**Long-term follow up for different varicose vein therapies: is surgery still
the best?**

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Introduction

Varicose vein disease is a common condition affecting a significant proportion of the population and is known to lead to worse quality of life^{1,2}. Early monographs of venous disease and their surgical treatment date back to 1550 BC. Celcus, in first century Rome, proposed the concept of ligation and division of bleeding varicosities, while Galen, in the second century, introduced ligation and vein avulsion using specialised hooks³. To a large extent, these early works inspired the current surgical techniques used to treat varicose veins.

Management of the condition has been transformed further over the past decade with surgical treatment of superficial venous incompetence no longer the mainstay of intervention. The introduction of endovenous thermal ablation, using either radiofrequency ablation (RFA) or endovenous laser ablation (EVLA), as well as improvement made in the use of foam sclerotherapy, however, gradually led to the desertion of surgery. The National Institute of Health and Clinical Excellence (NICE) guidelines (United Kingdom) on the management of varicose veins already recommend endothermal ablation as the first option to consider, relegating surgery only to a third line alternative⁴ (Table 1).

Despite endothermal methods being accessible, uncertainty remains as to the ideal long-term treatment for varicose veins which would offer the best outcomes.

Anatomical Success

Modern day surgical treatment of varicose vein disease typically involves ligation of the saphenofemoral junction (SFJ) (high ligation) or saphenopopliteal junction (SPJ) with or without stripping of the truncal vein. The technique allows the instant elimination of reflux in the offending vein and is often carried out under general or regional anaesthesia.

This type of surgical intervention has been found to be superior to ligation alone.

Dwerryhouse et al. (1999) looked at the reoperation rate for patients having surgery for GSV incompetence⁵. This was a randomised study comparing ligation of sapheno-femoral (SFJ) only to SFJ ligation and stripping, and patients were initially followed up for five years. The rate of reoperation at 5 years was found to be 17% in those receiving ligation only compared to 4% in those also having stripping⁵. After 11 years, the corresponding figures were 29% in the ligation only group and 11% in the ligation and stripping group⁶.

Occlusion rate comparisons have revealed some conflicting results between surgical and endovenous management of varicose veins.

In the EVOLVEs randomised controlled trial comparing RFA to surgery, in the form of high ligation and stripping (HL/S), Lurie et al. (2005) recruited 85 patients and followed them for 2 years. Both treatment modalities were found to have comparable closure rates by the end of the study period⁷.

However, later studies, such as another RCT comparing RFA and HL/S showed that endothermal ablation was superior. With 93 patients (98% CEAP class C2-3) randomised and treated as day-cases, all the patients receiving RFA had complete success of their treatment compared to 88% in those having surgery⁸.

Rasmussen et al. (2007) compared another endothermal ablation technique (EVLA) to surgery (HL/S) in patients with C2-4 disease and found that, after 6 months, the occlusion rate was 98% in the ligation and stripping group and 94.4% in the EVLA group⁹. After 5 years, there were more cases of open, refluxing GSVs in the EVLA group compared to the surgery group (18% vs. 10%; $p=NS$), while there were slightly more recurrent varicose veins in the surgery group than the EVLA group (54.6% vs. 46.6%; $p=NS$)¹⁰. The rate of re-operations was, however, comparable (38.6% in EVLA and 37.7% in surgery; $p=NS$).

Another comparison of endovenous laser treatment and surgery (high ligation and stripping) showed that, at 3 months, the occlusion rate was 94% in the thermal ablation group compared to 87.5% in the surgical group¹¹.

In a prospective randomised controlled trial comparing EVLA to surgery (HL/S), Christenson et al. (2010) randomised 204 patients, 97% of whom were in CEAP class C2-C4. They found that, at 1 year and 2 years, the GSV was absent in all patients who had surgery¹². There were 7 cases of treatment failure in the EVLA group (5 partial reopening and 2 complete reopening), but this did not reach significance ($p=0.51$)¹².

A comparison of the endothermal methods (RFA and EVLA), high ligation and stripping and ultrasound-guided foam sclerotherapy (UGFS) by Rasmussen et al. (2011) recruited and randomised 500 patients. Most (95%) of patients were of CEAP class C2-3. It showed that the failure rates (defined as an open segment of more than 10cm in length) at 1 year was 5.8% (RFA), 4.8% (EVLA), 4.8% (surgery) and 16.3% (UGFS)¹³.

