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Endovascular vein treatment (ELVeS™) for chronic venous insufficiency from varicose disease of lower limbs with reviparin sodium thromboprophylaxis

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Abstract

Chronic venous insufficiency (CVI) is a consequence of varicose disease (VD) or post-thrombotic syndrome (PTS). The cost of both diagnosis and treatment are high and the condition causes significant loss of working hours and impairs quality of life. Surgery of the superficial venous system represents a workload for departments of surgery and cause significant waiting lists. Recently, new endovascular venous surgery laser-based techniques, particularly Endo Laser Vein System (ELVeS, Biolitec, USA), have been introduced and demonstrated to be mini-invasive, less expensive, quicker and associated with a lower recurrence rate (5-7%) compared with traditional vein surgery (30-50%). Few data are available about the utility of low-molecular-weight heparins in the prevention of venous thromboembolism (VTE) in minor surgical procedures such as superficial venous surgery of the lower limbs. This was an open, observational clinical study to evaluate the efficacy and safety of thromboprophylaxis with reviparin sodium in patients undergoing ELVeS procedure for the treatment of CVI-related VD. From April 2001 to May 2004, 138 patients with CVI (CEAP C4-C6) cause by VD of the lower limbs (124 from great saphenous vein, GSV, and 14 from small saphenous vein, SSV) underwent ELVeS procedures as day cases according standardised criteria. Colour-coded Doppler of lower limbs was performed before, during and after the operation. All patients received post-surgical mechanical thromboprophylaxis with graduated compression stockings and subcutaneous reviparin sodium 1750 IU/daily during the first post-operative week. Immediate post-operative obliteration of GSV or SSV was achieved in all cases. There were only 2 cases (1.45%) of early recanalization, which were successfully re-treated, and no cases of late recanalisation (cumulative procedural success rate of 98.6%). Only 5 (3.6%) patients presented a thrombotic complication, namely superficial thrombophlebitis of the GSV, successfully resolved with short-term (one week) treatment with full weight-adjusted doses of reviparin sodium. No

patients experienced major bleeding or heparin-induced thrombocytopenia. The ELVeS technique with reviparin sodium thromboprophylaxis seems to be safe and effective in selected patients in the immediate, short- and medium-term follow-up periods. The results after long-term follow-up are required.

Introduction

Chronic venous insufficiency (CVI) is usually a consequence of the failure of peripheral veins, often caused by a varicose disease or a post-thrombotic syndrome. The first pathological stage of CVI is a localised or diffuse venous hypertension with subsequent haemorheological effects on the macro- and micro-circulation. Oedema is usually the principal clinical and pathophysiological manifestation.

CVI is an important clinical condition, epidemiologically and in socioeconomic terms, with a high prevalence in Western countries. The costs of both diagnosis and treatment are high and the condition causes significant loss of working hours and impairs quality of life.¹⁻³ The prevalence of CVI of the lower limbs ranges from 10% to 50% in adult males and from 50% to 55% in women, while varicose disease is clinically evident in 10-33% of women and 10-20% of men (Table 1).^{1,4-7} Surgery of the superficial venous system represents a large workload for departments of general and vascular surgery, and is responsible for significant waiting lists.

Table 1. Prevalence of clinical chronic venous insufficiency (CVI) and varicose disease (VD) of the lower limbs in adult males and females.

Diseases	Prevalence (%)	
	Male	Female
CVI	10-50	50-55
VD	10-20	10-33

Surgical treatment of lower limb varicose disease dates back to the beginning of the 20th Century, following the techniques introduced by Mayo (1906) and Babcock

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(1907). These procedures are still not outdated; they have long been confirmed and validated by common clinical experience and clinical trials.⁸⁻¹³

Recently, alternative endovascular venous surgery laser-based techniques have been introduced, alongside more conventional procedures. The newer techniques include both ablative (extended or short stripping, phlebectomy with or without Muller incisions, incisions of thrombosed collateral vessels for ablation or compression) and conservative surgery (sapheno-femoral external plastic valve reconstruction, conservative and haemodynamic treatment of venous insufficiency [CHIVA] type 1 and 2, and either simple crosssectomy or crosssectomy combined with phlebectomy).

In the past 15 years, several endovascular laser techniques have been introduced for the treatment of varicose disease. These include pulsed dye, long pulsed dye, argon, argon pumped dye, frequency doubled KIP:YAG, copper vapour, copper bromide alexandrite, diode, long pulsed Nd:YAG and intense pulsed laser treatments. These techniques have been of varying efficacy and, unfortunately, some have resulted in high morbidity rates due to inappropriate usage.

However, advances in technology have led to improvements in the efficacy and safety of surgical treatment of great and small saphenous veins, of reticular varicose veins and of venous ulcers.

ELVeS (Endo Laser Vein System; Biolitec, USA), the most recent mini-invasive standardised surgical procedure, is both less expensive and quicker (10–20 mins per procedure) compared with surgical or radiofrequency techniques. It is associated with a lower incidence of postoperative complications and a reduced recurrence rate (5–7%), compared with traditional venous surgery (30–50%).

