NICE National Institute for Health and Care Excellence

Surveillance report 2016 – Varicose veins in the legs (2013) NICE guideline CG168

Surveillance report

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Contents

Surveillance decision

We will not update the guideline at this time.

Reason for the decision

We found 17 new studies through surveillance of this guideline. None of the new evidence considered in surveillance of this guideline was thought to have an effect on current recommendations.

See how we made the decision for further information.

Commentary on selected new evidence

With advice from topic experts we selected 2 studies for further commentary.

Assessment and treatment in a vascular service – Interventional treatment – hierarchy of treatments

We selected the CLASS trial for a full commentary because it is a relevant new UK study which confirms endothermal ablation as the first line treatment for varicose veins and truncal reflux, affirming the sequence prescribed in the guideline.

What the guideline recommends

For interventional treatment of people with confirmed varicose veins and truncal reflux, the guideline endorses the following sequence (recommendation 1.3.2):

- endothermal ablation
- ultrasound-guided foam sclerotherapy, if endothermal ablation is unsuitable
- surgery, if ultrasound-guided foam sclerotherapy is unsuitable.

Methods

Brittenden et al. (2015) conducted a non-blinded, randomised controlled trial (the CLASS trial) designed primarily to assess the clinical effectiveness and cost-effectiveness of three treatment modalities: ultrasound-guided foam sclerotherapy, endovenous laser ablation and surgery.

Adult patients over 18 years of age referred from primary care to specialist vascular centres in the UK for treatment of primary varicose veins with symptomatic (CEAP grade 2 or above) great or small saphenous main truncal incompetence (reflux >1 second on duplex scanning) were included.

Patients were recruited from across 11 hospitals. Eight hospitals offered all three treatment options while three hospitals offered only foam sclerotherapy and surgery. Participants

were randomised to one of the available interventions at a given hospital.

A computer-generated randomisation system that was available to the hospitals as a web-based or telephone system was used to randomise participants.

Primary outcome measures were:

- disease-specific quality of life (measured by the Aberdeen Varicose Vein Questionnaire [AVVQ]) at 6 months
- generic quality of life (as measured by the European Quality of Life-5 Dimensions [EQ-5D] and Short Form questionnaire-36 items [SF-36]) at 6 months
- cost-effectiveness (measured as cost per quality-adjusted life-year [QALY] gained) at 6 months.

Secondary outcome measures were:

- disease-specific quality of life (measured by the AVVQ) at 6 weeks
- generic quality of life (measured by EQ-5D and SF-36) at 6 weeks
- clinical success of intervention assessed by:
  - the reduction in the venous clinical severity score (VCSS) at 6 weeks and 6 months
  - the presence of residual varicose veins (assessed by a visual analogue scale [VAS] by both patients and nurses) at 6 weeks and 6 months
  - patients' recollection of pain (measured on a VAS) at 6 weeks
  - complication rates
  - return to normal activities (behavioural recovery)
- anatomical success of intervention (assessed by duplex scan showing partial or complete ablation of, or the presence of reflux in, the great saphenous vein [GSV], the small saphenous vein [SSV] or both GSV and SSV [complete leg]) at 6 weeks and 6 months

- costs to the health service and participants of each intervention and any subsequent care.

Results

Recruitment and randomisation took place over a period of 48 months. In total 6592 patients with varicose veins were screened for eligibility in this time. Of those screened, 51% (n=3369) met the eligibility criteria, 43% (n=2847) were ineligible and the eligibility status of the remaining 6% (n=376) was unknown.

About a quarter of the eligible patients (n=798) agreed to take part in the trial and 2571 declined, the main reason for this being that a particular treatment was preferred. There were also 13 patients who were found to be ineligible after randomisation, leaving 785 participants in the study.

The mean age of study participants was 49 years and 57% were female. The mean body mass index was 27 kg/m^2, 61% were in employment and 28% of participants had varicose veins in both legs; these participants nominated their worst leg as their 'study leg'.

Eleven per cent of participants had undergone previous varicose vein treatment of their non-study leg and 1% had received previous sclerotherapy for varicose veins in their study leg.

An intention to treat analysis was carried out. The trial groups were as follows: foam sclerotherapy (n=292), surgery (n=294) and laser ablation (n=212). Results of the primary outcomes are presented below.

Surgery compared with foam sclerotherapy:

- There was significant health gain for AVVQ in favour of surgery at 6 months (effect size −1.74, 95% CI −2.97 to −0.50).
- There were no significant differences between sclerotherapy and surgery for SF-36 (8 domains or physical and mental components) or EQ-5D (overall score or ED-5D VAS) at 6 months.