Long-term follow-up for RFA confirms the effectiveness of this endothermal method. Indeed, Proebstle et al. (2015) conducted an international, prospective, multicentre study to investigate the effects of RF segmental thermal ablation on the GSV in 225 patients (295 limbs)¹⁴. At 5 years, using a Kaplan-Meier method, the GSV occlusion rates was found to be 91.9%, while 94.9% of GSVs were found to be free from reflux¹⁴.

Biemans et al. (2013) conducted an RCT comparing EVLA, UGFS and surgery and reported after one year. More than 90% of the study population had a CEAP class C2-C4. The anatomic success rate at that point for EVLA and surgery were comparable (88.5% vs. 88.2%), while that of UGFS was lower (72.7%)¹⁵. After 5 years, the GSV was successfully treated/absent in 85% of legs in the surgery group, 77% in the EVLA group and 23% in the UGFS group ($p<0.001$)¹⁶. At 5 years, patients receiving surgery or EVLA were also found to be four times more likely to have closure of the above-knee GSV than patients in the UGFS group¹⁶.

The CLASS trial is an ongoing multicentre study comparing foam sclerotherapy, surgery and EVLA. It has recruited 795 patients (96% of them in CEAP class C2-C4)

and preliminary results at 6 months show significantly higher closure rates in patients undergoing surgery (84.4%) or EVLA (83.0%) than those receiving foam sclerotherapy (53.6%; $p < 0.001$) (no significant differences in closure rates between EVLA and surgery)¹⁷.

The above studies demonstrate that surgery is a durable method and, at the very least, is comparable to endothermal methods, but superior to UGFS. However, anatomical success is considered more of a surrogate outcome measure, and the findings do not offer any indications as to the clinical or functional outcome following varicose vein intervention.

Clinical and Quality of Life Measures

The effect of surgery on quality of life (QoL) was investigated by Mackenzie and colleagues (2002) who recruited 203 patients undergoing surgery for varicose vein. Even though the Aberdeen Varicose Vein Symptom Severity Score (AVVSSS) was lower (improved) at the 4 week point, this was not significant (Wilcoxon signed rank test, $p = 0.44$) until 6 months and 2 years after intervention ($p = 0.001$)¹⁸. The same research group also found that the proportion of GSV removed in the thigh correlated with gains in QoL at 6 months and 2 years after the procedure ($p = 0.031$ and $p = 0.14$, respectively)¹⁹. They concluded that there is an improvement in QoL seen as early as 4 weeks from the surgical procedure which continues for as long as 2 years.

In the EVOLVeS study, the clinical score using the Venous Clinical Severity Score (VCSS) a few days after intervention (3 days and 1 week) showed that patients undergoing endothermal ablation (RFA) had a significantly more rapid clinical improvement than surgery, although that difference disappeared by the third week⁷.

The global QoL score (using CIVIQ2) also demonstrated a worsening of the QoL in surgery over the first few weeks and was still present by the end of the 2 years follow-up.

This early difference in clinical score was again shown in Rasmussen and colleagues' study with worse VCSS in patients having surgery compared to those having EVLA, but this was no longer the case by the end of the first month¹⁰. QoL, as measured using the AVVSS, improved significantly in both groups from the 3 month point onwards¹⁰.

Other studies, however, do not demonstrate such discrepancy in clinical or QoL scores. In their RCT, Christenson et al. found comparable improvement in both the EVLA group and surgery group, despite the EVLA group having a higher incidence of recurrence with symptoms¹².

Shadid et al. (2012) carried out a randomised controlled study comparing ultrasound-guided foam sclerotherapy (UGFS) and surgery in the treatment of incompetent GSV. At the 2 year follow-up, no difference was apparent between the two groups with regards to VCSS or the EuroQoL's EQ-5D²⁰. A similar finding was observed in the MAGNA trial with the CIVIQ and EQ-5D scores improving in all groups (EVLA, UGFS and surgery) at 3 months and remaining stable

In the CLASS trial, Brittenden et al. (2015) recruited 785 patients, randomising them to foam sclerotherapy, surgery or EVLA¹⁷. At 6 weeks, a greater improvement in the VCSS score was found in those undergoing surgery (and EVLA) compared to those receiving foam sclerotherapy (1.8 vs 2.2; $p < 0.001$). This difference was no longer present by 6 months though. The AVVQ also showed that patients having surgery achieved a better QoL at 6 months compared to foam sclerotherapy (7.8 vs. 9.1; $p < 0.01$).