The ELVeS procedure consists of a 'step-by-step' approach:

- Select patients appropriately
- Perform intraoperative venous mapping with colour-coded Doppler
- For the great saphenous vein (GSV), measure the GSV diameter at four different points: 2 cm below the sapheno-femoral junction, and in the upper, middle and lower third of the thigh and in the upper third of the leg
- For the small saphenous vein (SSV), measure the SSV diameter in two different sites: 1 cm below the sapheno-popliteal junction and in the posterior middle third of the leg
- Echo-guided tumescent anaesthesia
- Echo-guided introduction of the ELVeS device and of the laser fibre that is then chased up to the sapheno-femoral or sapheno-popliteal junction
- Finally, perform endovascular laser ablation of the vein according to the ELVeS criteria (12 watt power, 1 sec impulse duration, 1 sec interval between each impulse)

Even if it appears a safe surgical procedure, the use of laser energy is associated with a risk of thermal damage to the vessel wall, a risk that is greater at the sapheno-femoral or sapheno-popliteal junctions, which should not be treated by this procedure. Thermal damage correlates with increased thrombotic risk, mainly in the superficial venous system and, possibly, in the deep venous system. In previous studies, the risk of thromboembolic complications following laser procedures ranged from 2% to 12% without thromboprophylaxis.

As extensively reported, low-molecular-weight-heparins (LMWHs) have demonstrated their efficacy and safety in the prevention of venous thromboembolism (VTE) after major general and orthopaedic surgery. On the other hand, few data are available on their standardised use in the prevention of VTE in minor surgical procedures such as superficial venous surgery of the lower limbs.

Endovascular vein treatment (ELVeS™) for chronic venous insufficiency from varicose disease of lower limbs with rivaroxaban sodium thromboprophylaxis *continued*

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Aim of the study

This was an open, observational study designed to evaluate the efficacy and safety of thromboprophylaxis with rivaroxaban sodium (Clivarina®, Schwartz Pharma, Germany) in patients undergoing an endovascular laser procedure with the ELVeS technique for the treatment of CVI-related varicose disease.

Methods

From April 2001 to May 2004 we treated 138 patients affected by CVI of the lower limbs (Clinical Classification, Aetiology, Anatomy, Pathophysiology [CEAP] grades C4, C5, C6). Demographics of all patients are listed in Table 2. Most patients (124) presented with varicose disease of the GSV, while in 14 the SSV was affected. All surgical procedures were performed according to the standardised ELVeS criteria, with use of colour-coded Doppler before and during the operation. The mean diameter of the GSV was 6.8 mm (range 4–14), while that of the SSV was 5.2 mm (range 4–8).

Table 2. Demographics of the study population.

Patients, n	138
Age, years (range)	64.4 (42–83)
M:F, n (%)	44 (31.9):94 (68.1)
CEAP classification	C4–C6
*GSV treated, n (%)	124 (89.9)
*SSV treated, n (%)	14 (10.1)
GSV mean diameter, mm (range)	6.8 (4–14)
SSV mean diameter, mm (range)	5.2 (4–8)

*GSV: great saphenous vein; SSV: small saphenous vein

Access was percutaneous in six cases and mini-surgical in 132 patients. In 12 patients we used a Terumo® (Terumo Europe NV, Belgium) guide instead of a J guide to reach the sapheno–femoral junction, because of an important tortuosity of the vessel. Muller phlebectomy of collateral vessels, ligation of perforating veins and crosssection were performed in 85, 34 and 4 patients, respectively. The crosssection technique was adopted in two patients because guide-based cannulation of

the sapheno–femoral junction was not possible due to the strong tortuosity of the vessel. In the other two patients, crosssection was necessary for reintervention following early recanalisation.

A total of 136 patients received local anaesthesia (1 ml of 1% lidocaine) at the device insertion site, 60 ml of echo-guided tumescent mepivacaine hydrochloride 0.25% along the course of the GSV and short-term general anaesthesia with propofol (Diprivan®, AstraZeneca, UK) during the laser procedure. Two patients underwent spinal anaesthesia (Table 3).

Table 3. Interventions recorded in the study.

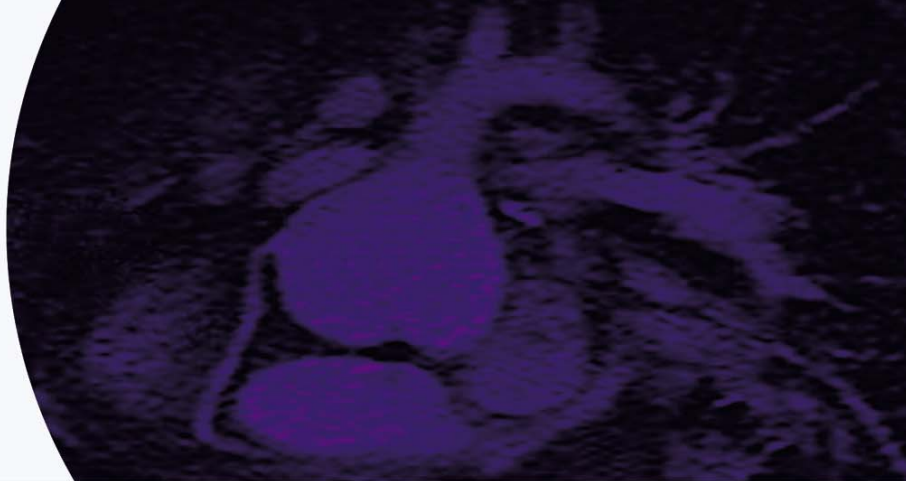
Mini-surgical access, n (%)	132 (95.6)
Percutaneous access	6 (4.4)
Muller-based varicectomy of collateral vessels	85 (61.6)
Ligation of perforating veins	34 (24.6)
Crosssection	4 (2.9)
Local anaesthesia in device insertion site	136 (98.5)
Spinal (locoregional) anaesthesia	2 (1.5)