Surgery compared with laser ablation:

- There was no significant difference between surgery and laser ablation for AVVQ at 6 months (effect size −0.63, 95% CI −2.16 to 0.90).
- There were no significant differences between surgery and laser ablation for SF-36 (domains or components scores) or EQ-5D (overall score or VAS) at 6 months.

Laser ablation compared with foam sclerotherapy:

- There was no significant difference between laser ablation and foam sclerotherapy for AVVQ at 6 months (effect size 0.90 and −1.06, 95% CI −2.56 to 0.43).
- There were no significant differences for SF-36 or EQ-5D at 6 months except for the mental component of SF-36 which showed benefit in favour of laser ablation (effect size 1.54, 95% CI 0.01 to 3.06).

Secondary outcomes:

- Health gains (EQ-5D) at 6 weeks were greater for laser ablation than for foam sclerotherapy (effect size 0.04, 95% CI 0.01 to 0.07).
- There were no differences in VCSS between the three treatments.
- Participants returned to a wide range of behaviours more quickly following foam sclerotherapy or laser ablation than following surgery ($p<0.05$).
- Truncal ablation rates were higher for surgery ($p<0.001$) and laser ablation ($p<0.001$) than for foam, and were similar for surgery and laser ablation.
- There were fewer procedural complications in the laser ablation group (1%) than after foam sclerotherapy (7%) and surgery (8%) ($p<0.001$).

Trial-based cost-effectiveness analysis:

- Laser ablation produced a small but non-significant increase in QALYs over both surgery and foam sclerotherapy at 6 months. In comparison with surgery, foam sclerotherapy had an ICER of £102,106 per QALY lost at 6 months, whereas laser ablation was found to be 'dominant'.
- Markov modelling showed that at 5 years, laser ablation had the highest probability (of about 79%) of being cost-effective at conventional thresholds, followed by foam (probability of about 17%) and surgery (probability of about 5%).

Strengths and limitations

Strengths

A strength of the study is that it is a relatively large, well conducted UK trial with a population that closely matched that looked at in the guideline. There is low risk of selection bias due to adequate randomisation as participants were randomised using a computer-generated randomisation system and also low risk of selective reporting as the study protocol is available and all of the study's pre-specified (primary and secondary) outcomes that are of interest in the trial have been reported in the pre-specified way.

Limitations

It is unclear whether allocation concealment was carried out prior to assignment, although the web based randomisation service would be adequate.

The following limitations were reported in the study:

- high proportion of ineligible patients and overall low recruitment rates.
- reduced target sample size due to low recruitment rates.
- lack of inclusion of radiofrequency ablation as a treatment option.

Impact on guideline

This RCT found that endovenous laser ablation is clinically and cost-effective compared to surgery and foam sclerotherapy. The study findings are consistent with the guideline which recommends endothermal ablation as first line treatment, followed by foam sclerotherapy and surgery. Therefore, this new evidence is unlikely to impact on guideline recommendations.

Assessment and treatment in a vascular service – Interventional treatment – treatment of tributaries

We selected the AVULS trial for a full commentary because it strengthens the recommendation on concomitant treatment of incompetent varicose tributaries and partly answers the research recommendation on whether tributary varicose veins should be

treated at the same time as the main truncal veins.

What the guideline recommends

Recommendation 1.3.2 of the guideline advocates treating incompetent varicose tributaries at the same time as truncal vein treatment in people with confirmed varicose veins and truncal reflux.

Methods

Lane et al. 2015 conducted a single centre randomised controlled trial (the AVULS trial) to ascertain the outcomes of delayed or simultaneous phlebectomy during radiofrequency ablation of incompetent truncal veins.

Power calculation showed that 64 participants were required per arm or 128 in total. However, the target recruitment was set at 120 participants per arm, or 240 in total, in consideration of losses to follow-up and protocol violation.

Patients with single truncal vein incompetence and visible symptomatic varicosities in the distribution of the target vein were included. Eligible patients who agreed to take part in the trial were randomised to the simultaneous or the delayed group. Randomisation was via computerised allocation at a remote location.

Participants in both arms of the trial received radiofrequency ablation of the truncal vein. Subsequently, the simultaneous group underwent tributary avulsions while the delayed group did not. All participants then received standardised above knee class II compression hosiery for 2 weeks.

The primary outcome was improvement in disease-specific quality of life (as measured by the AVVQ) at 6 months.

Secondary outcomes were:

- the need for further procedure over the intervention period
- anatomical success (assessed with colour duplex ultrasound)
- clinical disease severity (assessed using the VCSS)

- generic quality of life (as measured by the EQ-5D)
- the level of depression (assessed by the Centre for Epidemiological Studies – Depression Score [CES-D]) and
- the rate of complications.

