

Randomized clinical trial of endovenous laser ablation versus steam ablation (LAST trial) for great saphenous varicose veins

Renate van den Bos

Wendy Malskat

Marianne de Maeseneer

Kees-Peter de Roos

Dick Groeneweg

Michael Kockaert

Martino Neumann

Tamar Nijsten

Br J Surg; 2014 Aug;101(9):1077-83

ABSTRACT

Background: The aim was to compare endovenous laser ablation (EVLA) and endovenous steam ablation (EVSA) for great saphenous varicose veins in a non-inferiority study.

Methods: Patients with primary great saphenous vein reflux were randomized to EVLA (940 nm) or EVSA (SVS™). Primary outcomes were treatment success 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 EQ-5D™ scores after 12 weeks, and complications at 2 and 12 weeks.

Results: A total of 227 legs were treated (EVSA, 117; EVLA, 110); 36 legs treated with EVSA received a low dose and the remaining 81 a higher dose. At 1 year, the treatment success after high-dose EVSA was not inferior to that of EVLA: 92 (95 per cent confidence interval (CI) 86 to 98) *versus* 96 (92 to 100) per cent respectively. Changes in VCSS after 12 weeks were similar: -2.69 (95 per cent CI -2.34 to -3.04) and -2.51 (-2.10 to -2.93). AVVQ, EQ-5D™ and EQ VAS scores improved equally 12 weeks after both treatments. Patients treated with EVSA reported less postprocedural 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 EVLA. Several secondary outcomes were in favour of EVSA.

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 (1–4). 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. Two studies (5, 6) showed similar occlusion rates but faster recovery after segmental radiofrequency ablation (RFA) compared with laser ablation. Several studies (7–9) have tried to compare different endovenous laser ablation (EVLA) techniques to assess the possible advantages of higher wavelength or specific fiber tip design. However, these studies were not designed to compare a single variable, such as wavelength. Other parameters, such as power or fiber tip design also varied, making a valid comparison impossible.

The most recent innovation is endovenous steam ablation (EVSA). Its effectiveness and safety have been demonstrated in a small pilot study (10), in which microscopy of treated sheep veins showed thermally induced vein damage similar to that seen after RFA. A recent non-comparative case series (11) of EVSA reported a 96 per cent success 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 (12). 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 (similar to the temperature applied in RFA), there may be fewer treatment-related symptoms (pain and bruising) and complications than with EVLA.

The aim of the present randomized non-inferiority study was to compare anatomical success rates and patient-reported outcomes following EVLA 940 nm and EVSA for treatment of incompetent great saphenous veins (GSVs).

METHODS

Three medical centres participated in this multicentre trial. Patients referred to the Erasmus MC Rotterdam, DermaPark Uden and Flebologisch Centrum Grave were screened for suitability for the LAST trial. 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 EVLA or EVSA, using a computerized randomization list. The legs of patients with bilateral GSV incompetence were included separately, provided that there was at least 3 months between the two treatments. The two treatments differed too much in technique (materials and typical noise of steam pulses) to achieve blinding of both the patient and the attending physician; assessors were not blinded for practical reasons. The study was approved by the Medical Ethics Committee of Erasmus MC Rotterdam (MEC-2009-269). The trial is registered at <http://www.clinicaltrials.gov> with registration number NCT02046967.

Treatment

All treatments were performed as an outpatient using local tumescent anaesthesia (0.5 mg adrenaline (epinephrine), 4.2 mg bicarbonate and 35 mg lidocaine diluted in 500 ml saline solution). When needed, tributaries were treated with phlebectomies at least 3 months after EVLA or EVSA.

Endovenous laser ablation

EVLA was done with a 940-nm diode laser (Dornier MedTech GmbH, Wessling, Germany) using a bare fiber. In brief, the vein was punctured under DUS guidance, preferably at the distal point of reflux or at knee level, for ease of access, with a 19-G needle (13). A guidewire was passed through the needle up to the level of the saphenofemoral junction (SFJ). The needle was removed and a 5-Fr catheter was inserted over the guidewire. After removing the guidewire, the laser fiber was inserted and the tip positioned 1–1.5 cm distal to the SFJ. Tumescent anaesthesia was administered under DUS guidance (250–500 ml, depending on the length of treated vein). The laser fiber was withdrawn continuously (at a speed of 2 mm/s) with a power setting of 12 W, delivering approximately 60 J/cm.

