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# Comparable Effectiveness of Endovenous Laser Ablation and High Ligation With Stripping of the Great Saphenous Vein

## Two-Year Results of a Randomized Clinical Trial (RELACS Study)

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**Objective:** To compare the clinical efficacy and safety of endovenous laser treatment (EVLT) with high ligation and stripping (HLS) as standard treatment for great saphenous vein (GSV) insufficiency.

**Design:** Two-center randomized controlled trial with 2-year follow-up.

**Setting:** Interventions were performed on ambulatory and hospitalized patients at 2 vein centers, a university dermatology department (EVLT-treated group), and a specialized vein clinic (HLS-treated group).

**Patients:** Random sample of 400 patients with GSV insufficiency.

**Interventions:** Patients were assigned (1:1) to EVLT or HLS of the GSV from September 2004 through March 2007; 185 and 161 patients (limbs), respectively, were treated per protocol.

**Main Outcome Measures:** Clinically recurrent varicose veins after surgery (REVAS classification, primary study objective), duplex-detected saphenofemoral recurrence, clinical venous severity scoring (Homburg Varicose Vein Severity Score), hemodynamics (venous refilling time), quality of life (Chronic Venous Insufficiency

Questionnaire 2), adverse effects, and visual analog scale-based evaluations of patients' satisfaction.

**Results:** Clinically recurrent varicose veins after surgery were similarly observed in both groups: 16.2% (EVLT-treated group) vs 23.1% (HLS-treated group);  $P = .15$ . Duplex-detected saphenofemoral refluxes occurred significantly more frequently after EVLT (17.8% vs 1.3%;  $P < .001$ ). Both treatments equally improved medical condition (Homburg Varicose Vein Severity Score) and disease-related quality of life. Endovenous laser treatment caused more adverse effects (phlebitic reaction, tightness, dyspigmentation) but revealed advantages concerning hemodynamics, recovery, and cosmetic outcome.

**Conclusions:** Both EVLT and HLS are comparably safe and effective procedures to treat GSV incompetence. The significantly higher rate and the course of duplex-detected saphenofemoral recurrences after EVLT remain a matter of further investigations.

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**C**HRONIC VENOUS INSUFFICIENCY (CVI) caused by varicose veins is a common medical condition with prevalence rates as high as 28% to 35% in adults.<sup>1,2</sup> Treatment aims to eliminate pathological refluxes, thereby reducing symptoms, avoiding long-term complications of CVI, and improving disease-related quality of life (QOL). High ligation and

saphenous vein stripping (HLS) is still considered as standard treatment for saphenous vein insufficiency but is associated with ultrasonography-detected junctional recurrence rates of 30% to 40% at 5 years, which particularly at the saphenofemoral junction (SFJ) are often caused by neovascularization.<sup>3-5</sup> One strategy to reduce neovascularization as a risk factor for clinical recurrence consists in

applying different barrier techniques.<sup>6-8</sup> Endovenous procedures, which were implemented as minimally invasive approaches for varicose vein treatment in the late 1990s, might also be useful to circumvent neovascularogenesis.<sup>9-11</sup> These techniques—endovenous laser and radiofrequency ablation, as well as sclerotherapy—share the property of not transecting veins. Contact of endothelial or perivascular progenitor cells with the surrounding wounded tissue, which serves as putative trigger for neovascularization, is avoided.<sup>12</sup> However, endovenous procedures are associated with a risk for recanalization and neoreflux via junctional tributaries.<sup>11,13</sup>

Among these catheter- and ultrasonography-guided approaches, endovenous laser treatment (EVLT) represents the most commonly used technique.<sup>14</sup> The mode of action for laser wavelengths of 810 to 980 nm is hypothesized to be mediated by laser-induced steam bubble formation through energy absorption by hemoglobin and consecutive thrombotic vein occlusion.<sup>15</sup> The safety of EVLT and its efficacy in the early postoperative phase seem to be comparable with those of conventional surgery, as shown by recent randomized controlled trials (RCTs).<sup>16-21</sup> Although the procedure is considered to be highly variable in terms of wavelength, mode of application, power, and energy dose, EVLT is deemed to be safer and more effective compared with radiofrequency obliteration and ultrasonography-guided foam sclerotherapy.<sup>14,22</sup>

