



ELSEVIER



Randomised Clinical Trial Comparing Endovenous Laser Ablation with Stripping of the Great Saphenous Vein: Clinical Outcome and Recurrence After 2 Years[☆]

L.H. Rasmussen*, L. Bjoern, M. Lawaetz, B. Lawaetz, A. Blemings, B. Eklöf

The Danish Vein Centres – Åreknudeklinikken Naestved and Copenhagen and Surgical Centre Roskilde, Denmark

Submitted 26 August 2009; accepted 26 November 2009

KEYWORDS

Varicose veins;
Endovenous laser
ablation;
Surgical treatment;
Randomised trial

Abstract Objective: This study aims to compare the outcome 2 years after treatment of varicose veins by endovenous laser ablation (EVLA) or surgery by assessing recurrence, venous clinical severity score (VCSS) and quality of life.

Methods: A total of 121 patients (137 legs) were randomised to either EVLA or saphenofemoral ligation and stripping of the great saphenous vein (GSV). Follow-up included clinical and duplex ultrasound examinations, VCSS and quality of life questionnaires.

Results: A total of 18 (26%) and 25 patients (37%) in the EVLA and surgery group, respectively, developed recurrent varicose veins (not significant (NS) between groups). The source of reflux was not significantly different between the groups. Technical failure occurred in three EVLA and two surgery patients, reflux in the anterior accessory GSV, the groin, thigh and calf perforators was found in six, two, four, and three EVLA patients, and in three, three, nine and six surgery patients. VCSS, Aberdeen Varicose Vein Severity Score and several domains of the Medical Outcomes Study Short Form 36 (SF36) quality of life score improved significantly in both groups.

Conclusions: No significant differences in clinical or ultrasound recurrences were found between EVLA and surgery groups. Our study also shows that similar improvements in clinical severity scores and quality of life were gained in both treatments.

© 2009 European Society for Vascular Surgery. Published by Elsevier Ltd. All rights reserved.

[☆] Presented at the XXIII Annual Meeting 3-6 September, 2009, European Society for Vascular Surgery, Oslo, Norway.

* Corresponding author at: Åreknudeklinikken, Eskadronsvej 4A, 4700 Naestved, Denmark. Tel.: +45 4082 4418; fax: +45 5572 3038. E-mail address: Larshrasmussen@yahoo.com (L.H. Rasmussen).

Introduction

In recent years, endovenous laser ablation (EVLA) of the saphenous vein has gained popularity for the treatment of patients with saphenous vein incompetence resulting in varicose veins. Numerous reports have demonstrated a high degree of safety and efficacy of EVLA with respect to elimination of the incompetent vein, improvement in symptoms and quality of life, as well as a high degree of patient satisfaction with the treatment.^{1,2} Although recently published randomised clinical trials did not show major clinical differences in the short-term outcome of EVLA and surgery, they suggested that recurrence rates and pattern may differ in the longer term.^{3–6}

Recurrent varicose veins after surgery are a frequent problem, with recurrence rates ranging from 15 to 80% after 5 years or more; however, recurrence after EVLA has only been described to a limited extent.^{6,7} Most studies have been non-randomised and have focussed on re-canalisation of the great saphenous vein (GSV) rather than on varicose vein recurrence. Proper clinical evaluation with adequate follow-up in randomised trials is important before conventional surgical treatment is replaced by EVLA or other new endovascular methods. The present report describes the outcome 2 years after treatment with either EVLA or high ligation and stripping in a randomised clinical trial. The study was approved by the Regional Ethics Committee.

Patients and methods

The methodology and short-term outcome of this randomised clinical trial have been fully described in a previous publication.³ The study was conducted in two private surgical centres which work under contract to the national health-care system in Denmark. In brief, consecutive patients, with symptomatic varicose veins and GSV incompetence (clinical, etiologic, anatomic and pathophysiologic (CEAP) C_{2–4}E_pA_sP_r) were randomised by sealed envelopes to either surgery or EVLA. The preoperative assessment, including CEAP grading and venous clinical severity scoring (VCSS), was performed by one of two vascular and general surgeons, with experience in the management of venous disease. Bilateral treatment was permitted, provided both limbs received the same treatment during the same operation. Patients who had undergone previous saphenofemoral ligation were included in the trial. Exclusion criteria were duplication of the saphenous trunk or an incompetent anterior accessory GSV (AAGSV), small saphenous or deep vein incompetence, previous deep vein thrombosis, arterial insufficiency, or a tortuous GSV rendering the vein unsuitable for endovenous treatment.

