Endoluminal thermal ablation versus stripping of the saphenous vein: Meta-analysis of recurrence of reflux

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BACKGROUND: Catheter-based minimally invasive techniques developed to treat saphenous vein insufficiency include endovenous laser and radiofrequency ablation. Their long-term results are under evaluation. A meta-analysis of trials was performed, comparing endovenous versus surgical saphenous vein ablation with focus on long-term (greater than 365 days) outcomes of recurrence of varicosities, reflux and symptomatic disease.

METHODS: A systematic search of published studies reporting on the treatment of varicose veins was performed. The databases searched included Medline/PubMed, OVID, EMBASE, CINAHL, ClinicalTrials.gov, the Cochrane central register of controlled trials and the Cochrane database of systematic reviews. Search terms included saphenous vein ligation, stripping, radiofrequency ablation, laser ablation and endovenous ablation. Reports in all languages from 1966 to 2009 were considered. The 'related articles' function was used to broaden the search. All article titles, abstracts and subject headings were screened by one reviewer for potential relevance. Abstracts of articles selected by title were read online to reduce the number of articles for full-text examination. Finally, additional titles were sought in the bibliographies of the retrieved articles. Only studies reporting outcomes after more than 365 days were selected. Analyzed outcomes included recurrence of varicosities and reflux, as

documented by duplex ultrasound, and recurrence of signs and symptoms. Data extraction was performed from life tables, text or graphs. Statistical analysis was performed using the commercially available software CMA Version 2 (Biostat Inc, USA). The random effects model was used to calculate the ORs and 95% CIs. Statistical heterogeneity was evaluated using the Q value and considered present if $P < 0.05$.

RESULTS: Eight randomized controlled trials were included; these reported on 497 patients. Two hundred twenty-six patients underwent ligation and stripping and 271 underwent endoluminal thermal ablation. The mean ($\pm$ SD) follow-up period was 584 ± 182 days. There was no difference in the age and sex distribution between the groups. There was no difference in the long-term recurrence rate between the two techniques (OR 0.97, 95% CI 0.48 to 1.9, $P = 0.9$). Statistical heterogeneity was not significant (Q value $P = 0.5$) and publication bias was limited.

CONCLUSIONS: The analysis indicates that catheter-based treatments and traditional venous stripping with high ligation have similar long-term results. Establishing preoperative criteria for each method may improve outcomes but presently neither technique appears to confer an advantage in terms of mid- to long-term freedom from recurrent symptoms.

Key Words: Endovenous ablation; Radiofrequency ablation; Varicose veins; Vein reflux

Varicose veins are a common problem that affects approximately 25% of Western adults. Often, the cause is great saphenous vein (GSV) insufficiency. Common associated symptoms include pain, itching, night cramps, fatigue and a feeling of heaviness in the legs. Patients with chronic venous insufficiency develop lower leg chronic venous stasis changes, hyperactive pigmentation and leg ulceration. Recurrence after GSV ligation and stripping (L/S) is approximately 30%. The cause is not clear and may include surgical technique or development of new veins (neovascularization). A residual stump of the saphenous vein after L/S can lead to recurrence of varicosity in the groin several years after the original procedure (1). Cutaneous nerve injury was reported in 27% of patients after GSV stripping (2).

Catheter-based minimally invasive techniques (endovenous laser ablation and radiofrequency ablation [RFA]) have been developed that reduce postoperative recovery time and wound-related complications, and shorten the time needed before returning to normal activities and work (3,4). Endovenous laser ablation and RFA seem to be safe and effective modalities with good short- and mid-term results, but long-term recurrence data are lacking (5). We performed a meta-analysis of

prospective randomized trials comparing endoluminal thermal ablation (ETA) versus saphenous vein L/S with focus on long-term outcomes of recurrence of varicosities, reflux and symptomatic disease.