Endovenous steam ablation

EVSA was performed with the Steam Vein Sclerosis (SVSTM) 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, 2 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 experiments (14), 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. Prophylactic low molecular weight heparin was not administered routinely.

Outcomes assessed and follow-up protocol

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 VCSS recorded by a clinician at 12 weeks compared with the baseline score (15).

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 (16) and the EQ-5D™, a generic instrument measuring health status (<http://www.euroqol.org>). Changes in AVVQ, EQ-5D™ 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) (17).

Statistical analysis

The success rate of EVLA was assumed to be about 92 per cent after 1 year (18) 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 (CI), which were estimated using the Wald method, with analysis by χ^2 test. Continuous variables (such as pain scores) were distributed normally and interpreted using means, 95 per cent CI, and independent or paired *t* test. A per-protocol analysis was carried out. The CONSORT statement for non-inferiority trials was used as a guideline for reporting the results (19,20).

RESULTS

Between November 2009 and November 2011, a total of 237 legs (in 217 patients) met the eligibility criteria and were randomized to receive treatment (Figure 1). Ten patients (ten legs) did not receive the allocated treatment owing to technical treatment failure (1 EVSA, 4 EVLA) or because the treatment was declined (5 EVLA). 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 EVLA. Eleven patients had EVLA in one leg and EVSA in the contralateral leg, 4 patients had EVLA in both legs, and 5 patients had EVSA in both legs. For patients treated with EVLA, the mean(SD) energy delivered was 56.6(8.1) J/cm. 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(SD) of 2.1(0.6) pulses per cm of vein (higher dose 2.3(0.5) pulses/cm). Baseline characteristics were comparable between the treatment groups (Table 1).

Primary outcome primary outcomes: treatment success and Venous Clinical Severity Score

Table 2 summarizes the primary outcomes of the LAST trial. At 12 weeks, treatment success (obliteration of the treated GSV segment and/or absence of reflux) of all patients who had EVSA was not inferior to that of patients who had EVLA. After 1 year, EVSA was inferior to EVLA in achieving treatment success when all patients who had EVSA were considered (86.9 per cent *versus* 96 per cent who had EVLA; $p = 0.032$). Exclusion of patients who received low-dose EVSA resulted in similar success rates between EVSA and EVLA (92 *versus* 96 per cent; $p = 0.331$).

Of 107 legs treated with EVSA, 84 GSVs were obliterated, 9 were partially recanalized without reflux, and 14 treated GSVs were segmentally (more than 10 cm length of vein) or completely recanalized with reflux. Only 4 of 92 GSVs treated with EVLA were segmentally or completely recanalized, with reflux after 1 year. In both groups, the VCSS improved by 12 weeks after treatment: -2.51 (95 per cent CI -2.10 to -2.93) for EVLA and -2.90 (-2.42 to -3.58) for EVSA (all patients). Changes in VCSS scores between baseline