Treatment

All treatments were performed in a treatment room under tumescent local anaesthesia using a solution of 0.1% lidocaine with adrenaline and bicarbonate. Two experienced surgeons from the two study centres performed all the treatments and investigations.

The surgical procedure was carried out through a 4- to 6-cm incision in the groin, with flush division of the GSV and division of all tributaries behind the second level of division.⁸ The GSV was then removed using a pin-stripper to just below the knee.

The EVL procedure was performed under duplex guidance with a 980-nm diode laser (Ceralas D 980, Biolitec, Bonn, Germany) using pulse mode and a power of 12 W. The GSV was cannulated percutaneously just below the knee or at the lowest point of reflux on the thigh. In two cases, a small cut-down was performed. The laser fibre was advanced until 1–2 cm below the saphenofemoral junction after which the GSV was ablated during withdrawal of the fibre. The mean (range) energy used was 73.5 (57–95) joules cm⁻¹ GSV. All varicose veins were removed by phlebectomy during the same procedure in both groups of patients.

After the treatment, the leg was wrapped in sterile absorbent bandages and covered with a cohesive compression bandage for 48 h. The patients were instructed to wear a medical compression stocking (18 mmHg) during the day for at least 2 weeks after the bandage was removed.

Assessments

The patients attended follow-up at 12 days, and then after 1, 3 and 6 months and yearly thereafter. The present report describes the findings 2 years after surgery. The surgeon performed clinical and duplex ultrasound examinations (DUSs) at all visits. The clinical examinations were performed with the surgeon sitting in front of the standing patient. Ultrasound examinations for reflux were performed by manually compressing the calf with sudden release. Reflux >0.5 s was considered pathological. A Hawk ultrasound system (BK Medical, Denmark) was used for the DUS examinations. The track of the treated GSV, the deep veins and all axial veins were investigated with DUS for visibility, compressibility, blood flow and reflux. VCSS, the Aberdeen Varicose Vein Symptoms Severity Score (AVVSS) and the Medical Outcomes Study Short Form 36 (SF36) health-related quality of life score, were completed by the patient and recorded by a research nurse.^{9–11} A statistician performed the calculations. Just before each clinical investigation, the patients indicated, with a pen on the AVVSS form, if they considered varicose veins to be present. Subsequently, the surgeon would inspect the leg for varicose veins and other signs of venous insufficiency. In patients with evidence of varicose veins or signs of venous insufficiency (C2 or higher) the source of reflux, if possible, would be identified and categorised as reflux in the groin, the GSV, AAGSV and perforators in the thigh and/or calf.

Technical success was considered to have been achieved when the GSV was closed or absent. A re-canalised GSV or treatment failure was defined as an open section of the treated vein segment >5 cm in length. The criterion for a varicose vein was a visible or palpable varicosity with a diameter of more than 3 mm. At follow-up, a varicose vein, which had not been observed before or previously been marked by the patient on the AVVSS form, was considered to be a recurrent varicose vein.

Table 1 Baseline patient characteristics.

	Surgery	EVLA
No. of patients/legs	59/68	62/69
Age median (range)	54 (22–78)	53 (26–79)
Sex (F/M)	43/16	41/21
CEAP No. (%)		
C2	51 (86)	50 (81)
C3	5 (8)	3 (5)
C4	3 (5)	9 (15)

Statistical methods

The primary ultrasound end point was a closed or absent GSV and the clinical end point was the appearance of new varicose veins after surgery. *A priori* sample size calculations indicated, that to detect a 15% difference in closed or absent GSV or recurrence rate between the groups with $\alpha = 5$ and $\beta = 80$, 60 legs would be needed in each group. Efficacy end points AVVSS and SF36 score were analysed using analysis of variance for repeated measurements. For the VCSS, intergroup comparisons were made by Mann–Whitney statistics and intra-group comparisons by Friedman statistics. The time to failure or appearance of new varicose veins was analysed using log-rank statistics.