However, there is still a medical need for further RCTs comparing endovenous techniques with standard surgical treatment of saphenous vein incompetence to drive reliable conclusions, particularly concerning clinical efficacy.<sup>22</sup> The number of published RCTs on EVLT vs high ligation and stripping is small.<sup>16-21</sup> The sample sizes are largely less powered (mean study population, 124 patients [range, 40-200 patients]), primary study objectives are not always clearly defined, and the follow-up periods are short, ranging from 2 months to 2 years.

It was therefore our purpose to perform a suitably powered RCT to compare the clinical outcome of EVLT with that of conventional surgery (RELACS: Randomized Study Comparing Endovenous Laser Ablation With Crossectomy and Stripping of the Great Saphenous Vein). This report focuses on the early study results—clinical and duplex recurrence, adverse effects, functional outcome, QOL, and patients' evaluation—after a 2-year follow-up.

## METHODS

### PATIENTS

The study population derived from consecutive patients referred for varicose vein surgery to both study centers (Homburg and Bad Bertrich, Germany). Patients initially underwent routine venous diagnostics, were preselected according to defined inclusion criteria, and then further assessed for study eligibility.

### Inclusion Criteria

- Great saphenous vein (GSV) insufficiency with saphenofemoral incompetence and reflux at least down to the knee level
- CVI and/or symptoms caused by GSV incompetence and/or severe clinical findings at risk of varicose vein bleeding, thrombophlebitis or deep vein thrombosis
- Age, 18 to 65 years (at randomization)
- Performance status (according to the criteria of the American Society of Anesthesiologists, of class I-II)

### Exclusion Criteria

- Previous surgical interventions in the groin area with the exception of inguinal herniotomy
- Anterior or posterior accessory saphenous vein incompetence
- Small saphenous vein insufficiency requiring treatment at the same limb
- Acute deep venous thrombosis or postthrombotic syndrome
- Known thrombophilia associated with a high risk of thromboembolism
- Arterial occlusive disease classified as at least Fontaine stage IIA, and/or ankle-brachial index below 0.8
- Active malignant disease (diagnosed during the past 5 years)
- Poor compliance or inability to understand the study-related procedures
- Women who are pregnant or nursing

All patients who were eligible and willing to attend gave their written informed consent prior to randomization. The study protocol was approved by the local ethics committee (Ärzttekammer des Saarlandes, identification No. 98/2004).

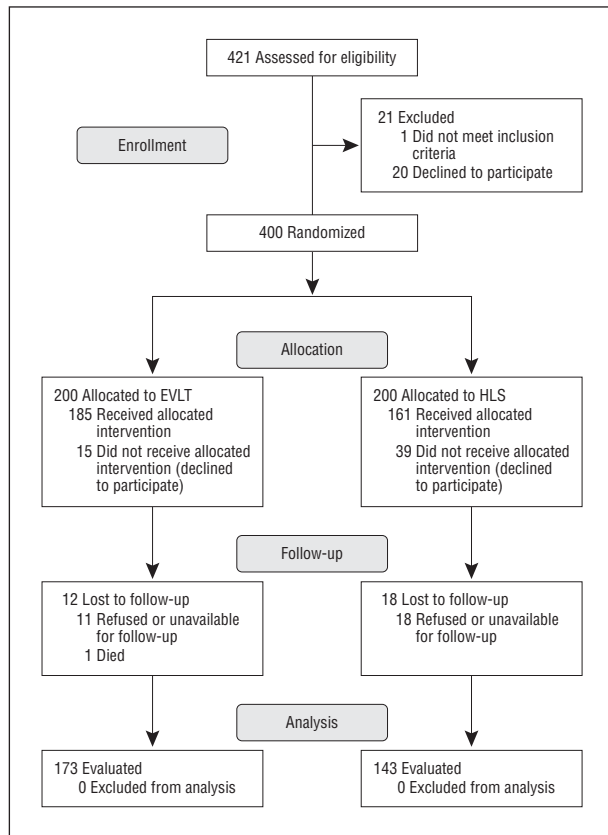
One limb per patient was allowed for randomization. In the event of both limbs being eligible, the one more affected by CVI was chosen for study participation. Patients were randomly allocated to receive EVLT (group A) or HLS (group B) of the GSV. Independent randomization was conducted via fax from a remote site (Institute of Medical Biometry, Epidemiology, and Medical Informatics, Saarland University Hospital, Homburg) in blocks of 10. For treatment, the patients of group A were assigned to Homburg and the group B patients to Bad Bertrich, where the surgical procedures were performed exclusively by appointed surgeons (EVLT treatment: K.R.; HLS treatment: N.F. and P.G.).

