Eur J Vasc Endovasc Surg (2009) **38**, 506–510

Influence of Warfarin on the Success of Endovenous Laser Ablation (EVLA) of the Great Saphenous Vein (GSV)

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Submitted 26 January 2009; accepted 17 May 2009
Available online 4 July 2009

KEYWORDS
Varicose veins;
Endovenous laser ablation (EVLA);
Warfarin

Abstract *Background:* Although warfarin is routinely stopped prior to varicose vein surgery the absence of incisions may make this unnecessary prior to EVLA. Nevertheless continuing therapy may compromise ablation rates resulting in treatment failure. Since EVLA is particularly suitable for older patients with co-morbidities this study investigates whether warfarin influences outcome.
Method: A prospective observational cohort study was designed to assess ablation rates (1 year, duplex ultrasound), Aberdeen varicose vein symptom severity scores (AVVSS) and patient satisfaction following GSV EVLA in 22 patients (''warfarin group'': 12 female, 10 male; 24 limbs) taking warfarin and 24 age/sex and disease-severity matched controls who were not taking anticoagulants (''no-warfarin group'').
Results: Complete ablation of the treated-length of GSV was achieved in 20/24 (83%) limbs in the ''warfarin group'' versus 23/24 (96%) in the ''no-warfarin'' group ($p = 0.347$, chi squared). Suboptimal energy densities were delivered to 3/4 failures in the ''warfarin group''. A similar, significant ($p < 0.001$, Wilcoxon) improvement in AVVSS occurred in both groups [warfarin: median 14.6 (inter-quartile range 8.9–19.1) to 3.8 (1.9–6.2), no-warfarin: median 13.9 (IQR 7.6–20.1) to 3.5 (2.2–6.4)]. Patients were equally satisfied with outcomes (warfarin = 92%, no-warfarin = 90%; $p = 0.391$, Mann–Whitney). No major complications occurred.
Conclusions: EVLA in patients taking warfarin is safe and effective. Since cessation of therapy is unnecessary it should provide a valuable alternative to surgery in these patients.

Introduction

Endovenous laser ablation (EVLA) employs thermal energy to cause irreversible vein wall injury leading to occlusion of an incompetent great, small or anterior accessory saphenous vein in the treatment of varicose veins. Previous studies have shown that laser energy density is the single

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1078-5884/$36
doi:10.1016/j.ejvs.2009.05.022

most important factor that determines the efficacy of laser ablation.[1,2]

In the short term it is likely that thrombotic occlusion of the treated vein occurs before vein contraction and fibrosis ensues. Thus it is possible that factors that inhibit thrombus formation such as anticoagulants may influence the success of EVLA.

Unlike surgery, EVLA may be particularly suitable for older patients and those with significant medical co-morbidities in whom the treatment of superficial venous reflux and varicose veins is indicated because of complications such as varicose eczema, lipodermatosclerosis and ulceration. A proportion of these patients may be prescribed long term anticoagulants such as warfarin for their co-existent medical conditions. Such drugs would usually be stopped prior to conventional varicose vein surgery because of the risk of intra-operative bleeding. Further, in-patient as opposed to day-case surgery is usually required with the duration of admission prolonged if pre-operative conversion to heparin therapy is needed or post-operative stabilisation of anticoagulant therapy necessary. A potential advantage of EVLA, given the absence of surgical incisions, is that anticoagulant therapy may not need to be stopped before undertaking EVLA although this might influence the success of axial vein ablation. This study therefore assesses the influence of warfarin on the outcome of EVLA.

Methods

Patients

Of 393 patients who underwent EVLA for varicose veins between May 2005 and January 2007 at the Leeds Vascular Institute, 22 patients (median age 62 years, range 51–77), 12 female, 10 male; 24 limbs, continued taking warfarin at the time of treatment (''warfarin group'') for varicosities secondary to sapheno-femoral junction (SFJ) and GSV reflux. Outcomes in these patients were compared with those for 24 age/sex and disease-severity (CEAP) matched control patients (''no-warfarin group'') who were not taking warfarin. The control patient for each study patient was the next age–sex and disease-severity matched patient undergoing EVLA and who subsequently completed 1 year follow-up. Patients with concomitant reflux in both the small saphenous vein and GSV and those with a previous deep vein thrombosis (DVT) were excluded from the study. The indication for warfarin therapy in the study group was atrial fibrillation ($n = 14$) or a metallic heart valve ($n = 8$). Informed consent was obtained from all patients for the both EVLA and data collection.