Results

A total of 121 consecutive patients (137 legs) gave written informed consent for inclusion in this study between August 2005 and July 2006 and were randomised to the surgical and EVLA groups. The groups were comparable with respect to patient characteristics and CEAP classification of treated legs (Table 1). There were two technical failures in the surgery group where the GSV broke during stripping. It was not possible to extract the remaining part of those veins through a distal incision because the stripper could not pass through the partially invaginated vein. In the EVLA group,

Table 2 Comparison of cumulative recurrence rates and source of reflux in patients 2 years after treatment with surgery or EVLA.

<i>n</i> = legs	Surgery (<i>n</i> = 68)	EVLA (<i>n</i> = 69)	<i>p</i>
Clinical recurrence (%)	25/68 (37)	18/69 (26)	0.20
Observed by patient (%)	9/68 (13)	8/69 (12)	0.80
Not seen at follow-up (%)	10/68 (15)	4/69 (6)	0.10
Technical failure (%)	2 (3)	3 (4)	1.00
Reflux into the AAGSV* (%)	3 (4)	6 (8)	0.49
Reflux in the groin (%)	3 (4)	2 (3)	0.68
Reflux in thigh perforators (%)	9 (13)	4 (6)	0.16
Reflux in lower leg perforators (%)	6 (9)	3 (4)	0.33

AAGSV*, anterior accessory great saphenous vein.

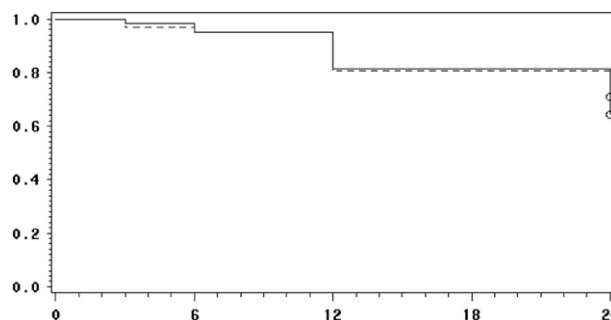


Figure 1 Kaplan–Meyer plot of recurrence during the first 2 years after treatment of varicose veins with either EVLA or conventional surgery. *p* = NS. Vertical axis: probability of freedom from varices. Horizontal axis, months after treatment. Legends: ——— surgery, - - - - - EVLA.

three GSVs completely re-canalised within the first 6 months. The lengths (diameters) of the GSVs that re-canalised were 25 cm (1.2 cm), 32 cm (0.7 cm) and 30 cm (1 cm), respectively. The laser energy in those GSVs was 61, 78 and 70 joules cm^{-1} vein, respectively. Such characteristics were not significantly different from the remaining veins. They were all retreated with foam sclerotherapy, considered to be treatment failures and were removed from the study. No GSVs were re-canalised thereafter. No clinically relevant differences between the groups were found within the first 6 postoperative months.³

The incidence of clinical recurrence increased gradually from 6 months onward. At 2 years follow-up, clinical recurrence was found in 25 (37%) and 18 legs (26%) in the surgery and EVLA groups, respectively (not significant (NS), Table 2). Six patients in the surgery group and nine in the EVLA group were retreated, mostly for cosmetic reasons. However, in only nine (13%) legs in the surgery group and eight legs (12%) in the EVLA group had the recurrence been observed by the patient. No significant difference in quality of life could be measured in patients with and without recurrence. Reflux developed in the anterior accessory GSV in three legs following surgery and six legs after EVLA (NS). Reflux after surgery was found in the groin (three legs), the thigh (nine legs) and the calf (six legs), respectively. In