Immediately prior to treatment (on the day before or day of surgery) all patients were again assessed by standard clinical and diagnostic procedures: (1) general demographics, clinical evaluation of medical history; (2) clinical, etiologic, anatomic, and pathological (CEAP) classification according to the Society for Vascular Surgery and the International Society for Cardiovascular Surgery recommendations<sup>23</sup>; and (3) clinical and functional impairment of CVI by the Homburg Varicose Vein Severity Score (HVVSS), including venous refilling time (RT) assessed by digital photoplethysmography (DPPG) (Vasoquant VQ 4000; ELCAT, Wolfratshausen, Germany), as detailed elsewhere.<sup>24</sup>

### DUPLEX ULTRASONOGRAPHY ASSESSMENTS

Full venous duplex ultrasonography was performed using Siemens Medical Solutions model Sonoline Antaris (transducer VF 10-5; Issaquah, Washington) and Hewlett Packard Image Point HX (Wilmington, Delaware) as previously described.<sup>24</sup> Reverse flow duration for more than 0.5 seconds at the junction was considered pathological.

Preoperatively, a detailed duplex mapping was performed, including measuring and recording the GSV diameters in the supine position at the SFJ and for EVLT also at the level of distal incompetence, which was marked for the planned GSV puncture on the skin. The proximal and distal GSV radius, as used for the vein surface calculation (see the next subsection), was defined as  $0.5 \times$  GSV diameter at the SFJ and puncture site level, respectively.



**Figure 1.** Patient disposition and study course concerning primary objective (REVAS at 2-year follow-up). EVLT indicates endovenous laser treatment; HLS, high ligation and stripping.

In addition, full duplex scans were postoperatively performed at any follow-up visit. During the first postoperative week, duplex ultrasonography served as quality control, confirming GSV occlusion (EVLT) and removal (HLS), respectively.

## SURGICAL PROCEDURES

### Group A: EVLT

Endovenous laser treatment was performed with bare fibers with an 810-nm diode laser (model 435; MedArt A/S, Hvidovre, Denmark) using Seldinger's technique as described in detail elsewhere.<sup>9</sup> The 20-W laser power was delivered in a continuous pull-back fashion. The applied energy fluence equivalent (EFE) was intended to be 20 J/cm<sup>2</sup> vein surface. The EVLT parameters were chosen from recommendations available at the time of study protocol drafting.<sup>25</sup> For this purpose, the vein surface ( $A_v$ ) was preoperatively calculated as  $[A_v = \pi \times \text{length of vein} \times (\text{radius}_1 (\text{proximal}) + \text{radius}_2 (\text{distal}))]$ .

### Group B: HLS

Standard surgical procedures were performed, consisting of transection of all groin tributaries, flush ligation of the SFJ with nonresorbable Ethibond (Ethicon, New Brunswick, New Jersey) 0-0 suture and neoreflux protection with an invaginating continuous Prolene 4-0 stump suture (Ethicon) as described previously,<sup>7</sup> followed by invagination stripping of the GSV just below the knee. The perioperative conditions were identical in both groups as determined in the study protocol.