Data collection

Prior to laser treatment all patients underwent a duplex ultrasound scan (DUS) [TITAN®, Sonosite Inc, Bothell, USA, 5–10 MHz linear probe] to confirm the site of superficial venous incompetence and the diameter of the GSV was recorded 10 cm distal to the SFJ, avoiding any localised dilatation. Suitability for GSV EVLA was established using criteria that have been described previously.[1] Patients' past medical history and drug history were documented. Disease severity was assessed using ''C'' of the CEAP clinical classification[4] (''EAP'' of CEAP were the same for all patients). Disease specific quality of life was assessed using the Aberdeen varicose vein symptom severity score (AVVSS) before and 1 year after EVLA.

EVLA was performed using an 810 nm diode pulsed laser at 12 W power and tumescent local anaesthesia (0.1% lignocaine) as described previously.[1] Neither concomitant phlebectomies nor foam sclerotherapy was undertaken although the latter was performed for residual varicosities at the first follow-up visit (6 weeks) if requested by the patient. Treatment details including the laser energy density (J/cm) were documented.

During follow-up patients were assessed at 6, 12 and 52 weeks for clinical signs of recurrence and successful GSV ablation (duplex ultrasound). The criteria for successful ablation have been described previously.[3] Patient satisfaction was assessed at 1 year using a 10 cm visual analogue scale which was then calculated as a percentage. A prospective log of complications was maintained throughout the study. These included deep vein thrombosis (DVT), phlebitis, nerve damage (sensor or motor), chronic pain, and skin pigmentation. These were assessed clinically and for DVT by ultrasound. All data were collected prospectively by a consultant vascular surgeon or vascular research fellow. This is a prospective observational cohort study with two groups.

Statistical analysis

All data were tested for normal distribution and are presented as median (inter-quartile range, IQR) unless stated otherwise. The AVVSS before and after laser ablation were compared within a group using a Wilcoxon test and the improvements in AVVSS between groups were compared by a Mann–Whitney U test. A chi squared test was used for contingency table analysis. All analyses were performed using the statistical package SPSS® for Windows (SPSS (14), Chicago, Illinois, USA).

Results

Disease severity and the demographic data of the two groups are summarised in Table 1. Pre-treatment vein diameters were similar in both groups (Table 2). Successful occlusion of the full length of the treated GSV was observed in 20/24 (83%) limbs in the ''warfarin group'' compared to 23/24 (96%) limbs in the ''no-warfarin group'' ($p = 0.347$, chi squared). Although the overall laser dose was not significantly different between the two groups, of the four patients in whom successful ablation was not achieved in the ''warfarin group'', three patients had received suboptimal laser energy densities (46, 44, and 52 J/cm). In these patients the GSV was patent and compressible on ultrasound examination at 6 weeks suggesting primary failure due to inadequate treatment. The most recent INR was recorded in 2/3 of these patients and was 2.7 and 3.1. For the group as a whole the range in INR was 2.3–4.1 and this suggests that the INR level was not an important factor in these treatment failures. Small numbers preclude formal

Table 1 Demography and CEAP classification of patients undergoing EVLA (CEAP score: clinical, etiology, anatomy, pathology)

Characteristics	''Warfarin group''	(%)	''No-warfarin group'' (age/sex/disease severity matched)	(%)
Male	10	(45%)	10	(45%)
Female	12	(55%)	12	(55%)
Age, median (range)	62 (51–77) years		62 (51–77) years	
Number of limbs treated	24		24	
CEAP				
C2	13	(54%)	13	(54%)
C3	4	(17%)	4	(17%)
C4	4	(17%)	4	(17%)
C5	2	(8%)	2	(8%)
C6	1	(4%)	1	(4%)

statistical analysis. In the remaining patient who received 62 J/cm laser energy the GSV was partially occluded at 6 week follow-up but was fully patent with reflux at 12 weeks. This is more likely to represent recanalisation. Similarly, the patient in whom treatment failed in the ''no-warfarin group'' received 58 J/cm laser energy, had a partially occluded vein at 6 weeks but a recanalised GSV at 12 weeks. These data are summarised in Table 2.

A significant improvement in AVVSS occurred in both groups: ''warfarin group'': median 14.6 (IQR 8.9–19.1) to 3.8 (1.9–6.2), ''no-warfarin group'': median 13.9 (IQR 7.6–20.1) to 3.5 (2.2–6.4); $p < 0.001$, Wilcoxon. However, there was no difference in either the improvement between the groups ($p = 0.446$, Mann–Whitney) or in patient satisfaction (A = 92% versus B = 90%, $p = 0.391$, Mann–Whitney).

