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A Randomised Controlled Study Comparing Flush Ligation to Steam Ablation for Great Saphenous Varicose Veins

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ABSTRACT

Background: *The aim was to compare Flush ligation and endovenous steam ablation (EVSA) for great saphenous varicose veins .* ***Methods:*** *Patients with primary great saphenous vein reflux were randomized to undergo Flush ligation or EVSA . Primary outcomes were treatment success (vein obliteration) at 52 weeks, and Venous Clinical Severity Score (VCSS) at 12 weeks. Secondary outcomes were pain, satisfaction with treatment, duration of analgesia use and days lost from daily activities, changes in Aberdeen Varicose Vein Questionnaire (AVVQ) and scores after 12 weeks, and complications at 2 and 12 weeks.* ***Results:*** *A total of 227 legs were treated (EVSA, 117; Flush ligation, 110). At 1 year, the treatment success rate after high-dose EVSA was not inferior to that of Flush ligation: 92 (95 per cent confidence interval (c.i.) 86 to 98) versus 96 (92 to 100) per cent respectively. Changes in VCSS after 12 weeks were similar: −2·69 (95 per cent c.i. −2·34 to −3·04) and −2·51 (−2·10 to −2·93). AVVQ scores improved equally 12 weeks after both treatments. Patients treated with EVSA reported less post procedural pain, fewer days of analgesia use, were more satisfied with therapy, and had a shorter convalescence. Complication rates were comparable.* ***Conclusion:*** *The 1-year treatment success of high-dose EVSA was not inferior to that of Flush ligation. Several secondary outcomes were in favour of EVSA.*

KEYWORDS : Varicose veins, Flush ligation, Steam ablation

Introduction

In many countries endovenous thermal ablation therapies have replaced high ligation and stripping as the treatment choice for primary incompetence of saphenous veins, as they are effective, have fewer complications, cause minimal postoperative pain and have faster recovery times. Because all endothermal treatments are effective, attention has shifted to finding the technique with the best side-effect profile, lowest pain scores and shortest convalescence. Only a few studies have compared the outcomes between different endothermal treatments with traditional flush ligation. The most recent innovation is endovenous steam ablation (EVSA). Its effectiveness and safety have been demonstrated in a small pilot study, in which microscopy of treated sheep veins showed thermally induced vein damage similar to that seen after RFA. A recent non-comparative case series of EVSA reported a 96 per cent vein obliteration rate after 12 months and favourable patient-reported outcomes. Possible advantages of this new steam procedure are: stable and relatively low temperature, easy procedure, potentially greater cost-effectiveness, low pain scores and greater patient satisfaction. EVSA uses sterile water, a natural fluid that does not have the possible disadvantage of inducing harm by generating exogenous substances

Another advantage of EVSA is strict temperature regulation; the steam produced has a constant temperature of 120◦C. Because the induced temperature rise is limited, there may be fewer treatment-related symptoms (pain and bruising) and complications

The aim of the present randomized study is to compare anatomical success rates and patient-reported outcomes following EVSA and flush ligation for treatment of incompetent great saphenous veins (GSVs).

Methods

Patients who presented with complaints suggestive of varicose veins at the OPD of a teaching medical college were included in the study.

Inclusion criteria were: age at least 18 years, informed consent, and symptomatic primary incompetence of the GSV with reflux time exceeding 0·5 s and diameter 5 mm or more (at mid-thigh level) according to duplex ultrasound (DUS) examination.

Exclusion criteria were: acute deep or superficial vein thrombosis, agenesis of the deep venous system, vascular malformation or syndrome, post-thrombotic syndrome of the obstruction type, pregnancy, immobility, allergy to lidocaine and arterial insufficiency (ankle : brachial pressure index below 0·9). Consenting patients were randomized to either Flush ligation or EVSA, using a computerized randomization list. The legs of patients with bilateral GSV incompetence were included separately.