All procedures—both EVLT and HLS—were performed exclusively in tumescent local anesthesia with sodium bicarbonate-buffered (0.084%) mepivacaine hydrochloride (0.1%) in isotonic saline. Analgo-sedation using intravenous midazolam hydrochloride and pethidine hydrochloride was allowed at the surgeon's discretion. All patients were covered with an infection prophylaxis with single-shot intravenous cefazolin sodium (1000 mg) or oral ofloxacin (400 mg) in case of  $\beta$ -lactam hypersensitivity. Incompetent perforators were ligated, and peripheral side branches were removed by multiple stab avulsions in the same session.

On treatment completion, an eccentric compression bandage was applied for the first 24 hours. Afterward, the bandages were replaced by class II thigh compression stockings that were recommended to be worn for 4 weeks. Anticoagulation was performed once daily with low molecular weight heparin (tinzaparin, 42.2 mg) for 6 days. In addition, the patients were provided with nonsteroidal antiinflammatories (paracetamol, metamizol sodium, or ibuprofen) that were recommended for 1 week in the EVLT group (ibuprofen, 400 mg, twice a day). All patients were assessed at a 3-month follow-up, and those with apparent residual varices and perforators could be treated with additional phlebectomies or sclerotherapy exclusively at this time point.

## Study Assessment Objectives

Follow-up visits were scheduled in the first postoperative week (days 1-7), at 3 months, 1 year, and 2 years by an active patient recall. The examinations were performed by the same physicians treating the patients (K.R. and N.F.), but a crossover follow-up was allowed (patients could be reevaluated at both centers irrespective of the treatment group). A 5-year follow-up is pending and not included in this report.

The 2-year clinical recurrence-free rate according to the classification of recurrent varices after surgery (REVAS)<sup>26</sup> was determined as the primary study objective. REVAS was defined as the presence of any new visible or palpable varicosity on the study leg that had been noticed by the examining clinician. Clinical recurrences originating from the operated site [nature of source: same site ( $N_{ss}$ )], defined as new varices linked to a saphenofemoral recurrence, to an incompetent GSV or perforator at medial thigh level, and with a medical indication for reoperation were defined as follow-up end point.

The secondary objectives were as follows:

1. The 2-year duplex recurrence-free rate at the SFJ. Duplex recurrence has been defined as a reappearance of reflux at the SFJ at more than 0.5 seconds, detected in vessels at least 2.0 mm in diameter connected with the common femoral vein. In the case of EVLT, reflux also had to be persuable over a distance of at least 2 cm distally from the SFJ.
2. Treatment-related adverse effects.
3. Clinical and functional outcome (HVVSS<sub>0-33</sub>). HVVSS includes varicose vein-associated symptoms (pain, heaviness, swelling, and itching), severity of varicose veins, CVI findings (varicose veins, edema, pigmentation, dermatitis, active ulceration), and semiquantitative venous RT assessed by DPPG.<sup>24</sup>
4. Disease-specific QOL measured by the Chronic Venous Insufficiency Questionnaire (CIVIQ-2).<sup>27</sup> The data collection of CIVIQ-2 was amended during the study course and assessed for the last 100 patients enrolled.
5. Patients' satisfaction, cosmetic outcome, and recovery using questionnaires and visual analog scales (VAS) (range, 1-5).

All scores used in these analyses (HVVSS, CIVIQ, VAS) increased with disease severity, respectively, with a worse outcome.