METHODS

A systematic search of published studies reporting saphenous vein interventions was performed. The following databases were searched: Medline/PubMed, OVID, EMBASE, CINAHL, ClinicalTrials.gov, the Cochrane central register of controlled trials and the Cochrane database of systematic reviews. Search terms included saphenous vein ligation, stripping, cryostripping, radiofrequency ablation, laser ablation/surgery, endovenous ablation, thermal ablation, endovascular ablation and varicose vein ablation/surgery. Clinical data registries were also searched. Reports in all languages from 1966 to 2009 were considered. The 'related articles' function was used to broaden the search. Specialty journals such as *Dermatologic Surgery*, *Phlebology*, *Journal of Vascular Surgery*, *Acta Phlebologica* and the *International Journal of Angiology* were searched for relevant articles. All article titles, abstracts and subject headings were screened for potential relevance. Abstracts of articles selected

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TABLE 1
Distribution of treatment modalities in the eight randomized controlled trials

Author	Study design	Legs, n			Total
		L/S	EVLA	RFA	
De Medeiros, 2006 (10)	Prospective randomized trial	20	20		40
Darwood et al, 2008 (14)	Prospective randomized trial	12	49		61
Disselhoff et al, 2008 (9)	Prospective randomized trial	55	56		111
Hinchcliffe et al, 2006 (15)	Double-blind randomized trial	16		16	32
Lurie et al, 2005 (6)	Multicentre randomized trial	36		44	80
Rasmussen et al, 2007 (7)	Randomized trial	68	67		135
Perala et al, 2005 (11)	Randomized trial	13		15	28
Stotter et al, 2006 (16)	Prospective randomized trial	19		19	38

EVLA Endovenous laser ablation; L/S Ligation and stripping; RFA Radiofrequency ablation

TABLE 2
Demographic characteristics and Class, Etiology, Anatomy and Pathophysiology (CEAP) classification for each treated patient

	ETA	L/S	P
Age, years, mean $\pm$ SD	47 $\pm$ 7.48	48.4 $\pm$ 5.44	0.69
Women, %, mean $\pm$ SD	78.05 $\pm$ 15.23	76.48 $\pm$ 17.43	0.86
CEAP 2, %	36.4	32.4	0.791
CEAP 3, %	9.4	11.4	0.526
CEAP 4, %	4.5	2.3	0.375
CEAP 5, %	0.8	0.8	0.407
CEAP 6, %	0.4	0	0.337

ETA Endoluminal thermal ablation; L/S Ligation and stripping

by title were read online to reduce the number of articles for full-text examination. Finally, additional titles were sought in the bibliographies of the retrieved articles.

Studies that fulfilled the following criteria were included: comparative randomized controlled trials with follow-up of one year or longer, use of duplex ultrasound (DUS) as an outcome measure, and class, etiology, anatomy and pathophysiology patient classification. Excluded were studies that performed saphenofemoral junction ligation without stripping. Studies with cryostripping were included. Studies that used sclerotherapy were also excluded. Outcomes analyzed included recurrence as documented by DUS (GSV recanalization, reflux) and recurrent varicosities with symptoms. Data extraction was performed from life tables, text or graphs. Statistical analysis was performed using the commercially available software CMA Version 2 (Biostat Inc, USA). The random effects model was used to calculate ORs and 95% CIs. Statistical heterogeneity was evaluated using the Q value and considered present if $P < 0.05$.

RESULTS

Eight comparative trials were identified. These studies reported on 497 patients (Table 1). Reported studies included the use of

Figure 1) Forest plot with relative weights for each study. There appears to be no significant difference in the recurrence rate between the two modalities. ETA Endoluminal thermal ablation; L/S Ligation and stripping

Figure 2) No single study overinfluences the results of the meta-analysis. ETA Endoluminal thermal ablation; L/S Ligation and stripping

standard symptom grading systems such as the Varicose Vein Severity Score and the Aberdeen Varicose Vein Symptoms Severity Score (6,7). The intervention site was the GSV in all studies. Two hundred twenty-six patients (239 legs) underwent L/S and 271 (286 legs) underwent ETA. The mean ($\pm$ SD) follow-up period was 584 $\pm$ 182 days. Table 1 summarizes the distribution in the treatment arms, which reflects patients who were followed for a year or longer.

The demographic characteristics, as well as class, etiology, anatomy and pathophysiology classification distribution, were similar between the ETA and L/S groups (Table 2).