Treatment

All treatments were done as a in-patient procedure,When needed, tributaries were treated with phlebectomies at least 3 months after flush ligation and EVSA. Flush ligation was done as traditionally described and the importance of elaborating on the steps of the procedure not highlighted in view of the vast knowledge among the medical professionals about the procedure,but the steps in EVSA is explained in detail. EVSA was performed with the Steam Vein Sclerosis (SVS™) system (cermaVEIN, Archamps, France). Venous access was obtained by puncture with a 19-G cannula under DUS guidance. The steam ablation catheter (diameter 1·2 mm) was passed through the cannula into the vein and positioned 2–3 cm distal to the SFJ. Some 250–500 ml (depending on the length of treated vein) of tumescent anaesthesia was administered. First, two pulses of steam were delivered to dispel condensed water in the catheter. Three pulses were then delivered at the catheter tip. The catheter was withdrawn by 1 cm and 1–4 pulses per cm of vein were emitted, depending on the diameter. For the first 36 procedures the treatment protocol was to apply 1 pulse/cm in veins smaller than 7 mm, 2 pulses/cm in veins of 7–10 mm, and 3 pulses/cm in veins larger than 10 mm. With insight and after temperature experiments14, this was increased to 2, 3 and 4 pulses/cm respectively during the study. After treatment Following both treatments, patients were advised to wear medical elastic compression stockings for 1 week and to mobilize immediately.

Outcomes

Follow-up visits were scheduled at 2, 12 and 52 weeks after the initial procedure. Primary outcomes were treatment success, defined as obliteration of the GSV and/or absence of reflux (more than 0·5 s of retrograde flow) along the treated segment of the GSV, according to DUS examination at 12 and 52 weeks, and change in the Venous Clinical Severity Score (VCSS) recorded by a clinician at 12 weeks compared with the baseline score. Secondary outcomes were divided into patient-reported outcomes and treatment safety. Pain was assessed by means of a visual analogue scale (VAS) and duration of painkiller use; satisfaction with treatment was measured on a VAS, and convalescence as number of days lost from work/daily activities. These were all assessed at 2 weeks after treatment. Health-related quality-of-life

(HRQoL) was assessed with two questionnaires at 0 and 12 weeks: the Dutch translation of the Aberdeen Varicose Vein Questionnaire (AVVQ), which is a validated disease-specific quality-of-life questionnaire for varicose veins, Changes in AVVQ, and EQ VAS scores were calculated as differences between scores at 12 weeks and baseline values. To evaluate treatment safety, major and minor complications were reported at 2 and 12 weeks.

Major complications were: deep venous thrombosis (DVT), superficial thrombophlebitis in tributaries, nerve injury, skin burns and (sub)cutaneous infections. Minor complications were ecchymosis and hyperpigmentation, both measured as an area (cm2) .

Statistical analysis

The obliteration rate of Flush ligation was assumed to be about 92 per cent after 1 year and 2 months and was unknown for EVSA. The non-inferiority interval was set at 10 per cent with a β of 0·80 and one-sided α of 0·025. Based on these assumptions, the number of legs needed in this study was 116 per study group. Success rates and other categorical variables for the two treatments were compared using proportions and 95 per cent confidence intervals (c.i.), which were estimated using the Wald method, with analysis by $\chi 2$ test. Continuous variables (such as pain scores) were distributed normally and interpreted using means, 95 per cent c.i., and independent or paired t test. A per-protocol analysis was carried out.

Results

Between November 2011 and November 2013, a total of 237 legs (in 217 patients) met the eligibility criteria and were randomized to receive treatment. Ten patients (10 legs) did not receive the allocated treatment owing to technical treatment failure (4 EVSA, 1 Flush ligation) or because the treatment was declined (5 EVSA). They were not included in the analysis because of the per-protocol design. A total of 227 legs were treated in 207 patients; 117 legs in 112 patients had EVSA and 110 legs in 106 patients had Flush ligation. Eleven patients had Flush ligation in one leg and EVSA in the contralateral leg, four patients had Flush ligation in both legs, and five patients had EVSA in both legs. Thirty-six patients treated with EVSA received the low dose, and the remaining 81 had the higher dose. Patients treated with EVSA received a mean(s.d.) of 2·1(0·6) pulses per cm of vein (higher dose 2·3(0·5) pulses/cm).

Primary outcome measures: treatment success and Venous Clinical Severity Score

At 12 weeks, treatment success of all patients who had EVSA was not inferior to that of patients who had Flush ligation. After 1 year, EVSA was inferior to Flush ligation in achieving treatment success when all patients who had EVSA were considered (86·9 per cent versus 96 per cent who had Flush ligation; P =0·032). Exclusion of patients who received low-dose EVSA resulted in similar success rates between EVSA and Flush ligation (92 versus 96 per cent; P =0·331). Of 107 legs treated with EVSA, 84 GSVs were obliterated, nine were partially recanalized without reflux, and 14 treated GSVs were segmentally (more than 10 cm length of vein) or completely recanalized with reflux. Only four of 92 GSVs treated with Flush ligation were segmentally or completely recanalized, with reflux after 1 year. In both groups, the VCSS improved by 12 weeks after treatment.