**Table 1. Baseline Patient Demographics, Clinical Characteristics, and Follow-up Rates**

Characteristic <sup>a</sup>	Treatment Group, No. (%)		P Value
	EVLT (n = 185 Patients)	HLS (n = 161 Patients)	
Patient demographics			
Age, mean (SD) [range], y	47.9 (10.9) [22-67]	48.0 (10.7) [18-66]	.95
Female	124 (67)	113 (70)	.56
BMI, mean (SD) [range]	26.2 (4.1) [18.4-39.1]	26.3 (4.9) [15.7-48.4]	.90
Limb characteristics			
Left side	91 (49)	68 (42)	.23
CEAP			
C2	53 (29)	47 (29)	.75
C3	95 (52)	76 (47)	
C4	36 (20)	35 (22)	
C5	1 (1)	2 (1)	
C6	0	1 (1)	
HVVSS (0-33), mean (SD) [range]	13.0 (4.8) [4-27]	12.6 (4.3) [2-24]	.44
GSV diameter at SFJ (supine position), mean (SD) [range], mm	8.7 (2.8) [3.8-22.0]	8.7 (2.2) [4.4-16.5]	.32
Duration of follow-up			
3 mo	181 (98)	155 (96)	.52
1 y	172 (93)	136 (84)	.02
2 y	172 (93)	143 (89)	.19

Abbreviations: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); CEAP, clinical (C), etiologic, anatomic, and pathological; EVLT, endovenous laser treatment; GSV, great saphenous vein; HLS, high ligation and stripping; HVVSS, Homburg Varicose Vein Severity Score; SFJ, saphenofemoral junction.

<sup>a</sup>Age, BMI, HVVSS, and GSV diameter are expressed as mean (SD) [range]. Other values are expressed as number (percentage).

### Determination of Sample Size

Because no reports dealing with clinical recurrence after EVLT in 2004 were available, we chose duplex recurrence as the surrogate parameter.<sup>28</sup> The duplex recurrence-free rates from prospective studies with a 2- to 3-year follow-up were reported to be 93% after EVLT in a single study and approximately 82% (range, 75%-89%) after HLS in several studies.<sup>3,29-31</sup> Based on log-rank test, a sample size of 180 participants per group would be required to detect this difference of 11% as significant on a 2-sided 5% significance level ( $\alpha=0.05$ ) with 90% statistical power ( $\beta=0.1$ ). We assumed a dropout rate of 10% and accordingly decided to enroll 400 patients into the study.

### STATISTICAL ANALYSIS

Qualitative variables were compared by  $\chi^2$  test between groups. Quantitative variables were analyzed by the Mann-Whitney test and presented as box plots (HVVSS). Intragroup differences of preoperative and postoperative continuous variables were compared by Wilcoxon ranked-sum test. For the recurrence-free rates, Kaplan-Meier analyses were performed, and groups were compared with log-rank test.  $P < .05$  was considered statistically significant. All statistical analyses were performed with PASW Statistics software (version 18; SPSS Inc, Chicago, Illinois).

## RESULTS

### DEMOGRAPHICS

A total of 421 patients meeting the study selection criteria were invited to participate from September 2004 through March 2007. Twenty patients declined randomization, and 1 patient revealed an anterior accessory saphenous vein incompetence, which was defined

as exclusion criterion. Therefore, 400 patients (400 limbs) could be enrolled in the study and were randomized according to the schedule (**Figure 1**). Fifty-four patients declined study participation after receiving the randomization result, in most of the cases owing to a preference for the treatment not assigned. Most (39) were patients from the HLS group. Finally, 185 patients were treated by EVLT, 161 with HLS. All study analyses were performed on this per-protocol (PP) population (n=346). Baseline patient demographics and limb characteristics were well balanced between the groups (**Table 1**).

### TREATMENT SUCCESS AND CHARACTERISTICS

The early treatment success was determined by duplex scan in the first postoperative week. Endovenous laser treatment was applied with a mean energy fluence equivalent of 22.5 J/cm<sup>2</sup>, resulting in an immediate occlusion rate of 98.9% (183 of 185 patients). High ligation and GSV stripping were successful in all cases. The detailed EVLT data are summarized in **Table 2**.

### CLINICAL RECURRENCE AND DUPLEX FINDINGS IN VIEW OF REVAS CLASSIFICATION

For the recurrence analyses, all patients presenting at the 2-year follow-up and patients with additional recurrences at the 1-year follow-up were included (316 [91.3% of the PP population]). The overall clinical recurrence-free rates after a median follow-up of 24.5 months were 83.8% (EVLT group) and 76.9% (HLS group) ( $P=.15$ ) (**Table 3**). Log-rank testing revealed no significant difference as well ( $P=.14$ ) (**Figure 2A**).

