EDITORIAL

Comparison of Laser Ablation, Foam Sclerotherapy and Surgery (CLASS) Trial

The five year outcomes of the CLASS trial, which compared three treatments for patients with symptomatic primary varicose veins, were published recently.[1] In that study, 798 participants were randomised to endovenous laser ablation of the main incompetent venous trunk, with foam sclerotherapy for residual non-trunk varicosities, ultrasound guided foam sclerotherapy alone, or surgery. Study recruitment occurred between November 2008 and October 2012. At that time all the three treatments had been shown to have good technical and short term clinician reported outcomes. However, there was little evidence about patient reported outcomes, medium term clinical outcomes (up to five years), and cost effectiveness of the endovenous treatments.[2–4]

The primary outcome measures were quality of life at six months and five years; and cost effectiveness (cost per quality adjusted life year [QALY] gained). Secondary outcomes were complication rates and measures of clinical success, such as presence of varicose veins, return to activities, and Venous Clinical Severity Score; and technical success (truncal ablation). Return to normal activities was assessed, using a specially developed questionnaire.[5]

Six month results of the trial were published in 2014:[5–7] all three treatments were shown to be safe and effective, but laser ablation and foam sclerotherapy were associated with a quicker return to normal activities than surgery. After five years there was still a substantial response rate, with 75% of patients reporting their outcomes. For the five year analysis, to account for multiple testing, only primary outcomes with a $p < .003$ were considered to be significant. QoL was improved in all groups compared with baseline.

QoL measures after laser ablation and surgical treatment were superior to those after foam sclerotherapy: this significant clinical difference was much more marked at five year follow up than at six month follow up. There were no differences in disease specific QoL between the laser ablation and surgery groups; or in generic quality of life between the three groups.

The proportion of patients who reported having no varicose veins after five years was lower than predicted in previously published cost effective analysis models: foam sclerotherapy 47%, surgery 54%, and laser 58%.[8] The extent of varicose veins at five years, by participant reported visual analogue score was less for laser ablation ($p < .001$) and for surgery ($p < .001$) than for foam sclerotherapy. Nevertheless, patient satisfaction was high across all three groups, and the majority of participants would recommend the treatment they had received to family or friends. The re-intervention rate over the five year period was low (surgery 7%, laser 11%, and foam sclerotherapy 14%).

With regard to cost effectiveness, our previously constructed Markov model was updated to take account of all the five year findings. This has not altered our previous conclusion, despite a lower rate of re-intervention and a higher recurrence rate than previously predicted, laser ablation under local anaesthetic in a treatment room setting had the highest probability (77%) of being cost effective (using a ceiling willingness to pay ratio of £20 000 per QALY gained). The trial based analysis showed a similar outcome for the three way comparison. There was considerable uncertainty in the two way analysis comparing foam sclerotherapy and surgery, with differences in the model and trial based analysis.

Our findings provide clinical, quality of life, and cost information to guide choices of patients and venous specialists between the several treatment options available for varicose veins. The trial did not include radiofrequency ablation (RFA), which is a commonly used endothermal alternative to laser ablation. By and large, the evidence shows little difference in outcomes between laser ablation and RFA, so RFA probably has similar advantages, provided that it can be done at similar cost to laser.[8] When using endothermal ablation (laser or RFA), practice varies substantially in terms of whether and when varicosities are treated, concomitantly or at a later date, and by foam or phlebectomies. These variations will affect both costs and outcomes, and they need to be considered alongside the findings of the CLASS trial in which later treatment with foam sclerotherapy was performed in 31% of participants in the laser ablation group.

Foam sclerotherapy is technically possible in most patients, and a case has been made previously that it is so inexpensive that it dominates other treatments in terms of cost.[9] However, the poorer long term clinical outcomes and cost effectiveness documented in the CLASS trial should prompt caution in promoting foam sclerotherapy as a routine treatment for patients with primary varicose veins. Guidance from NICE (the National Institute for Health and Care Excellence) in the UK, published in 2013, recommends foam as second choice after endothermal ablation, for treating varicose veins. When the guidance is reviewed, this recommendation may need to be reconsidered in the light of the CLASS results.[8]

Finally, CLASS has shown how commonly varicose veins recur, five years after apparently thorough treatment. This

https://doi.org/10.1016/j.ejvs.2020.03.040

highlights the chronic tendency that many people have for developing more veins and could call into question the value of treatment, especially in publicly funded health services. In the UK, NICE recommendations that patients with troublesome symptomatic varicose veins (CEAP classes C2—C3) should be eligible for treatment have been widely ignored by health service commissioners and providers, who restrict treatment to those with ulcer, bleeding, or phlebitis. Balancing cost and value is a challenge for healthcare systems worldwide. The CLASS trial provides important new evidence that should help to influence the decisions of policy makers, payers, clinicians, and patients with varicose veins.

Acknowledgements

The project was funded by the NIHR Health Technology Assessment Programme (Project number: 06/45/02).

REFERENCES

1 Brittenden J, Cooper D, Dimitrova M, Scotland G, Cotton SC, Elders A, et al. Five year outcomes of a randomized trial of treatments for varicose veins. *N Engl J Med* 2019;**381**:912—22.
2 Darwood RJ, Theivacumar N, Dellagrammaticas D, Mavor AI, Gough MJ. Randomized clinical trial comparing endovenous laser ablation with surgery for the treatment of primary great saphenous varicose veins. *Br J Surg* 2008;**95**:294—301.
3 Rasmussen LH, Bjoern L, Lawaetz M, Blemings A, Lawaetz B, Eklof B. Randomised trial comparing endovenous laser ablation of the great saphenous vein with high ligation and stripping in patients with varicose veins: short-term results. *J Vasc Surg* 2007;**46**:308—15.
4 Wright D, Gobin JP, Bradbury A. Varisolve polidocanol microfoam compared with surgery or sclerotherapy in the management of varicose veins in the presence of trunk vein incompetence: European randomised controlled trial. *Phlebol* 2006;**221**:180—90.
5 Cotton SC, MacLennan G, Brittenden J, Prior M, Francis J. Behavioural recovery after treatment for varicose veins. *Br J Surg* 2016;**103**:374—81.
6 Brittenden J, Cotton SC, Elders A, Ramsay CR, Norrie J, Burr J, et al. A randomised trial of varicose vein treatments. *N Engl J Med* 2014;**371**:1218—27.
7 Tassie E, Scotland G, Brittenden J, Cotton SC, Elders A, Campbell MK, et al. Cost-effectiveness of ultrasound guided foam sclerotherapy (UGFS), endovenous laser ablation (EVLA), and surgery as treatments for primary varicose veins: from the randomized CLASS trial. *Br J Surg* 2014;**101**:1532—40.
8 National Institute for Health and Care Excellence. *Varicose veins in the legs CG168*. Available at: http://guidance.nice.org.uk/CG168.
9 Carroll C, Hummel S, Leaviss J, Ren S, Stevens JW, Cantrell A, et al. Systematic review, network analysis and exploratory cost-effectiveness model of randomised trials of minimally invasive techniques versus surgery for varicose veins. *Br J Surg* 2014;**101**:1040—52.

Julie Brittenden*
Institute of Cardiovascular Research, University of Glasgow, Glasgow, UK

Bruce Campbell
University of Exeter Medical School, Honorary Vascular Consultant, Royal Devon and Exeter Hospital, Exeter, UK

*Corresponding author. Vascular Surgery, Institute of Cardiovascular Research, University of Glasgow, Glasgow, G81 4HX, UK.
Email-address: Julie.brittenden@glasgow.ac.uk (Julie Brittenden)