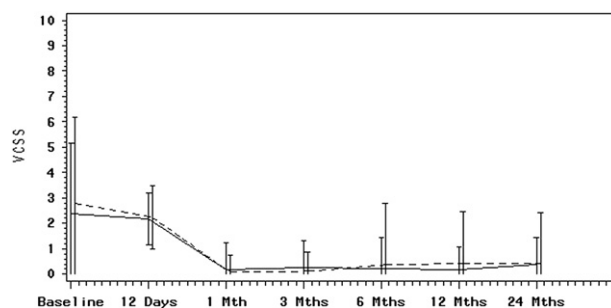


Figure 2 VCSS in patients treated with EVLA or surgery. No significant difference between groups. For improvement over time *p* < 0.01. Legends: ——— surgery, - - - - - EVLA. Error bars: mean \pm 2 standard deviations. Abbreviations: VCSS, venous clinical symptoms score; Mth, months.

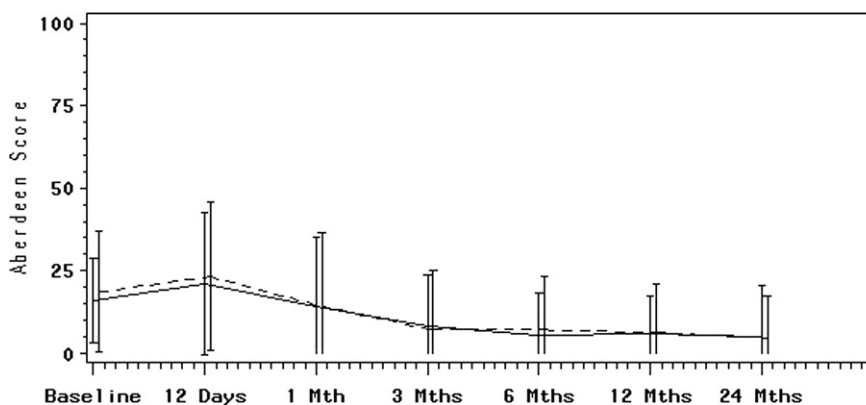


Figure 3 Aberdeen varicose veins severity score in patients treated with EVLA or surgery. No significant difference between groups. For improvement over time $p < 0.01$. Legends: ——— surgery, - - - - - EVLA. Error bars: mean \pm 2 standard deviations. Abbreviations: Mth, months after treatment.

comparison, in the EVLA group, reflux was found in the groin (two legs), the thigh (four legs) and the calf (three legs) (NS). A Kaplan–Meier plot of recurrence over time is shown in Fig. 1. There was no difference between groups. Improvements in both groups in the clinical scoring and quality of life measures were observed from 3 months onwards ($p < 0.01$). For the SF36 scores, improvements were seen in the domains bodily pain, vitality and social functioning ($p < 0.01$). The improvement in VCSS and quality of life scores were still present after 2 years (Figs. 2–6).

Discussion

The recurrence of varicose veins and reflux were not significantly different between the groups. However, recurrence among our patients was substantially higher than in a recent study, where only 6.6 and 7% of legs had developed new varicose veins 2 years after surgery and EVLA, respectively.⁶ In both studies, varices noticed by the patient or the surgeons were counted, and apparently the same criteria for evaluation were used. We have no clear explanation for such discrepancy. The fact that some of the

varices classified as recurrent in our study might have been residual may have influenced the results however. In another randomised clinical trial, recurrence was found in 23 and 34% of patients for up to 2 years after EVLA or cryostripping, respectively.⁷ In two other studies, clinical recurrence was found in 25 and 51% of patients, respectively, 5 years after conventional surgery.^{12,13} This differs little from our results. Technical failure occurred in two and three of our patients in the surgery and EVLA groups, respectively. Failures due to technical problems, where the GSV breaks during stripping are not uncommon.^{12,13} Similarly, early re-canalisation after EVLA may happen, but most cases can be avoided if the laser energy used for ablation is more than $80 \text{ joules cm}^{-1}$ of GSV.¹⁴ In addition, using the laser in continuous mode instead of pulse mode might reduce re-canalisation.

