

OHTAC Recommendation: Endovascular Ablation for Varicose Veins

Ontario Health Technology Advisory Committee

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Background

Health Quality Ontario (HQO) reviewed *Endovascular Laser Therapy for Varicose Veins* in April 2010 (http://www.health.gov.on.ca/english/providers/program/mas/tech/reviews/pdf/rev_EVLT_20100422.pdf) and *Endovascular Radiofrequency Ablation for Varicose Veins* in February 2011 (http://www.health.gov.on.ca/english/providers/program/mas/tech/reviews/pdf/rev_rfa_vv_20110216.pdf). The evidence-based analyses for endovascular laser therapy (ELT) and endovascular radiofrequency ablation (RFA) assessed the following:

- safety profile of ELT and RFA
- treatment effectiveness of ELT and RFA for varicose vein (VV) reflux
- treatment effectiveness of ELT and RFA for VV symptoms
- impact of ELT and RFA on health-related quality of life (HRQOL)
- durability of ELT and RFA
- patient satisfaction with ELT and RFA
- effectiveness of ELT and of RFA compared with surgical ligation and vein stripping
- effectiveness of RFA compared with ELT

The primary focus of both reviews was to compare nonsurgical endovascular ablation techniques with surgery by examining clinical effectiveness, safety, costs, and budgetary implications for the health system.

Conclusions

Endovascular Laser Therapy

The Medical Advisory Secretariat (MAS) evidence-based review of endovascular laser therapy (ELT) for varicose veins (VV) was performed as an update to the 2007 health technology review by the Australian Medical Services Advisory Committee (MSAC) to support public financing decisions. The Health Quality Ontario (HQO) evidence search on ELT for VV identified 14 systematic reviews, 29 cohort studies on safety and effectiveness, 4 cost studies, and 12 randomized controlled trials (RCTs) of which 6 compared ELT with surgical ligation and vein stripping.

Since 2007 alone, 22 cohort studies that involved 10,883 patients who underwent ELT of the great saphenous vein have been published. Imaging-defined treatment effectiveness of mean vein closure rates were reported to be greater than 90% (range 93%–99%) at short-term follow-up. Longer than 1-year follow-up was reported in 5 studies with life table analysis performed in 4 but with limited follow-up to 3 and 4 years. The overall pooled major adverse event rate (including deep vein thrombosis, pulmonary embolism, skin burns, or nerve damage) was 0.63% (69/10,883).

The overall level of evidence of RCTs comparing ELT with surgical ligation and vein stripping ($n = 6$) was graded as moderate to high. In the trials, recovery after treatment (median number of days to return to work) was significantly shorter after ELT (4 days after ELT vs. 17 days after surgery; $P = .005$). Major adverse events occurring after surgery were not significantly more numerous than those after ELT (0.4%; $n = 1$). Treatment effectiveness as measured by imaging-defined vein absence or closure, symptom relief, or health-related quality of life (HRQOL) were similar in the 2 treatment groups, and both treatments resulted in significant improvements in these outcomes. Recurrence was low after both treatments at follow-up but neovascularization (growth of new vessels), a key predictor of long-term recurrence, was significantly more common (18% vs. 1%; $P = .001$) after surgery. Although patient satisfaction was reported to be high (> 80%) with both treatments, patient preferences evaluated through recruitment process, physician reports, and consumer groups were strongly in favour of ELT. For patients with VV, minimal complications, quick recovery, and dependability of outpatient scheduling were key considerations.

Cost Analysis

As the clinical effectiveness of the 2 treatments was similar, a cost analysis was performed to compare the differences in resource use and costs. A budget impact analysis was also performed to evaluate potential costs of introducing ELT as an Ontario health service. The average case cost (based on direct hospital costs and medical resources) for surgical vein stripping was estimated to be \$1,799 (Cdn). The estimated average case cost for ELT, which included device-related costs, physician fees, and hospital costs, was \$2,025 (Cdn) (where hospital-ELT costs are the same as surgery) or \$1,602 (Cdn) (where ELT hospital costs 40% less than surgery).