The recurrence-free rates concerning varicose veins originating from the operated site ( $N_{ss}$ ) were 96.5% in both groups. Log-rank testing also revealed no significant differences ( $P > .99$ ) (Figure 2B).

Topographically, recurrent varices occurred most frequently at the lower limb and thigh. The source of recurrence was located at the SFJ in 6 patients after EVLT and

in 2 cases after HLS. In most patients, the origin of recurrent varices assessed was not detectable (ie, only refluxive side branches were present; 61% in both groups). New varicose veins, independent from the operation site [nature of source: different site ( $N_{ds}$ )], were more frequently found in the HLS group ( $P = .04$ ), especially originating from lower leg perforators. Most of these patients were treated by sclerotherapy or miniphlebectomy without differences between groups. One patient who underwent EVLT developed an extensive recurrence during pregnancy, and the decision was made to retreat her by HLS. In all patients who developed a clinical recurrence, 43% and 30% were considered for a wait-and-see approach. Table 3 shows the detailed REVAS data.

## SECONDARY OBJECTIVES

### Duplex Recurrence

The incidence of duplex ultrasonography-detected recurrences at the SFJ was significantly higher in the EVLT group. The duplex recurrence-free rates were 82.2% (EVLT group) and 98.7% (HLS group) at the 2-year follow-up ( $P < .001$ ) (Figure 2C).

**Table 2. Technical Details of Endovenous Laser Treatment**

Characteristic <sup>a</sup>	Mean (SD) [range]
Length of treated GSV, cm	45.1 (13.3) [12-80]
Surface of treated GSV, cm <sup>2</sup>	98.7 (42.1) [25.6-235.4]
Vein access by puncture	180 (97)
Laser tip position (distance from SFJ), mm	14.0 (2.3) [10.0-19.8]
Pullback velocity, mm/s	4.4 (1.0) [1.9-7.2]
EFE, J/cm <sup>2</sup>	22.5 (2.3) [16.5-29.0]
EFE below threshold, <20 J/cm <sup>2</sup>	15 (8)
LEED, J/cm	48.7 (12.7) [27.9-108.0]
LEED by GSV diameter $\geq 10$ mm	62.6 (11.9) [48.0-108.0]

Abbreviations: EFE, endovenous fluence equivalent; GSV, great saphenous vein; LEED, linear endovenous energy dose; SFJ, saphenofemoral junction.

<sup>a</sup>Vein access and EFE below threshold are expressed as number (percentage); all other parameters are expressed as mean (SD) [range].

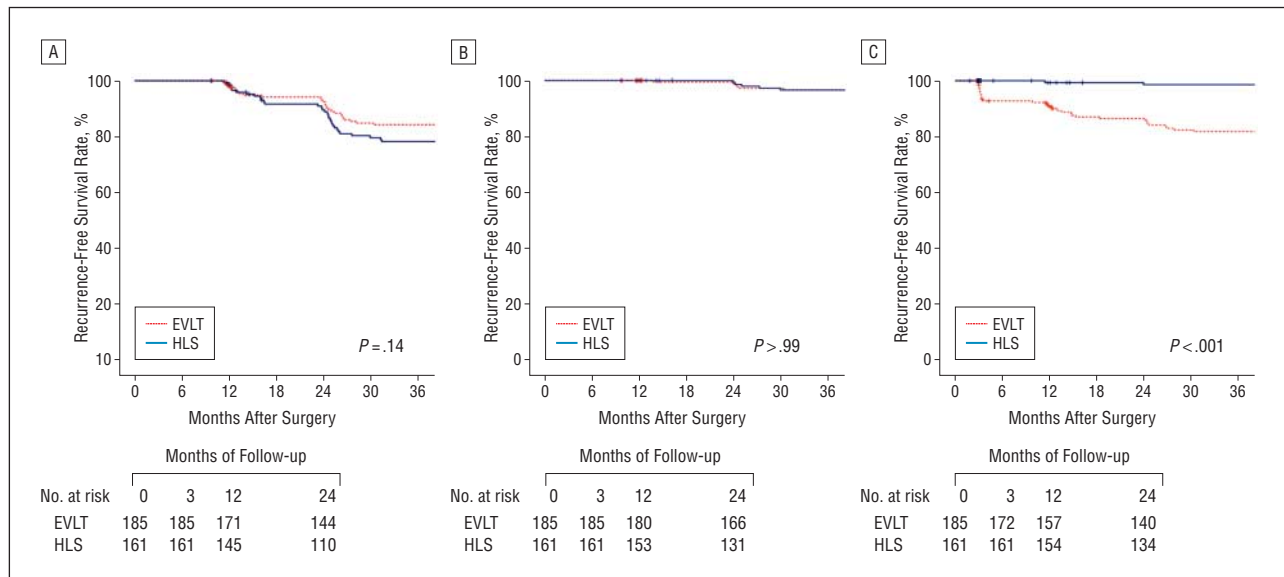
**Table 3. Cumulative Clinical Recurrences Characterized by REVAS Classification<sup>a</sup> and Management**