The primary causes of recurrence after surgery are tactical errors, technical errors, neo-vascularisation and progression of the disease.¹⁵ Tactical errors, where the source of reflux is anatomically misjudged, will probably have minor importance when DUS is used preoperatively as in our patients. Only two studies have previously detailed the distribution of reflux after EVLA compared to surgery.^{6,7} Two years after conventional surgery, in the study by

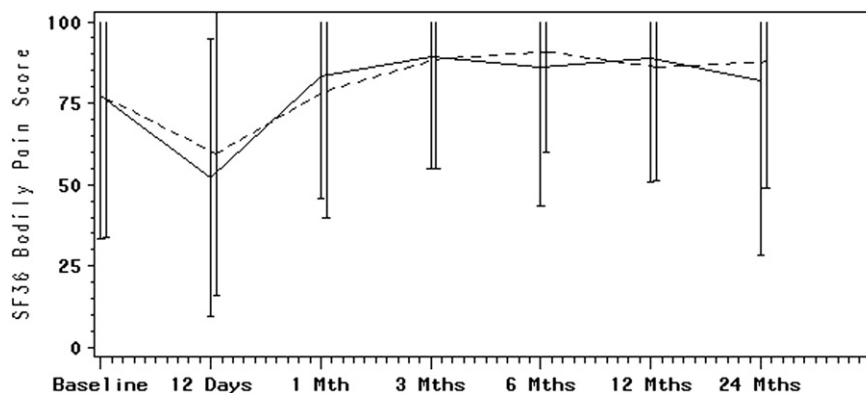


Figure 4 SF36 health-related quality of life score in patients treated with EVLA or surgery, domain bodily pain. No significant difference between groups. For improvement over time $p < 0.01$. Legends: ——— surgery, - - - - - EVLA. Error bars: mean \pm 2 standard deviations.

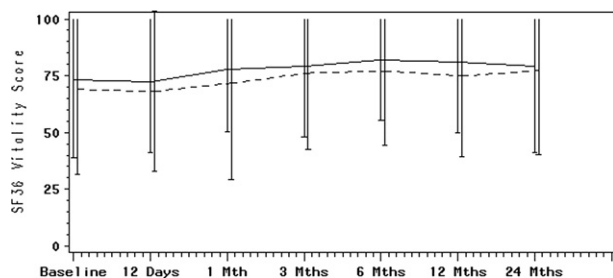


Figure 5 SF36 health-related quality of life score in patients treated with EVLA or surgery: domain vitality. No significant difference between groups. For improvement over time $p < 0.01$. Legends: ——— surgery, - - - - - EVLA. Error bars: mean \pm 2 standard deviations.

Theivacumar et al., recurrent varices were due to neo-vascularisation in the groin in two cases (3%) and mid-thigh perforator reflux in another two cases. After EVLA, re-canalisation was the cause in three patients (4%), mid-thigh perforator reflux in one (1%) and a refluxing AAGSV the cause in another patient.⁶ In the study by Disselhoff et al., the pattern of recurrence was similar to ours.⁷ The distribution of reflux in our patients with new varicose veins was not statistically different between the groups. Reflux into the AAGSV accounted for a substantial number of recurrences. We do not believe that tactical or technical errors were the cause of reflux in these cases, since it developed after the first 6 months. Accordingly, reflux in six AAGSVs after EVLA probably indicates disease progression, whereas in the three cases in the surgical group, neo-vascularisation must also play a role. The relatively high incidence of late reflux in the AAGSV in our patients may make it worthwhile considering primary ablation of this vein if possible, even if it is competent. However, some authors have suggested avoiding ablation of this vein at the initial operation.^{7,16} Alternatively, it can be treated easily with ultrasound-guided foam sclerotherapy at a later stage should it become incompetent resulting in the development of varices. Reflux in the groin and in thigh perforators in our patients was probably caused by neo-vascularisation or disease progression, since the GSV had been completely ablated in these patients. Reflux in calf perforators may