A 5-year projection model was constructed to estimate annual volumes and costs based on historical patterns of surgical vein stripping for VV in the province. In 2007/2008, there were 3,481 surgical vein stripping procedures (28% of which were for repeat surgical procedures) performed in Ontario. The annual volume of ELT procedures currently performed in 20 private clinics in Ontario was estimated to be approximately 840 cases. If ELT were to be publicly reimbursed, it would capture approximately 35% of the vein stripping surgeries in the first year, increasing to 55% in subsequent years. The cost to the

province to meet needs for vein stripping surgery would be approximately \$5.9 million. Reimbursed ELT would cost between \$7.1 million (Cdn) and \$8.2 million (Cdn), depending upon the real hospital costs.

The conclusions on the comparative outcomes between ELT and surgery are summarized in the table below.

Table 1: Outcome Comparisons of ELT Versus Surgery for Varicose Veins

Outcome Comparators	
Postprocedural pain, minor complications	ELT < Surgery
Length of recovery	ELT < Surgery
Major adverse events	ELT < Surgery
Effectiveness – imaging-defined vein occlusion	ELT ~ Surgery
Effectiveness – vein symptom improvement	ELT ~ Surgery
Effectiveness – HRQOL	ELT ~ Surgery
Recurrence	ELT ~ Surgery
Patient satisfaction	ELT ~ Surgery
Patient preference	ELT > Surgery
Procedure costs	ELT ~ < Surgery
Budget impact	ELT > Surgery

Abbreviations: ELT, endovascular laser therapy; HRQOL, health-related quality of life.

The results of the evidence-based review on ELT for VV are summarized below:

Patient Outcomes – ELT versus Surgery

- ELT has been shown to result in faster recovery than surgery. This is attributable to a reduction in pain, fewer minor complications, and the use of local anesthesia with immediate ambulation.
- ELT is as effective as surgery in the short term as assessed by imaging anatomic outcomes, symptomatic relief, and HRQOL outcomes.
- Recurrence rate after treatment is similar between the 2 modalities, but neovascularization, a key predictor of long-term recurrence, is significantly higher with surgery.
- Patient satisfaction is equally high after both treatments, but patient preference is much more heavily weighted toward ELT. Surgeons performing ELT are satisfied with treatment outcomes and offer ELT as an alternative to surgery.

Clinical or Technical Advantages – ELT Over Surgery

- An endovascular approach can more easily and more precisely treat multilevel disease and difficult-to-treat areas.
- ELT is an effective and a less invasive treatment for the elderly with venous reflux and those with venous leg ulcers.

System Outcomes – ELT Replacing Surgery

- ELT may offer system advantages in that the treatment can be offered by several medical specialties in outpatient settings.
- ELT does not require an operating room (OR) or general anesthesia but rather decants patients from the OR, it could result in fewer pre-surgical investigations, less demand on anesthetists' time, shorter hospital stays, decreased wait times for VV treatment, and more reliable outpatient scheduling.
- Depending on the reimbursement mechanism for the service, however, it may also result in closure of outpatient clinics with an increasingly centralization of procedures in selected hospitals with large capital budgets resulting in larger and longer waiting lists.
- Procedure costs may be similar for the 2 treatments, but budget impact may be greater with insurance of ELT because of the transfer of the cases from the private market to the public payer system.

Endovascular Radiofrequency Ablation

The Medical Advisory Secretariat (MAS) performed an evidence-based review of the safety and effectiveness of endovascular radiofrequency ablation (RFA) ablation of VV to support public financing decisions. A literature search was performed on March 9, 2010, using standard bibliographic databases for studies published up until March 2010. The MAS search identified the following evidence: 3 health technology assessments, 9 systematic reviews, 8 RCTs (5 comparing RFA to surgery and 3 comparing RFA to ELT), 5 controlled clinical trials, and 14 cohort case series (4 were multicentre registry studies).