Participants were followed up for 12 months following the procedure, with repeated quality of life measures done at 6 weeks, 6 months and 12 months and an assessment of anatomical success carried out at 6 months.

At the 6-week follow-up, participants were evaluated for the need for further intervention by independent clinicians unaware of the initial treatment group. If both patient and clinician identified symptomatic residual varicose veins, further intervention, either as foam sclerotherapy or multiple stab avulsions under local anesthesia, was carried out.

All further treatments were completed as soon as possible after the 6-week follow-up and all before the 6-month follow-up. Avulsion surgeries at the 6-week follow-up were performed under local anesthesia in the same way as the simultaneous treatment was done, with compression hosiery to be used for 2 weeks after treatment.

At the 6-month follow-up, a duplex ultrasound scan was completed to ensure closure of the treated truncal vein. This was categorised as fully occluded, predominantly occluded and fully patent. The duplex scan was performed by an independent vascular scientist blinded to the treatment allocation.

Results

From a screened population of 393 patients that presented to the Charing Cross Local Anesthetic Varicose Vein Unit for treatment there were 221 suitable patients. Of this number, 101 participants consented to randomisation and were recruited to the trial (n=50 to the delayed phlebectomy group and n=51 to the simultaneous phlebectomy group).

Primary outcome: There was a significant improvement in AVVQ scores in the simultaneous group compared to the delayed group at 6 weeks (p=0.029) but not at 6 months (p=0.120) or 12 months (p=0.387). The AVVQ score between those in the delayed group who needed further treatment compared with the simultaneous group showed a significant difference in favour of simultaneous treatment at 6 weeks (p=0.005) and 6 months (p=0.033) but not 12 months (p=0.258).

Secondary outcomes:

- There was a significant increase in the need for further treatment in the delayed group compared to the simultaneous group (36% in the delayed group required further treatment compared to 2% in the simultaneous group, RR 18.36, p<0.0001).
- There was no difference in truncal veins ablation rates between the delayed and simultaneous groups at 6 months (p=0.849).
- There was a significant improvement in the VCSS scores in the simultaneous group compared to the delayed group at all time points (6 weeks p<0.001, 6 months p=0.012, 12 months p=0.011).
- There was a significant improvement in the EQ-5D scores in the simultaneous group compared to the delayed group at 6 weeks (p=0.033) but not at 6 months or 12 months.
- There was no difference in depression scores between the groups at any time point during follow-up.
- There was 1 superficial venous thrombosis in each group but no deep vein thromboses (DVTs).

Strengths and limitations

Strengths

The strengths of the AVULS trial are its UK setting and its RCT design with a relatively low risk of selection bias due to random sequence generation.

Limitations

It is unclear whether allocation concealment was carried out prior to assignment, although the central allocation at a remote location provided by a randomisation service should be fine.

The authors noted that a significant limitation of the study is the failure to reach target recruitment over the 18-month recruitment period.

Impact on guideline

This RCT found that simultaneous treatment of varicose veins (combining truncal treatment with tributary treatment) is beneficial compared to delayed treatment. The study findings are consistent with the guideline which advocates treating incompetent varicose tributaries at the same time as the treatment of the truncal vein in people with confirmed varicose veins and truncal reflux. Therefore, this new evidence strengthens the guideline recommendations. It also partly answers the research recommendation on whether tributary varicose veins should be treated at the same time as the main truncal veins. It does not fully answer the research recommendation as further research is required.

How we made the decision

We check our guidelines regularly to ensure they remain up to date. We based the decision on surveillance 2 years after the publication of varicose veins (2013) NICE guideline CG168.

For details of the process and update decisions that are available, see ensuring that published guidelines are current and accurate in 'Developing NICE guidelines: the manual'.

New evidence

We found 17 new studies in a search for randomised controlled trials published between 1 October 2012 and 29 June 2015.

We also checked for relevant ongoing research, which will be evaluated again at the next surveillance review of the guideline.

See appendix A: decision matrix for summaries and references for all new evidence considered.

Views of topic experts

We considered the views of topic experts, including those who helped to develop the guideline and other correspondence we have received since the publication of the guideline.

Views of stakeholders

Stakeholders are consulted only if we decide not to update the guideline following checks at 4 and 8 years after publication. Because this was a 2-year surveillance review, and the decision was not to update, we did not consult on the decision.

See ensuring that published guidelines are current and accurate in 'Developing NICE guidelines: the manual' for more details on our consultation processes.

Date of next surveillance

Our next surveillance to decide whether the guideline should be updated is scheduled for 2017.

NICE Surveillance programme project team

Sarah Willett
Associate Director

Philip Alderson
Consultant Clinical Adviser

Katrina Sparrow
Technical Adviser

Khalid Ashfaq
Technical Analyst

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