out under local anesthesia in an outpatient treatment facility. UGFS was carried in an outpatient treatment facility (no anesthesia required). Duplex ultrasound examinations were performed prior to treatment and up to one year after treatment. The primary outcome measure was presence of reflux measured with duplex imaging. Success of treatment was defined as complete occlusion of the treated vein. Secondary outcome measures were pain associated with the procedure using the VAS, and the rate of deep vein thrombosis, phlebitis, ecchymosis, and paraesthesia. The cohorts showed no statistically significant differences in clinical or demographic characteristics prior to treatment. After one year, the number of limbs with confirmed occlusion of the great saphenous vein was higher in the EVLT group compared with UGFS (93.4% versus 77.4%; p<0.0465). There were no significant differences between treatment groups in the incidence of phlebitis, ecchymosis, and paraesthesia after treatment. However, procedure-associated pain and induration were significantly higher in the EVLT group compared with the UGFS group (p<0.0082 and p<0.0047, respectively). Deep vein thrombosis was detected in two patients following UGFS procedures but no cases were detected in the EVLT group. No episodes of pulmonary embolism or other cardiovascular complications were observed. The authors concluded that overall, EVLT achieved higher occlusion rates than UGFS with similar minor complication rates at one year following treatment. Limitations of this trial include an absence of random allocation of treatment group which does not control for confounding factors and selection bias.

**Economic evaluations**

Disselhoff et al. compared the costs and cost-effectiveness of surgical cryostripping with EVLT in the Netherlands. The perspective of this economic study was not stated. Data from a RCT comparing surgical cryostripping with EVLT in 120 patients were used for estimates of clinical and cost-effectiveness. The comparison of costs included both direct medical costs (including costs of initial treatment and additional treatment required up to two years following therapy) and costs resulting from lost productivity of the patient. The principle outcome measure was clinical-effectiveness at two years as measured using the SF-6D. The SF-6D is a single preference-based measure of health representing overall quality of life. A value of 1 represents the best health state and 0 represents death. Utility scores for SF-6D were recorded at baseline and at six, 12, and 26 months of follow-up. Incremental cost per quality-adjusted life year (QALY) gained two years after treatment was calculated. The quality-adjusted SF-6D,
calculated in terms of QALYs gained was 1.59 (95% CI, 1.53 to 1.64) in patients who underwent surgery and 1.60 (95% CI, 1.55 to 1.64) for patients who underwent EVLT two years after treatment. While the time to return to work (an average of 1.3 days for EVLT versus 2.2 days for surgery) and costs of lost productivity (€10,262 for EVLT versus €17,812 for surgery) were in favor of EVLT, the total costs of EVLT were higher than those for surgery. The costs of surgery and EVLT per patient were €2,651 and €2,783, respectively. The costs of EVLT equipment including the laser apparatus, fiber kit and duplex ultrasound were major factors that increased costs in the EVLT group (€21,600 compared with €3,460 for surgical equipment). Costs for additional treatment including surgical interventions and sclerotherapy required at 6 weeks (€16,941 for surgery versus €17,304 for EVLT) and two years (€10,843 for surgery versus €11,479 for EVLT) following initial treatment were similar between groups. Comparing surgery and EVLT, the cost-effectiveness ratio (cost in Euros per QALY gained) was in favor of surgery at €1,730 (95% CI, €1,591 to €1,891) versus €1,760 (95% CI, €1,633 to €1,898), respectively. The incremental cost-effectiveness ratio (cost in Euros per QALY gained) favored surgery (€-32, 95% CI, €-240 to €173). When different strategies including day-case and outpatient procedures were compared, outpatient surgery appeared to be the least costly and most effective two years after treatment. The authors concluded that outpatient surgical cryostripping was superior to EVLT in terms of costs per QALY gained at two years after treatment. However, the authors noted that EVLT yielded comparable clinical-effectiveness outcomes for a relatively small additional cost. The conclusions of this study directly apply to the Netherlands and may not be generalizable to the Canadian health-care system.

Vuylsteke et al. assessed the cost-effectiveness of EVLT compared with conventional surgical stripping for the management of varicose veins caused by great saphenous vein insufficiency. A prospective cohort study was conducted in Belgium to determine whether the additional medical costs of EVLT could be offset by improvements in efficacy and quality of life as well as shorter time off work. The economic analysis was carried out from a societal perspective. A total of 164 patients were assigned to surgery (n=84, 124 limbs) or EVLT (n=80, 118 limbs). Patients were assessed at week one, four, and nine months post-operatively. No patient was lost to the follow-up assessment. Blinding was not performed. The clinical and economic data were gathered from January 2002 to December 2003. The comparison of costs included both direct medical costs (including costs of vein stripper, laser fiber, catheter generator, surgeon and anesthesiologist fees, duplex ultrasound, surgeon visits, day stay in hospital, and compression stockings) and costs resulting from lost productivity of the patient. The cost of a lost working day was derived from the average gross wage level in Belgium in 2002. Resource use was estimated from the patients involved in the effectiveness analysis but sources of cost estimates were not explicitly stated. The effectiveness analysis showed that the laser procedure led to significant improvements in quality of life, non-steroidal anti-inflammatory use, patient satisfaction, and duration of sick leave in comparison with surgery. For unilateral procedures, the total direct treatment costs per patient were higher for EVLT compared with surgery (€853 versus €716, respectively). However, once productivity was accounted for, the costs of the EVLT group were lower compared with surgery (€1,277 versus €2,659, respectively). Similar results were obtained for patients receiving bilateral procedures. The authors concluded that EVLT procedures for varicose veins produced lower societal costs than conventional surgical stripping. As the study was limited to full-time working patients, these results may not be generalizable to older patients. Furthermore, clinical and cost estimates were derived from a single institution in Belgium in a cohort study which might not be representative of the patient population and treatment patterns in Canadian medical centers.