Return to Activity and Work

Post-surgical patients tend to take longer to go back to their normal activities or work. Lurie and his colleagues (2003) showed that patients from the surgery group were back to their normal activities a mean 3.89 days after their procedure compared to a

mean of 1.15 days for RFA ($p=0.2$)²¹. Patients were back at work a mean 4.7 days after their radiofrequency ablation and 12.4 days after having surgery. When compared to EVLA, a similar picture becomes apparent. Similar differences in return to activities was also noted in Darwood (2008) and Subramonia's studies¹¹⁸. Rasmussen et al. (2011) also found that patients undergoing surgery took longer to return to their normal activities (median 4 days compared to less than 2 days for the endovenous methods)¹³. Such a difference was no longer apparent though when the time to return to work was looked at with patients returning to work a median 4.3 days following surgery compared to 3.6 days for EVLA¹³.

Complications

Commonly reported complications following varicose vein surgery are wound infections, haematoma formation, recurrence, numbness, paraesthesia, neuralgia, lymphatic damage, major vessel injury, residual veins and venous thromboembolism (deep vein thrombosis (DVT) and pulmonary embolus (PE))^{23, 24}.

In their comparative RCT, Rasmussen et al. (2011) recorded one incidence of DVT, 5 cases of paraesthesia and 6 of hyperpigmentation in patients having surgery¹³. The rate of these latter two complications was similar to those reported for the endovenous procedures, however. There was a significantly higher incidence of phlebitis in the endovenous ablation methods ($p=0.006$)¹³.

Christenson et al. (2010) noted significantly more cases of bruising in their surgical group compared to the EVLA group (15 vs. 2)¹². No cases of wound infection or DVT were reported.

In the MAGNA study, a significantly higher number of patients undergoing surgery suffered from wound infection requiring systemic antibiotics ($p=0.03$)¹⁵. The overall rate of complications was also higher with surgery, but this was not significant ($p=0.64$).

In the CLASS trial, the surgery group had a comparable overall complication rate to UGFS and EVLA (3.5%, 3.8% and 3.3%, respectively) and similar serious adverse events related to treatment with the endovenous procedures (1.4%)¹⁷. A rather high incidence of numbness (15.6%) and persistent bruising (17.0%) was found to be still present at 6 months.

Cost-Effectiveness

As the cost of healthcare is increasingly becoming a worldwide issue, there is a drive to use the most cost-effective interventions to achieve the best outcomes in varicose vein disease management.

Rasmussen et al. (2011) conducted a randomised trial comparing EVLA, RFA, UGFS and surgery and looked at the cost of each procedure based on the reimbursement rates and productivity level in Denmark. Foam sclerotherapy was found to be the cheapest, while both surgery and EVLA were found to be the most expensive treatment options¹³.

The National Institute of Health and Care Excellence (NICE, United Kingdom) uses a threshold of £20,000 to indicate the cost-effectiveness of treatments in the National Health Service (NHS). In their cost-effectiveness analysis, the CLASS trial investigators found that, at such a ceiling, EVLA had the highest probability of being the most cost-effective treatment for varicose vein disease compared to surgery²⁵.

Cost-effectiveness analysis conducted by NICE itself showed that surgery produced fewer gains in quality of life years (QALYs) at an increased cost compared to the endothermal methods²⁶. Despite being more costly than foam sclerotherapy, endothermal ablation was also found to produce the greatest QALY gain and was the most clinically effective treatment. The incremental cost-effectiveness ratio (ICER, difference in cost between two possible interventions, divided by their effect) was in

favour of endothermal ablation, making this method the most cost-effective strategy in treating varicose veins²⁶.

Conclusion

The case for the continuing use of surgical treatment options in contemporary practice soon becomes very apparent. It is a proven technique providing good anatomic success and instantaneous elimination of the cause of superficial incompetence. However, once clinical and quality of life scores are taken into account, deficiencies start appearing with this intervention, with slower improvement noted. Moreover, it often results in a delay before patients can resume their normal activities and work, and can often lead to serious complications. The cost of surgical intervention is also quite prohibitive and it is proving to be a less cost-effective treatment option compared to the endovenous methods. The choice of varicose vein treatment to use in current practice is dictated by its cost-effectiveness, thereby, making surgery increasingly harder to justify.

Surgery, however, remains a very efficient method to treat venous incompetence and refinement of the technique could potentially enable it to improve some of the outcomes and hopefully make it a more cost viable alternative. Hence, endovenous ablation, most specifically endothermal methods, will be around for the foreseeable future, unless the newer non-thermal, non-tumescent (NTNT) methods prove to be more advantageous²⁷⁻²⁹.

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