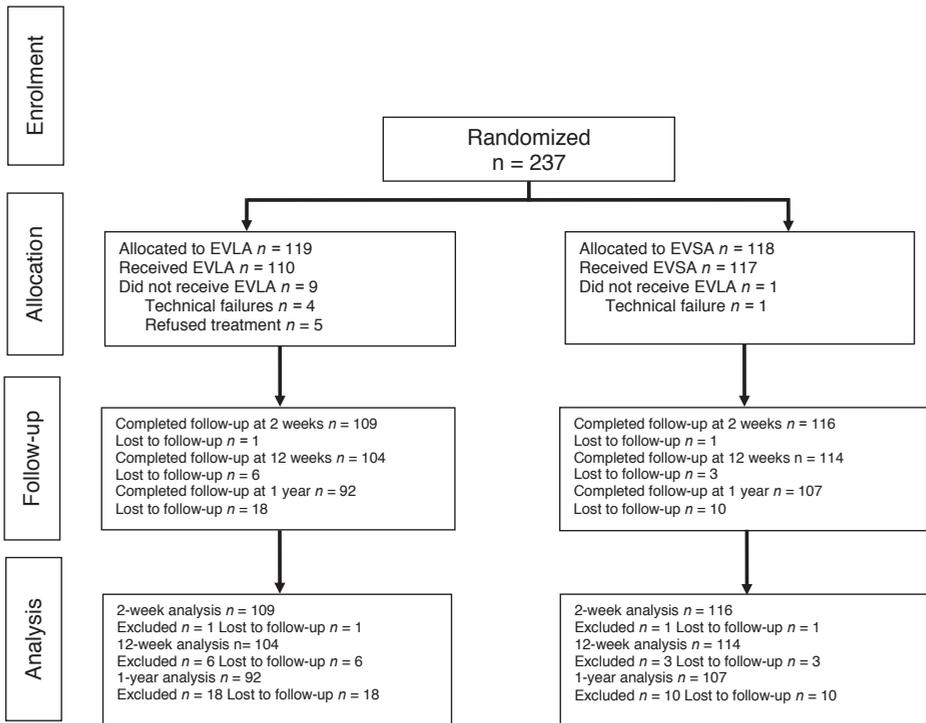


Figure 1. CONSORT diagram for the trial. EVLA, endovenous laser ablation; EVSA, endovenous steam ablation.

and 12 weeks were similar in the two groups, and there was no difference when patients who had low-dose EVSA were excluded.

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 EVLA (mean (95 per cent CI) 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 CI) 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 (Table 3).

Satisfaction and convalescence

Patients who had EVSA were more satisfied with the therapy (mean (95 per cent CI) 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 CI) 1.6 (1.0 to 2.1) *versus* 4.2 (3.4 to 5.0) days). The higher dose made no difference (Table 3).

Table 1. Demographic data and treatment characteristics

		EVLA	EVSA (all)	P†	EVSA (high-dose)	P‡
No. of legs		110	117		81	
No. of patients		106	112			
Age (years)*		55 (±12)	56 (±13)	0.801§	55 (±13)	0.824§
Sex				0.185¶		0.275¶
Male	patients	45 (42)	39 (35)			
	legs	48 (44)	41 (35)		29 (36)	
Female	patients	61 (58)	73(65)			
	legs	62 (56)	76 (65)		52 (64)	
C(EAP) class				0.186#		0.824#
C1		0 (0)	0 (0)		0 (0)	
C2		77 (70)	72 (62)		55 (68)	
C3		28 (25)	40 (34)		23 (28)	
C4		3(3)	3 (3)		1 (1)	
C5		1 (1)	1 (1)		1 (1)	
C6		1 (1)	1 (1)		1 (1)	
GSV diameter (mm)				0.342#		0.535#
<7 mm		84 (76)	91 (78)		66 (82)	
7-10 mm		26 (24)	24 (21)		14 (17)	
>10 mm		0 (0)	2 (2)		1 (1)	
Length treated GSV (cm)*		32.5 (±6.8)	31.2 (±6.7)	0.172§	31.0 (±6.8)	0.164§
Energy (Joules per cm/pulses)*		56 (±8.1)	2.1 (±0.6)		2.3 (±0.5)	

Values in parentheses are percentages unless indicated otherwise; *Values are mean (±standard deviation). EVLA, endovenous laser ablation; EVSA, endovenous steam ablation; CEAP, Clinical Etiologic Anatomic Pathophysiologic; GSV, great saphenous vein. †EVLA versus EVSA (all), ‡EVLA versus EVSA (high dose); §In-dependent T-test; ¶Chi-square test; #Chi-square test, linear by linear association.

Quality-of-life questionnaires

In both groups, all HRQoL outcomes improved 12 weeks after treatment, compared with scores at baseline ($p < 0.001$). The disease-specific questionnaire (AVVQ) improved substantially (by more than 30 per cent), but the generic questionnaires improved very little (less than 5 per cent). Changes in AVVQ, EQ-5D™ and EQ VAS scores between baseline and 12 weeks were comparable for EVSA and EVLA (Table 3).