There were no instances of DVT in either group and only one patient in the ''no-warfarin group'' reported marked post-EVLA discomfort (''phlebitis''). None of the patients described either extensive bruising or haematoma formation.

Details of subsequent treatment and their outcome for patients with either primary treatment failure or recanalisation are shown in Table 2.

Discussion

Unlike conventional surgery, EVLA ablates the target incompetent axial vein in-situ without the need for surgical incisions. When varicose vein surgery is performed in patients who are taking anticoagulants such as warfarin it is common practise to discontinue therapy 3 days (with or without heparin cover) prior to operation. The results of this study show that EVLA remains effective in most patients who continue to take warfarin throughout the treatment period. Although there were more treatment failures in warfarin patients it seems likely that this was associated with suboptimal laser energy delivery in most instances although a larger study would be required to confirm this. Nevertheless it is possible that warfarin might have contributed to these failures and thus it is reasonable to conclude that a laser energy density $\geq$60 J/cm[1,2] is required in these patients. Even if warfarin therapy was the primary reason for these treatment failures successful ablation occurred in the majority of patients thus justifying both the adoption of this technique in these patients and the continuation of anticoagulant therapy.

A diode laser of 810 nm wavelength produces temperatures above 700 °C at the tip of the laser fibre.[4] Nevertheless the temperature recorded 3 mm from the vein wall in the surrounding tumescent anaesthesia is only 43 °C.[5] It is therefore clear that the vein wall absorbs a significant proportion of the thermal energy that is delivered. Although Proebstle et al[6] suggested that heat conduction from the laser fibre to the vein wall is the result of steam bubble formation in blood a more recent study suggests that direct contact between the fibre and the vein is the most likely mechanism of action.[7] These high temperatures result in a range of injuries to the vein including denaturation of protein, tissue desiccation, necrosis, and possibly carbonisation with charring depending on the temperature to which it is exposed.[7,8] This type of transmural damage results in a progressive fibrosis and permanent occlusion of the vein rather than a temporary thrombotic occlusion[7,9] and previous studies have provided ultrasound-based evidence for this.[3,4] Data from the present study confirm that these same changes occur in patients who undergo EVLA whilst taking warfarin (Fig. 1). Thus anticoagulants do not appear to interfere with the fibrotic occlusion that occurs following EVLA.

Currently there are no reports describing the outcome of other minimally invasive therapies in patients receiving anticoagulants. A recent study suggests that foam sclerotherapy only inflicts patchy endothelial damage and minimal subendothelial injury.[10] Thus thrombotic occlusion is likely to be a major component of its success and anticoagulants could prevent this. Further studies are required to assess the impact of warfarin on this and radiofrequency ablation.

Although EVLA avoids surgical incisions peri-venous bruising may occur in some patients, presumably related to vein wall perforation following direct contact with the laser fibre or from the tumescent needle. Thus warfarin could result in more extensive bruising or haematoma. This did not seem to be the case in the present study. Although the extent of bruising was not quantified patient satisfaction was no different to that in patients who were not on warfarin.

Given that EVLA appears an effective therapy for superficial venous incompetence in patients taking warfarin the longer hospital stay associated with conventional surgery in anticoagulated patients can be avoided. This will

Table 2 Treatment details, ablation status and presence of significant reflux (>1 s) in patients with treatment failure at 6, 12 and 52 week follow-up compared to patients who had successful treatment in the warfarin and no-warfarin groups

Patient/group	Laser energy (J/cm)	Total laser energy (J)	DUS findings (ablation status, reflux status and diameter)			
			Pre-EVLA	6 weeks	12 weeks	52 weeks
Warfarin (1)	46[a]	1380	Patent, reflux, 7.6 mm	Patent, reflux, 7.4 mm	Patent, reflux, 7.6 mm	Patient had successful re-do EVLA at 6 m
Warfarin (2)	44[a]	1408	Patent, reflux, 8.2 mm	Patent, reflux, 8.3 mm	Patent, reflux, 8.1 mm	Patient had successful re-do EVLA at 7 m
Warfarin (3)	52[a]	1456	Patent, reflux, 7.7 mm	Patent, reflux, 7.9 mm	Patent, reflux, 7.6 mm	Patient had successful re-do EVLA at 13 m
Warfarin (4)	62	2260	Patent, reflux, 8.4 mm	Partially occluded, 7.8 mm	Patent, reflux, 5.1 mm	Patient had successful re-do EVLA at 18 m
No-warfarin (1)	58	2320	Patent, reflux, 7.3 mm	Partially occluded, 7.0 mm	Patent, reflux, 4.3 mm	Patient had successful DUS guided foam sclerotherapy at 12 m
Warfarin group: median (IQR)	64 (54—72)	1997 (1686—2350)	Patent, reflux, 7.9 ± 2.1	Fully occluded, 5.0 ± 1.4	Fully occluded, 3.1 ± 1.3	Fully ablated, GSV not visible
No-warfarin group: median (IQR)	66 (55—74)	2016 (1640—2460)	Patent, reflux, 7.6 ± 2.2	Fully occluded, 5.2 ± 1.5	Fully occluded, 3.0 ± 1.4	Fully ablated, GSV not visible
p (warfarin versus no-warfarin)	0.09	0.15	0.19	0.21	0.24	—