The majority (86%) of the cohort studies (n = 3,664 patients) evaluating RFA for VV involved treatment with first-generation RFA catheters, and in all studies, the great saphenous vein was the target vein. Major adverse events were not frequently reported and the overall pooled major adverse event rate extracted from these cohort studies was 2.9% (105/3,664). Imaging-defined treatment effectiveness of vein closure rates were variable, ranging from 68% to 96% at post-operative follow-up. Vein ablation rates at 6-month follow-up were reported in 4 studies with rates close to 90%. Only 1 study reported vein closure rates at 2 years but only for a minority of the eligible cases. A large prospective registry trial that recruited over 1,000 patients in 34 largely European centres reported on treatment success on selected patient subgroups at various follow-up points up to 5 years. However, the follow-up of eligible recruited patients at all the time points was low, resulting in inadequate estimates of longer-term treatment efficacy. The 2 studies reporting on RFA ablation with second-generation catheters involved better follow-up and reported higher ablation rates at close to 100% at 6-month follow-up with no major adverse events.

The overall level of evidence of RCTs comparing RFA with surgical ligation and vein stripping (n= 5) was graded as low to moderate. In all trials, RFA ablation was performed with first-generation catheters in the OR under general anesthesia, usually without tumescent anesthesia. Procedure times were significantly longer for RFA than for surgery. Recovery after treatment was significantly quicker after RFA, both in terms of returning to usual activity and returning to work with, on average, 1 week less of work loss for RFA. The occurrence of major adverse events after surgery was higher than after RFA, but not significantly so (1.8% [n = 4] vs. 0.4% [n = 1]). Treatment effectiveness measured by imaging-defined vein absence or vein closure was comparable in the 2 treatment groups. Significant improvements in vein symptoms and HRQOL over baseline were reported for both treatment groups. Improvements in these outcomes were significantly greater in the RFA group than the surgery group in the post-operative period but not at later follow-up. Follow-up in these trials was inadequate to evaluate longer-term recurrence after either treatment. Patient satisfaction was reported to be higher for RFA.

The RCTs comparing the 2 endovascular treatment approaches were more limited. Three RCT studies compared RFA (2 with the second-generation catheters) with ELT but mainly focused on post-operative outcomes such as pain, complications, and recovery. Except for 1 small trial involving bilateral VV, vein ablation rates were not evaluated. Pain responses in patients undergoing ablation were extremely variable, and mean pain levels were significantly less with RFA than ELT for up to 2 weeks but not at 1 month. Recovery, evaluated as return to usual activity or return to work, was similar in the treatment groups. Vein symptoms and HRQOL improved in both groups but were significantly better in the RFA group than the ELT group, once again at 2 weeks but not at 1 month. Several controlled clinical studies evaluated vein ablation rates by comparing the treatments between centres or within centres between individuals or over time. Comparisons in these studies were inconsistent with vein ablation rates for RFA reported to be similar to, higher than, and lower than those with ELT.

Cost Analysis

RFA and surgical vein stripping, the main comparator reimbursed by the public system, are comparable in clinical benefits. A cost analysis was therefore conducted to identify the differences in resources and costs involved in both procedures, and a budgetary impact analysis (BIA) was conducted to project costs over a 5-year period in Ontario. The target population of this economic analysis was patients with symptomatic VV, and the primary analytic perspective was that of the Ministry of Health and Long-Term Care.

The average case cost (based on Ontario hospital costs and medical resources) for surgical vein stripping was estimated to be \$1,799 (Cdn). In order to calculate a procedural cost for RFA, it was assumed that the hospital cost and physician labour fees, excluding anesthesia and surgical assistance, were the same as for vein stripping surgery. The manufacturer also provided details on the RFA generator, with a capital cost of \$27,500 and a lifespan of 5 years) and the disposables (catheter, sheath, guidewire) with a cost of \$673 (Cdn) per case. The average case cost for RFA was therefore estimated to be \$1,356 (Cdn). One-way sensitivity analysis was also conducted with hospital cost of RFA varied to 60% that of vein stripping surgery (average cost per case = \$627.08) to calculate an impact to the province.