Complications

Complications were mostly minor, and the side-effect profiles of EVSA and EVLA treatment appeared to be similar (Table 4). One patient who had EVLA developed a DVT in the common femoral vein of the treated leg 2 weeks after the intervention. Thrombophlebitis in tributaries was reported in ten legs (9.2 per cent) in the EVSA and ten (8.5

Table 2. Treatment success

	Anatomical success after 12 weeks*	Anatomical success after 1 year*	Change in VCSS after 12 weekst
EVLA	101/104 (97; 94 to 100)	88/92 (96; 92 to 100)	-2.51 (-2.10 to -2.93)
EVSA (all)	107/114 (94; 90 to 98)	93/107 (87; 81 to 93)	-2.90 (-2.42 to -3.58)
P‡	0.251¶	0.032¶	0.242#
EVSA (high-dose)	76/78 (97; 94 to 100)	68/74 (92; 86 to 98)	-2.69 (-2.34 to -3.04)
P	0.896¶	0.311¶	0.279#

Values in parentheses are *percentages with 95 per cent confidence intervals (CI) and †mean with 95 per cent CI. VCSS, Venous Clinical Severity Score; EVLA, endovenous laser ablation; EVSA, endovenous steam ablation. ‡EVLA versus EVSA (all), SEVLA versus EVSA (high dose); ¶Chi-square test; #independent T-test.

Table 3. Secondary outcome measures

	EVLA N=109	EVSA (all) N=116	P*	EVSA (high-dose) N=81	P†
2 weeks after intervention	<i>n</i> = 109	<i>n</i> = 116		<i>n</i> = 81	
Pain (VAS)	5.1 (4.7, 5.6)	2.6 (2.1, 3.1)	<0.001	2.7 (2.1, 3.3)	<0.001
Satisfaction (VAS)	7.7 (7.3, 8.1)	8.6 (8.3, 9.0)	0.001	8.5 (8.1, 8.9)	0.007
Duration of analgesia use (days)	3.3 (2.6, 4.1)	0.9 (0.5, 1.4)	<0.001	1.5 (0.5, 1.8)	<0.001
Limited in daily life (days)	4.2 (3.4, 5.0)	1.6 (1.0, 2.1)	<0.001	1.6 (0.9, 2.3)	<0.001
Changes in HRQoL (12 weeks after intervention versus baseline)					
AVVQ	-5.47 (-3.93, -7.01)	-5.17 (-3.63, -6.70)		-5.10 (-3.14, -7.06)	
EQ-5D™	0.039 (0.010, 0.067)	0.035 (0.011, 0.059)		0.033 (0.003, 0.062)	
EQ VAS	1.9 (0.4, 3.4)	0.8 (-0.9, 2.4)		0.0 (-2.1, 2.1)	

Values in parentheses are 95 per cent confidence intervals. EVLA, endovenous laser ablation; EVSA, endovenous steam ablation; VAS, visual analogue scale; HRQoL, Health Related Quality of Life; AVVQ, Aberdeen Varicose Vein Questionnaire. *EVLA versus EVSA (all); †EVLA versus EVSA (high dose); all T-test.

Table 4. Complications

	EVLA	EVSA
2 weeks after intervention	<i>n</i> = 109	<i>n</i> = 117
Deep venous thrombosis	1 (0.9)	0 (0)
Superficial venous thrombosis	10 (9.2)	10 (8.5)
Nerve injury	0 (0)	1 (0.9)
Skin burn	0 (0)	0 (0)
Skin infection	0 (0)	1 (0.9)
Ecchymosis (cm ²)*	4.5 (13.1)	1.0 (3.1)
Hyperpigmentation (cm ²)*	0.9 (3.9)	0.9 (4.6)
12 weeks after intervention	<i>n</i> = 98	<i>n</i> = 107
Superficial venous thrombosis	0 (0)	3 (2.8)
Nerve injury	0 (0)	2 (1.9)
Ecchymosis (cm ²)*	0.0 (0.4)	0.0 (0.0)
Hyperpigmentation (cm ²)*	0.1 (0.5)	0.3 (1.8)

Values in parentheses are percentages unless indicates otherwise; *values are mean (SD). EVLA, endovenous laser ablation; EVSA, endovenous steam ablation

per cent) in the EVLA group 2 weeks after treatment. 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. Two weeks after EVLA the mean area of ecchymosis was 5 cm², which was larger than the mean of 1 cm² after EVSA.