Secondary outcomes

Postprocedural pain and analgesia use

Pain scores were available for 225 patients. EVSA-treated patients reported less postprocedural pain than those treated with flush ligation (mean (95 per cent c.i.) VAS score 2·6 (2·1 to 3·1) versus 5·1 (4·7 to 5·6)) and a shorter duration of analgesia use (mean (95 per cent c.i.) 0·9 (0·5 to 1·4) versus 3·3 (2·6 to 4·1) days). There was no difference between the low-dose and high-dose EVSA groups.

Satisfaction and convalescence

Patients who had EVSA were more satisfied with the therapy (mean (95 per cent c.i.) VAS score 8·6 (8·3 to 9·0) versus 7·7 (7·3 to 8·1), and had a shorter convalescence (mean (95 per cent c.i.) 1·6 (1·0 to 2·1) versus 4·2 (3·4 to 5·0) days). The higher dose made no difference.

Quality-of-life questionnaires

In both groups, all HRQoL outcomes improved 12 weeks after treatment, compared with scores at baseline (P<0.001) Scores on the disease-specific questionnaire improved substantially (by more than 30 per cent), but those on the generic questionnaires improved very little (less than 5 per cent). Changes in AVVQ and EQ VAS scores between baseline and 12 weeks were comparable for EVSA and Flush Ligation.

Complications

They were mostly minor, One patient who underwent Flush ligation developed a DVT in the common femoral vein of the treated leg 2 weeks after the intervention,mabe due to prolonged rest with no exercise and other contributing factors, thrombophlebitis was reported EVSA in ten legs (8·5 per cent) . Three legs (2·8 per cent) in the EVSA group still had thrombophlebitis at 12 weeks. Two patients reported a sensory nerve injury 12 weeks after EVSA.

Discussion

This trial compared EVSA with Flush ligation. With the appropriate (high) dose, EVSA was not inferior to Flush ligation regarding obliteration of the treated GSV segment after 1 year. The patient-reported outcomes were all in favour of EVSA: pain scores, duration of painkiller use and satisfaction with treatment. Quality of life improved similarly in both groups. The initial dosing of EVSA was based on the short-term outcome of a pilot study, in which 1 or 2 pulses/cm resulted in seven of 20 treated veins being incompletely obliterated and two having a remaining segment with reflux after 6 months. The present randomized clinical trial was initiated after the pilot study,showing that 2 pulses/cm should be sufficient for a homogeneous temperature rise exceeding 50∘C, explaining the rationale for violation of the protocol by increasing the number of pulses from at least 1 to at least 2 pulses per cm vein during the trial. The patients who received at least 2 pulses per cm vein had a success rate of 92 per cent, which is close to the 96 per cent in a recently published large case series in which 2–4 pulses/cm were administered. Altogether, these findings suggest a clear dose–response relationship. Therefore, diameter of the veins and presence of tributaries should be taken into account when determining optimal EVSA methodology. To determine the optimal schedule for EVSA, further evaluation should be undertaken. The difficulty of designing dose-finding studies is a problem common to all endovenous thermal therapies. In vivo measurements (temperature profile in the vein during treatment) are difficult to obtain. Ideally, these data should be investigated before setting up a randomized trial. Increasing the number of pulses per centimetre might influence the volume of tumescent anaesthesia needed for a painless procedure. However, it is unlikely to influence patient-reported outcomes at 2 weeks because the intravenous temperature rise is limited. Vein wall perforation and perivenous damage are usually responsible for side-effects of endothermal treatments; these are not found on histological examination of veins treated with EVSA. Of the secondary outcomes, HRQoL scores improved equally after both treatments, but the remaining patient-reported outcomes were in favour of EVSA. Reduction in pain translated into quicker recovery after EVSA, which is an important advantage from a societal perspective. The minimal clinically important difference is unknown for the HRQoL questionnaires, making it difficult to evaluate their clinical relevance. The relatively low temperature in EVSA does not seem to cause perforation of the vein wall, similar to previous findings for RFA in a bovine model. The lack of perforations after EVSA has been confirmed in experimental studies. The gap in knowledge concerning optimal EVSA dosing is an important limitation of this study. A second limitation is that patients and practitioners were not blinded. Owing to the different materials and the typical noise that EVSA makes, blinding was impossible.But in total endothermal procedures are never inferior to flush ligation.

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