Historical volumes of vein stripping surgeries in Ontario were used to project surgeries in a linear fashion up to 5 years into the future. Volumes for RFA and ELT were calculated based on share capture from the surgery market (based on discussion with clinical expert opinion) and existing private data (based on discussion with the device manufacturer). RFA is expected to compete with ELT and capture some of the market. If ELT is reimbursed by the public sector, numbers will continue to increase from previous private data and share capture from the conventional surgical treatment market. Therefore, the number of RFA cases will also increase since RFA will be capturing a share of the ELT market. A budget impact to the province was then calculated by multiplying volumes by the cost of the procedure.

RFA is comparable in clinical benefits to vein stripping surgery. It has the extra upfront cost of the generator and cost per case for disposables but does not require an OR or anesthetist or surgical assistant. The impact to the province is expected to be \$5 million (Cdn) by Year 5 with the introduction of new ELT and RFA image-guided endovascular technologies and existing surgery for VV.

The conclusions on the major comparative outcomes between RFA and surgical ligation and saphenous vein stripping and between RFA and laser ablation for VV treatment are summarized below.

Table 2. Outcome Comparisons of Endovascular Radiofrequency Ablation for Varicose Veins

Outcome Comparators	RFA vs. Surgery	RFA vs. ELT
Postprocedural pain, minor complications	RFA < Surgery	RFA < ELT
Length of recovery	RFA < Surgery	RFA ~ ELT
Major adverse events	RFA < Surgery	RFA ~ ELT
Effectiveness – imaging-defined vein occlusion	RFA ~ Surgery	RFA ? ELT
Effectiveness – vein symptom improvement	RFA ~ Surgery	RFA ~ ELT
Effectiveness – HRQOL	RFA ~ Surgery	RFA ~ ELT
Recurrence	RFA ? Surgery	RFA ? ELT
Patient satisfaction	RFA > Surgery	RFA ? ELT
Patient preference	RFA > Surgery	RFA ? ELT
Procedure costs	RFA < Surgery	RFA ~ ELT
Budget impact	RFA < Surgery	RFA ~ ELT

Abbreviations: ELT, endovascular laser ablation; QOL, quality of life; RFA, radiofrequency ablation.

The outcomes of the evidence-based review on these treatments for VV based on different perspectives are summarized below:

RFA First-generation Versus Second-generation Catheter with Segmental Delivery

- Ablation with second-generation catheters and segmental ablation offered the technical advantages of improved ease and significant decreases in procedure time. RFA ablation with second-generation catheters is also no longer restricted to smaller (< 12 mm diameter) saphenous veins.
- The safety profile with the new device and method of energy delivery is at least as good as or better than that of the first-generation device. No major adverse events were reported in 2 multicentre prospective cohort studies at the 6-month follow-up with over 500 patients. There were significantly fewer postoperative minor complications with RFA ablation than with ELT in 2 RCTs.
- The ablation rates of RFA treatment using second-generation catheters were higher than when using first-generation catheters and more comparable with the consistently high rates of ELT.

Endovascular RFA Versus Surgery

- RFA has a quicker recovery attributable to decreased pain and fewer minor complications.
- In the short term, RFA is comparable to surgery in treatment effectiveness as assessed by imaging-defined outcomes such as vein closure, flow, or reflux. Other treatment outcomes such as symptomatic relief and HRQOL were significantly improved in both groups.
- Longer-term follow-up was inadequate to evaluate recurrence. .
- Patient satisfaction was higher for RFA than for surgery at various follow-up times, and patient preference was stronger for an endovascular approach.

Endovascular RFA Versus ELT

- There was significantly less postoperative pain with RFA compared to ELT, but differences are not significant when pain was adjusted for analgesic use, and differences did not persist at 1-month follow-up.
- Treatment effectiveness between groups was similar in the short term (within 1 month) when measured as symptom relief and improvement in HRQOL.
- Treatment effectiveness measured as imaging-defined vein ablation was not reported in any RCTs, and results were inconsistently reported in observational trials.
- Follow-up was inadequate to assess longer-term recurrence after either treatment.
- There is insufficient evidence, particularly on treatment effectiveness or durability, to recommend one method of endovascular thermal ablation, RFA or ELT, over the other.