The mean intervention time was 26 minutes. All patients received postsurgical mechanical thromboprophylaxis with 30–40 mmHg graduated compression stockings and pharmacological thromboprophylaxis with subcutaneous rivaroxaban sodium (1750 IU/day) during the first postoperative week.

Results

Immediate postoperative obliteration of the GSV or SSV during intraoperative ultrasound control, as well as full compression of the relevant deep venous system (common and superficial femoral veins and popliteal vein), was recorded in all patients. No intra- or postoperative major complications (bleeding, deep venous thrombosis, skin burns) occurred.

Most patients treated as day cases, while four patients were discharged the day after the procedure. In 132 patients there was mild pain from the third to the



seventh postoperative day, with full relief of symptoms following short-term treatment with an NSAID (nimesulide). In six patients pain was prolonged up to the twelfth postoperative day with poor relief following administration of the NSAID but with subsequent spontaneous resolution.

Postoperative complications of this surgical approach are reported in Table 4. Only five patients (3.6%) experienced a thrombotic complication, namely superficial thrombophlebitis of the GSV. These cases all resolved successfully with short-term treatment (7 days) with weight-adjusted rivaroxaban. Twenty patients (14.5%) presented diffuse ecchymosis, which resolved spontaneously and a cutaneous vesicle occurred in one patient. Light skin tattooing was observed in six cases.

Table 4. Postoperative complications.

Events	Patients, n (%)
Superficial thrombophlebitis*	5 (3.6)
Deep venous thrombosis	0 (0)
Pulmonary embolism	0 (0)
Light cutaneous discoloration	6 (4.3)
Cutaneous vesicle	1 (0.7)
Soft-tissue haemorrhage in injection site	20 (14.5)
Major bleeding	0 (0)
Early recanalisation of GSV**	2 (1.4)
Late recanalisation†	0 (0)

*GSV (great saphenous vein) collateral veins with complete resolution following 7 days' full doses of rivaroxaban. **Two cases at 4 and 6 months after surgery: in both cases, incomplete occlusion of the proximal site of the vessel. †'No late recanalisation' is equivalent to a 98.6% success for the laser procedure.

Overall, 132 patients were fully satisfied with the endovascular laser procedure, while six patients considered this surgical approach 'good'. All patients underwent 1-, 3-, 6- and 12-month follow-up visits and colour-coded Doppler evaluation, with a mean follow-up of 13.7 months. Only two (1.45%) early recanalisations of the GSV were detected – at 4 and 6 months postoperatively, respectively. In both cases,

the proximal part of the vessel had not been fully occluded. Both patients underwent 'redo' surgery consisting of crossotomy along with a caudo–cranial ELVeS procedure, with a good result. No cases of late recanalisation were detected. Thus, the cumulative procedural success rate was 98.6%. Furthermore, no patient developed major bleeding or heparin-induced thrombocytopenia as a consequence of prophylactic treatment with rivaroxaban. Thus, this treatment was well tolerated, and the study was associated with a compliance rate of 100% with rivaroxaban.

Conclusions

The ELVeS technique seems to be safe and effective in well-selected patients who meet the criteria that provide a clear indication for an endovascular laser-based procedure. Obviously, the best clinical results are obtained when the procedure is performed by experienced operators. Our approach led to a reduction in operating time and to an improvement in patient comfort, compared with a traditional surgical procedure such as stripping. The lower thrombotic complication rate of 3.6% – which involved only collateral superficial vessels and fully resolved with short-term LMWH treatment – as well as the absence of major bleeding complications indicates the efficacy and safety of thromboprophylaxis with low, fixed doses of rivaroxaban. Further, the absence of other complications such as infections confirmed the safety of this surgical procedure in the immediate postoperative period and its efficacy in the short- and middle-term follow-up periods. Efficacy results after long-term follow-up remain to be obtained.

Our study was limited by the small sample size and lack of a control group. However, it showed a very low thrombotic complication rate (all cases resolved in a short period), good tolerability, short intervention time and good patient comfort with this new surgical approach, compared with traditional techniques.

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Thus, the study represents, in our opinion, clear evidence that the ELVeS surgical approach, with a short period of thromboprophylaxis with low, fixed doses of rivaroxaban sodium, is safe and effective in the treatment of varicose disease and its thrombotic complications. Randomised clinical studies with large numbers of patients are now needed to confirm these observational clinical findings.

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