[a] Three patients in the warfarin group received suboptimal laser energy density(<60 J/cm)[1,2] for their initial treatment.

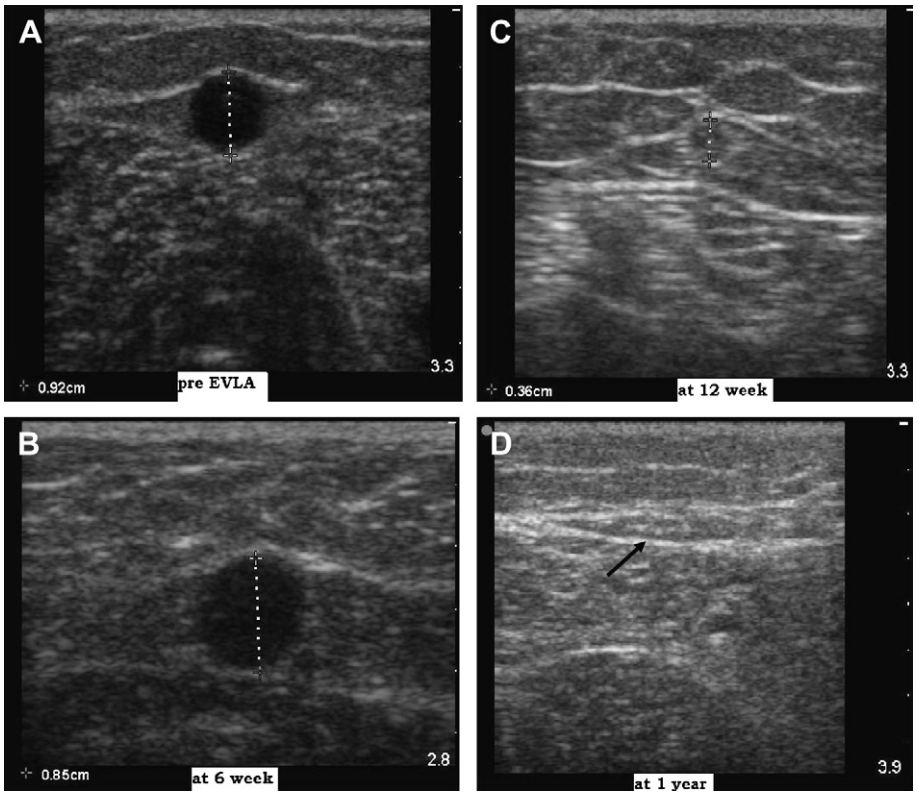

Figure 1 Sequential ultrasound appearance of GSV in a patient from the ''warfarin group'' after successful EVLA. These changes are identical to those occurring in patients who are not anticoagulated.[3] (A) GSV pre-EVLA (9.2 mm, hypo-echoic, compressible). (B) GSV 6 weeks post-EVLA (8.5 mm, hypo-echoic, non-compressible, vein occluded). (C) GSV 12 weeks post-EVLA (3.6 mm, iso-echoic, not compressible, vein ablated). (D) GSV 1 year post-EVLA (not visible — arrow shows empty saphenous space).

inevitably improve the cost effectiveness of treatment in these patients. Further, since patients who are taking warfarin are generally older and less fit than the majority of those requesting treatment for varicose veins the risks of intervention should be reduced. This may be particularly important given that these patients are more likely to require treatment for complications of their venous disease. That this is the case is reflected by a relatively high proportion of patients classified as C3—C6 in this study.

In conclusion, EVLA in patients who continue to take warfarin is safe and effective. Although warfarin can be continued during EVLA, adequate laser energy density or fluence should be administered to ensure a satisfactory outcome.

Conflict of Interest/Funding

None.

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