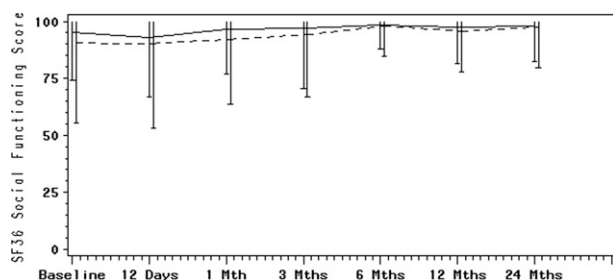


Figure 6 SF36 health-related quality of life score in patients treated with EVLA or surgery: domain social functioning. No significant difference between groups. For improvement over time $p < 0.01$. Legends: ——— surgery, - - - - - EVLA. Error bars: mean \pm 2 standard deviations.

have been present initially, since we did not exclude patients with incompetent perforators. Neither did we record them preoperatively. It is possible that ablation of an incompetent GSV in the calf as well in the thigh may influence recurrence after EVLA.

The recurrence of varicose veins in our patients was mostly minor, in many cases not noticed by the patient, and was not associated with a significant increase in mean VCSS. The disease-specific quality of life (AVVSS) remained similarly improved. The same was true for several domains of SF36. Such improvements after treatment of primary varicose veins with surgery, EVLA and radio-frequency ablation, have been demonstrated before, confirming that treatment of primary varicose veins is worthwhile.^{3-5,17-19} The present study is the first to demonstrate in a randomised trial that improvement in quality of life after EVLA is prolonged beyond the first 6 months following treatment. This prolonged improvement in quality of life was the same in both treatment groups.

One shortcoming of the present study is the fact, that for practical reasons, the treatment and follow-up examinations were not blinded. The patient completed the quality of life questionnaires however, including drawing of varices on the AVVSS form. Ideally, studies such as the present should be blinded as much as possible, and it is technically possible to blind the observer at follow-up, but not the patient. Another shortcoming of the study is our recording of recurrent varicose veins after surgery. This was not formally performed according to the recurrent varices after surgery (REVAS) classification, which is thought to be a useful tool when comparing different studies and treatments.²⁰ However, our classification of the recurrent varices follows the definitions of REVAS and presents most of the information. The present study was powered to show a 15% difference in success rate. Because such difference was not demonstrated, there is a 20% risk of a type 2 error. In our opinion, the present study represents a robust comparison of the two treatments.

In conclusion, our study showed no difference in recurrence and reflux after EVLA compared to conventional surgery in the treatment of primary varicose veins. Our results have shown that the improvement in quality of life gained from the minimally invasive EVLA is the same as that achieved by conventional surgery. The choice of treatment should be tailored to each individual patient taking into account factors such as the anatomy of the veins, the patient's wishes, economy and the surgeon's preferences. Future studies should include more patients if possible, and perform at least 5 years' follow-up.

Conflict of Interest

None.

Sponsor information

The study was supported by a grant from the Public Health Insurance Research Foundation of Denmark. EVLA catheters were provided, in part, by Biolitec AG (Bonn, Germany) and Micronmed (Kristianstad, Sweden). The sponsors had no involvement in the study.