DISCUSSION

This trial compared EVSA with EVLA, which is the most commonly used thermal treatment for varicose veins. With the appropriate (high) dose, EVSA was not inferior to EVLA (940 nm, bare fiber) regarding success rate 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.

EVLA occlusion rates are usually in the range 90–95 per cent (18), similar to the rate in the present study. In patients who had low-dose EVSA, the occlusion rate after 1 year was lower than that after EVLA. The initial dosing of EVSA was based on the short-term outcome of a pilot study (10), 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, but before an experimental study (14) 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 (11) 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, including EVLA for which there are numerous different laser parameters and little consensus on the optimal treatment.

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/cm 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 histology of veins treated with EVSA (10).

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 (21). The explanation for the favourable side-effect profile may be that the peak temperature in EVSA is far lower than that of EVLA (22). Peak temperatures of over 600°C at the fiber tip have been reported for EVLA, potentially leading to perforation and perivenous inflammation when the bare fiber tip is in direct contact with the vein wall (12,23–25). 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 (25). The lack of perforations after EVSA has been confirmed in experimental studies (10, 26). In another recent experimental study (22), temperature profiles of EVSA, EVLA and segmental RFA were compared. The LAST trial was performed with 940-nm bare-fiber EVLA, which was the most frequently used EVLA method when the study began. Developments in EVLA methodology aiming to improve the secondary outcomes are ongoing. Innovations in fiber tip design (such as tulip fiber) and power administered may result in better secondary outcomes, decreasing the difference between EVLA and EVSA (27).

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.

Endovenous thermal ablation is very successful for the treatment of varicose veins. The 1-year success rate of high-dose EVSA is not inferior to that of EVLA (940 nm, bare fiber). The efficacy of EVSA might be improved by increasing the dose of the pulses, which will require formal assessment in future studies.

REFERENCES

1. 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.
2. Lurie F, Creton D, Eklof B, Kabnick LS, Kistner RL, Pichot O et al. Prospective randomized study of endovenous radiofrequency obliteration (closure procedure) versus ligation and stripping in a selected patient population (EVOLVEs Study). *J Vasc Surg* 2003; 38: 207–214.
3. Rasmussen LH, Lawaetz M, Bjoern L, Vennits B, Blemings A, Eklof B. Randomized clinical trial comparing endovenous laser ablation, radiofrequency ablation, foam sclerotherapy and surgical stripping for great saphenous varicose veins. *Br J Surg* 2011; 98: 1079–1087.
4. De Maeseener M. The endovenous revolution. *Br J Surg* 2011; 98: 1037–1038.
5. Shepherd AC, Gohel MS, Brown LC, Metcalfe MJ, Hamish M, Davies AH. Randomized clinical trial of VNU ClosureFAST radiofrequency ablation versus laser for varicose veins. *Br J Surg* 2010; 97: 810–818.
6. Almeida JJ, Kaufman J, Göckeritz O, Chopra P, Evans MT, Hoheim DF et al. Radiofrequency endovenous ClosureFAST versus laser ablation for the treatment of great saphenous reflux: a multicenter, single-blinded, randomized study (RECOVERY study). *J Vasc Interv Radiol* 2009; 20: 752–759.
7. Almeida J, Mackay E, Javier J, Mauriello J, Raines J. Saphenous laser ablation at 1470 nm targets the vein wall, not blood. *Vasc Endovascular Surg* 2009; 43: 467–472.
8. Doganci S, Demirkilic U. Comparison of 980 nm laser and bare-tip fibre with 1470 nm laser and radial fibre in the treatment of great saphenous vein varicosities: a prospective randomised clinical trial. *Eur J Vasc Endovasc Surg* 2010; 40: 254–259.
9. Proebstle TM, Moehler T, Gül D, Herdemann S. Endovenous treatment of the great saphenous vein using a 1320 nm Nd : YAG laser causes fewer side effects than using a 940 nm diode laser. *Dermatol Surg* 2005; 31: 1678–1683.
10. van den Bos RR, Milleret R, Neumann M, Nijsten T. Proof-of-principle study of steam ablation as novel thermal therapy for saphenous varicose veins. *J Vasc Surg* 2010; 53: 181–186.
11. Milleret R, Huot L, Nicolini P, Creton D, Roux AS, Decullier E et al. Great saphenous vein ablation with steam injection: results of a multicentre study. *Eur J Vasc Endovasc Surg* 2013; 45: 391–396.
12. Amzayyb M, van den Bos RR, Kodach VM, de Bruin DM, Nijsten T, Neumann HA et al. Carbonized blood deposited on fibres during 810, 940 and 1470 nm endovenous laser ablation: thickness and absorption by optical coherence tomography. *Lasers Med Sci* 2010; 25: 439–447.
13. van den Bos RR, Kockaert MA, Neumann HA, Nijsten T. Technical review of endovenous laser therapy for varicose veins. *Eur J Vasc Endovasc Surg* 2008; 35: 88–95.
14. van Ruijven PW, van den Bos RR, Alazard LM, van der Geld CW, Nijsten T. Temperature measurements for dose-finding in steam ablation. *J Vasc Surg* 2011; 53: 1454–1456.
15. Rutherford RB, Padberg FT Jr, Comerota AJ, Kistner RL, Meissner MH, Moneta GL. Venous severity scoring: an adjunct to venous outcome assessment. *J Vasc Surg* 2000; 31: 1307–1312.
16. Klem TM, Sybrandy JE, Wittens CH, Essink Bot ML. Reliability and validity of the Dutch translated Aberdeen Varicose Vein Questionnaire. *Eur J Vasc Endovasc Surg* 2009; 37: 232–238.
17. Van Den Bos RR, Neumann M, De Roos KP, Nijsten T. Endovenous laser ablation-induced complications: review of the literature and new cases. *Dermatol Surg* 2009; 35: 1206–1214.
18. van den Bos R, Arends L, Kockaert M, Neumann M, Nijsten T. Endovenous therapies of lower extremity varicosities: a meta-analysis. *J Vasc Surg* 2009; 49: 230–239.