System Outcomes – RFA Replacing Surgery or Competing with ELT

- RFA, like ELT, may offer system advantages in that the treatment can be offered by several medical specialties in outpatient settings since it does not require an OR or general anesthesia.
- The treatment may result in decanting patients from OR, decreased presurgical investigations, decreased demand on anesthesiologists' time, decreased hospital stay, and decreased wait time for VV treatment, leading to more reliable outpatient scheduling.
- Procedure costs may be less for endovascular approaches than surgery, but the budget impact will be greater with insurance of endovascular treatments because of the transfer of cases from the private market to the public payer system.
- Competition between RFA and ELT endovascular approaches is likely to continue to stimulate innovation and technical changes to advance patient care and result in competitive pricing.

Decision Determinants

The Ontario Health Technology Advisory Committee (OHTAC) has developed a decision-making framework that consists of 7 guiding principles for decision making and a decision-making tool called the Decision Determinants tool. When making a decision, OHTAC considers 4 explicit main criteria: overall clinical benefit, value for money, feasibility of adoption into health system, and consistency with expected societal and ethical values. For more information on the decision-making framework, please refer to the *Decision Determinants Guidance Document* (http://www.health.gov.on.ca/english/providers/program/mas/pub/guide_decision.pdf).

A summary of the Decision Determinants is shown in Appendix 1.

OHTAC Recommendations

In considering the evidence-based analyses, the Ontario Health Technology Advisory Committee (OHTAC) took into account the following:

- high burden of venous disease, need, and moderate evidence of effectiveness and safety;
- consistency with expected societal and ethical values;
- moderate uncertainty of cost-effectiveness due to similarities of treatment costs and effects and limited economic studies; and
- moderate uncertainty of feasibility of adoption into the health system.

Based on these considerations, OHTAC made the following recommendations for both endovascular laser treatment (ELT) and radiofrequency ablation (RFA).





- ELT and RFA are less invasive, safe, and cost-effective alternatives to surgical vein stripping that should be made available to people with symptomatic varicose veins (VV) and saphenous venous reflux demonstrated on a full duplex ultrasound investigation and, when feasible, following a failed trial of conservative management.
- There is an absolute medical necessity for a surgical approach including RFA or ELT treatment of VV associated with venous ulcer, thrombophlebitis, or bleeding. However, the decision to recommend a similar treatment approach based on other symptoms attributed to chronic venous reflux should be made on an individual basis and guided by validated disease severity scales such as the Venous Clinical Severity Score.
- Any intervention for VV for cosmetic indications should not be provided as an insured service.
- Mechanisms to ensure quality assurance for both the physicians performing endovascular treatments and the facility where the treatments are being performed should be considered as part of any implementation plan.

Appendix 1 – Decision Determinants

Endovascular Laser Therapy

Based on the evidence reported in the *Endovascular Laser Therapy for Varicose Veins* review and the deliberations of the Ontario Health Technology Advisory Committee (OHTAC) on November 27, 2009, pertaining to this evidence, OHTAC rated the following decision determinants criteria:





Table A1: Decision Determinants for Endovascular Laser Therapy for Varicose Veins

Criterion		Rating
Overall clinical benefit		High
Consistency with expected societal and ethical values		Moderate
Value for money		Moderate with uncertainty
Feasibility of adoption into the health system		Moderate with uncertainty

Endovascular Radiofrequency Ablation

Based on the evidence reported in the *Endovascular Radiofrequency Ablation for Varicose Veins* review and the deliberations of OHTAC on August 28, 2010, pertaining to this evidence, OHTAC rated the following with respect to the decision determinants criteria:

Table A2: Decision Determinants for Endovascular Radiofrequency Ablation for Varicose Veins

Criterion		Rating
Overall clinical benefit		High
Consistency with expected societal and ethical values		Moderate
Value for money		Moderate with uncertainty
Feasibility of adoption into the health system		Moderate with uncertainty