References

- 1 Min RJ, Khilnani N, Zimmet SE. Endovenous laser treatment of saphenous vein reflux: long-term results. *J Vasc Interv Radiol* 2003;**14**:991–6.
- 2 Mundy L, Merlin TL, Fitrudge RA, Hiller JE. Systematic review of endovenous EVL treatment for varicose veins. *Br J Surg* 2005;**92**: 1189–94.
- 3 Rasmussen LH, Bjoern L, Lawaetz M, Blemings A, Birgit Lawaetz, Eklof B. Randomised trial comparing endovenous laser ablation of the great saphenous vein with high ligation and stripping in patients with varicose veins: short term results. *J Vasc Surg* 2007;**46**:308–15.
- 4 Darwood R, Theivacumar N, Dellagrammaticus D, Marvor AID, Gough MJ. Randomised clinical trial comparing endovenous laser ablation with surgery for the treatment of primary great saphenous veins. *Br J Surg* 2008;**95**:294–301.
- 5 Kalteis M, Berger I, Messie-Werndl S, Pistrich R, Schimetta W, Pölz W, et al. High ligation combined with stripping and endovenous laser: early results of a randomised controlled study. *J Vasc Surg* 2008;**47**:822–9.
- 6 Theivacumar NS, Darwood MJ, Gough MJ. Neovascularisation and recurrence rates 2 years after varicose vein treatment for saphenofemoral and great saphenous vein reflux: a comparison of surgery and endovenous laser ablation. *Eur J Vasc Endovasc Surg* 2009;**38**:203–7.
- 7 Disselhoff BCVM, Kinderen DJ, Kelder JC, Moll FL. Randomised clinical trial comparing endovenous laser with cryostripping for great saphenous varicose veins. *Br J Surg* 2008;**95**:1232–8.
- 8 Bergan JJ. Inversion stripping of the saphenous vein. In: Bergan JJ, editor. *The vein book*. San Diego, Calif: Elsevier Academic Press; 2007. p. 231–9.
- 9 Rutherford RB, Padberg Jr FT, Comerota AJ, Kistner RL, Meissner MH, Moneta GL. Venous severity scoring: an adjunct to venous outcome assessment. *J Vasc Surg* 2000;**1**:1307–12.
- 10 Garrat AM, Macdonald LM, Ruta DA, Russel IT, Buckingham JK, Zygmunt HK. Towards measurement of outcome for patients with varicose veins. *Qual Health Care* 1993;**2**:5–10.
- 11 Smith JJ, Garrat AM, Guest M, Greenhalgh MA, Davies AH. Evaluating and improving health-related quality of life in patients with varicose veins. *J Vasc Surg* 1999;**30**:710–9.
- 12 Kostas T, Loannou CV, Toulouopakis E, Daskalaki E, Giannoukas AD, Tsetis D, et al. Recurrent varicose veins after surgery: a new appraisal of a common and complex problem in vascular surgery. *Eur J Vasc Endovasc Surg* 2004;**27**:275–82.
- 13 van Rij AM, Jiang P, Solomon C, Christie RA, Hill GB. Recurrence after varicose vein surgery: a prospective long-term clinical study with duplex ultrasound scanning and air plethysmography. *J Vasc Surg* 2003;**38**:935–43.
- 14 Rasmussen L. Laser treatment as an alternative for the treatment of GSV and SSV incompetence, in: Wittens C (ed.). *Innovative treatment of venous disorders*. EVC Edizioni Minerva Medica Turin, 2009.
- 15 Perrin MR, Guex JJ, Ruckley CV, dePalma RG, Royle JP, Eklof B, et al. Recurrent varices after surgery (REVAS), a consensus document. REVAS group. *Cardiovasc Surg* 2000 Jun;**8**(4): 233–45.
- 16 Theivacumar NS, Dellagrammaticas D, Beale RJ, Mavor AI, Gough MJ. Fate and clinical significance of saphenofemoral junction tributaries following endovenous laser ablation of the great saphenous vein. *Br J Surg* 2007;**94**:722–5.
- 17 Sam RC, Mackenzie RK, Paisly AM, Ruckley CV, Bradbury AW. The effect of superficial venous surgery on generic health-related quality of life. *Eur J Vasc Endovasc Surg* 2004;**28**: 253–6.
- 18 Durkin MT, Turton EP, Wijesinghe LD, Scott DJ, Berridge DC. Long saphenous vein stripping and quality of life – a randomised trial. *Eur J Vasc Endovasc Surg* 2001;**21**:545–9.
- 19 Lurie F, Creton D, Eklof B, Kabnick LS, Kistner RL, Pichot O, et al. Prospective randomised study of endovenous radiofrequency obliteration (closure procedure) versus ligation and stripping in a selected patient population (EVOLVES Study). *J Vasc Surg* 2003;**38**:207–14.
- 20 Perrin M. Recurrent varicose veins: etiology and management. In: Glovicki P, editor. *Handbook of venous disorders*. 3rd edition. UK: Hodder Arnold; 2009. p. 446–65.