19. Piaggio G, Elbourne DR, Altman DG, Pocock SJ, Evans SJ, CONSORT Group. Reporting of noninferiority and equivalence randomized trials: an extension of the CONSORT statement. *JAMA* 2006; 295: 1152–1160.
20. Piaggio G, Elbourne DR, Pocock SJ, Evans SJ, Altman DG; CONSORT Group. Reporting of noninferiority and equivalence randomized trials: extension of the CONSORT 2010 statement. *JAMA* 2012; 308: 2594–2604.
21. Norman GR, Sloan JA, Wyrwich KW. Interpretation of changes in health-related quality of life: the remarkable universality of half a standard deviation. *Med Care* 2003; 41: 582–592.
22. Malskat WS, Stokbroekx MA, van der Geld CW, Nijsten TE, van den Bos RR. Temperature profiles of 980- and 1470-nm endovenous laser ablation, endovenous radiofrequency ablation and endovenous steam ablation. *Lasers Med Sci* 2014; 29: 423–429.
23. Fan CM, Rox-Anderson R. Endovenous laser ablation: mechanism of action. *Phlebology* 2008; 23: 206–213.
24. Disselhoff BC, Rem AI, Verdaasdonk RM, Kinderen DJ, Moll FL. Endovenous laser ablation: an experimental study on the mechanism of action. *Phlebology* 2008; 23: 69–76.
25. Schmedt CG, Sroka R, Steckmeier S, Meissner OA, Babaryka G, Hunger K et al. Investigation on radiofrequency and laser (980 nm) effects after endoluminal treatment of saphenous vein insufficiency in an ex-vivo model. *Eur J Vasc Endovasc Surg* 2006; 32: 318–325.
26. Thomis S, Verbrugghe P, Milleret R, Verbeken E, Fourneau I, Herijgers P. Steam ablation versus radiofrequency and laser ablation: an in vivo histological comparative trial. *Eur J Vasc Endovasc Surg* 2013; 46: 378–382.
27. Proebstle TM, Alm J, Gockeritz O, Wenzel C, Noppeney T, Lebard C et al.; European Closure Fast Clinical Study Group. Three-year European follow-up of endovenous radiofrequency-powered segmental thermal ablation of the great saphenous vein with or without treatment of calf varicosities. *J Vasc Surg* 2011; 54: 146–152.