As part of the HTA conducted by MSAC (2008) a costing study from the perspective of the Australian health-care system was conducted based on clinical-effectiveness estimates.
obtained from a systematic review. This showed EVLT to be at least as effective as surgical
vein stripping. A cost-analysis was conducted based on the assumption of no significant
differences between treatments in clinical outcomes. The analysis showed an incremental cost
per patient receiving EVLT rather than surgery of A$ -171, indicating a cost-saving. The bulk of
the additional cost of EVLT was associated with higher procedural fee (A$606 versus
A$481.85), the additional capital cost of buying EVLT equipment (A$128), duplex imaging
(A$111.05), and consumables including the laser fiber (A$600) and catheters (A$50). These
costs were offset by reduced staffing costs and the lower costs of day surgery as opposed to
hospitalization (A$1500 versus A$2500). The authors concluded that EVLT appears to be at
least as cost-effective as surgical vein stripping for the treatment of varicose veins. Although
effectiveness estimates were derived from a systematic review, the economic evaluation was
performed from the perspective of the Australian health-care system which may not be
generalizable to the Canadian health-care system.

Rasmussen et al. compared the costs associated with EVLT to surgical ligation and stripping.19
A total of 121 patients with varicose veins were assigned to EVLT (n=62, 69 limbs) or surgery
(n=59, 68 limbs). This study was not restricted to working individuals. Cost calculations were
based on the standard fee for surgery, the additional costs for EVLT equipment, and the
standard salary and productivity in Denmark. The impact of sick leave on costs was corrected
for weekends. Results showed that the treatment costs were higher in the EVLT group (€1,391)
compared with surgery (€924). The additional cost was associated with the capital costs of the
EVLT equipment (€334) and duplex imaging (€134). However, this difference was offset by
lower indirect costs due to time of work (€2,006 for EVLT versus €2,160 for surgery). Taking this
into account, the total estimated cost of EVLT was €3,396 compared with €3,085 for surgery.
Calculations were based on the fixed procedure-related price system and the productivity level
in Denmark. Therefore, these costing comparisons may not directly apply to Canada.

Limitations

The majority studies identified in the HTA and systematic reviews were relatively short-term,
uncontrolled case series assessing low numbers of patients and were subject to selection bias.
Definitions of treatment success varied considerably among the trials hindering assessments of
comparative clinical-effectiveness. Some RCTs have been published comparing EVLT with
surgical interventions but none were powered to detect differences in rare, but serious adverse
effects such as pulmonary embolism. Furthermore, there is a lack of trials with sufficient follow-
up duration to indicate the long-term clinical-effectiveness and safety of EVLT compared to
surgical interventions. There is a paucity of high quality evidence to support the clinical-
effectiveness and safety of EVLT in comparison to other minimally invasive techniques.
Although most economic evaluations indicate that EVLT may be at least as cost-effective as
surgery, these results may not be generalizable to the treatment patterns and resource use in
Canada.

CONCLUSIONS AND IMPLICATIONS FOR DECISION OR POLICY MAKING:

There is some evidence that the short-term clinical-effectiveness of EVLT is similar to that of
surgical interventions for the management of varicose veins but with lower rates of adverse
effects such as post-operative pain, hematomas, edema, bruising, and infection. While serious
adverse events such as thromboembolic events and nerve damage were rare in comparative
trials, occurrence rates of these events seemed to be lower in patients receiving EVLT.
However, these comparative studies were underpowered to detect differences in these
infrequent events. There is evidence that patients receiving EVLT experience superior short-
term quality of life of up to two months following treatment and return to normal activity sooner compared with patients undergoing surgery. The long-term clinical-effectiveness and safety of EVLT compared with surgical interventions remains to be established. Although economic evaluations suggest that EVLT may be at least as cost-effective as surgery despite additional equipment and imaging costs, these results may not be generalizable to the Canadian healthcare system. There is limited evidence that EVLT may be at least, if not more, effective than other minimally invasive treatment options such as UGFS and RFA. Well-designed RCTs with sufficient sample size and follow-up duration are required to confirm this finding. Results from an unpublished conference abstract and ongoing studies are of particular interest.

In conclusion, long-term comparative RCTs of sufficient sample size assessing clinical effectiveness (particularly with regard to the formation of recurrent varicose veins), safety, quality of life, and cost-effectiveness are needed to fully characterize the role of EVLT for the management of varicose veins relative to other treatments.

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