In all randomized clinical trials, follow-up included DUS evaluation of the saphenous vein. The criterion for technical success was an obliterated GSV with lack of flow. Recanalized GSV or treatment failure was defined as an open part of the treated vein segment (segment length varied in each reported study). Recurrence was documented if venous reflux was present on ultrasound, the vein was recanalized or new varicosities were evident. Frequency of ultrasound evaluation varied among studies.

Meta-analysis did not reveal significant differences in the recurrence rates between the two methods (OR 0.97, 95% CI 0.48 to 1.9, $P=0.9$) (Figure 1). Omitting each study and repeating the analysis did not change the findings, indicating that no single study overinfluenced the results (Figure 2). Statistical heterogeneity was not significant (Q value $P=0.5$).

Publication bias was not significant, as shown in the funnel plot (Figure 3).

DISCUSSION

New, less invasive methods have been developed as alternatives to L/S to treat saphenous vein incompetence. Randomized trials have shown that ETA has the advantages of less postprocedure pain and faster recovery (4,8). In addition, quality of life scores are higher after ETA than after L/S (9). Recurrence remains a significant problem after either endovenous or open surgical ablation. After L/S, neovascularization in the subcutaneous tissue around the saphenofemoral junction can lead to recurrence (3,10). The process of neovascularization may be associated with a groin incision. The presence of incompetent tributaries after L/S is another possible cause of recurrence. Clinical problems are caused by a connection between a remaining segment of GSV and new vessels or incompetent tributaries (4). Endoluminal ablation leaves a patent small proximal lumen of GSV and its proximal tributaries, which may affect long-term results. Another potential event leading to recurrence is recanalization of the GSV. During the two-year follow-up of the EVOLVeS trial (8), neovascularization was observed in four L/S patients and one RFA patient.

Dwerryhouse et al (8) suggested the events that may lead to recurrence occur within two years after treatment. The only study reporting longer than two-year follow-up after ETA is by Peralta et al (11). They reported an increase in the recanalization of the GSV from 1.7% one week after the procedure to 11.3% at two years, without any sonographic evidence of neovascularization. Recanalization was associated with the presence of varicose veins in more than one-half of the patients.

Another potential factor affecting recurrence is the preoperative venous function and extent of venous reflux (superficial versus superficial/deep/perforator reflux). Van Rij et al (12) demonstrated that a preoperative venous filling index of greater than 2 s was present in 58% of patients with late recurrences. Reflux of perforators and deep venous reflux were present in 83% of limbs with recurrent disease. Furthermore, Bhatti et al (13) reported that patients with deep venous incompetence have an increased incidence of recurrence.

Overall, it appears that recurrence after either L/S or ETA is a complex phenomenon. Neither technique completely addresses all potential causes. ETA is not associated with a groin incision; thus, it should have minimal neovascularization. On the other hand, the tributaries of the saphenofemoral junction are not ligated and the obliterated vein can recanalize because it remains in situ. Overall, venous function is an additional factor that can influence long-term results; this was not

Figure 3) Funnel plot of standard error by log OR. The shape of the funnel plot is not suggestive of significant publication bias

studied extensively in the reports included in our meta-analysis.

One limitation of our study is that a heterogeneous mix of trials was included – one involved cryostripping and one recurrent long saphenous vein treatment (9,14). Our findings did not change by omitting these trials one by one and repeating the analyses. We used the definition of success as stated by the investigators of each report to quantify recurrence and restricted analysis to studies that used DUS to increase comparability.

Registries of clinical trials, meeting abstracts and non-English literature were searched to minimize the effect of publication bias.

CONCLUSION

Our analysis indicates that catheter-based treatments and traditional venous stripping with high ligation have similar long-term results. Further studies with long-term follow-up and thorough preoperative evaluation of venous function, as well as clinical classification of the severity of the disease, are needed to determine whether either approach is superior or whether the choice of saphenous vein ablation should be tailored to each patient. Establishing preoperative criteria for each method may improve outcomes but, presently, neither technique appears to confer an advantage in terms of mid- to long-term freedom from recurrent symptoms.

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