Characteristic	Treatment Group, No. (%)		P Value
	EVLT (n = 173 Patients)	HLS (n = 143 Patients)	
Overall REVAS	28 (16.2)	33 (23.1)	.15
Follow-up, median [range], mo	24.4 [13.7-45.9]	24.7 [20.5-47.7]	.26
Topography <sup>b</sup>			
Groin	0	1 (3)	>.99
Thigh	16 (57)	15 (46)	.44
Popliteal fossa	3 (11)	4 (12)	>.99
Lower leg	19 (68)	25 (76)	.57
Other	0	1 (3)	>.99
Source of recurrence <sup>b</sup>			
Not detectable	17 (61)	20 (61)	>.99
Saphenofemoral junction	6 (21)	2 (6)	.13
Thigh perforator	5 (18)	4 (12)	.72
Saphenopopliteal junction	0	3 (9)	.24
Lower leg perforator	1 (4)	8 (24)	.03
Nature of source <sup>b</sup>			
Same site	6 (21)	5 (15)	
Technical failure	6	2	.74
Neovascularization	0	1	
Uncertain	0	2	
Different site	22 (79)	32 (97)	
Persistent	0	1	.04
New	21	31	
Uncertain	1	0	
Contribution from persistent incompetent GSV			
Not detectable	23 (82)	28 (85)	.88
Above knee	2 (7)	3 (9)	
Below knee	3 (11)	2 (6)	
Management of REVAS			
Wait-and-see approach	12 (43)	10 (30)	.23
Sclerotherapy and/or phlebectomy	15 (54)	23 (70)	
GSV surgery reoperated	1 (4)	0	

Abbreviations: EVLT, endovenous laser treatment; GSV, great saphenous vein; HLS, high ligation and stripping; REVAS, recurrent varices after surgery.

<sup>a</sup>See Perrin et al.<sup>26</sup>

<sup>b</sup>Multiple selections were applicable for these topics (topography, source of recurrences, nature of source), resulting in possible percentages greater than 100%. All parameters are expressed as number (percentages). Nonapplicable items of REVAS were left out.



**Figure 2.** Kaplan-Meier curves showing recurrence-free survival. A, Survival for overall clinical recurrent varices after surgery (REVAS) (any site); B, for clinical recurrence with a nature of source at the operated site (REVAS NSs); and C, for duplex recurrence at the saphenofemoral junction. Differences between groups were compared with log-rank test. EVLT indicates endovenous laser treatment; HLS, high ligation and stripping.

**Table 4. Treatment-Related Adverse Effects<sup>a</sup>**

Adverse Effect	Treatment Group, No. (%)		P Value
	EVLT (n = 185 Patients)	HLS (n = 161 Patients)	
Deep vein thrombosis	1 (0.6) <sup>b</sup>	1 (0.6) <sup>b</sup>	
Thrombus propagation into CFV	2 (1.1)	0	
Wound infection	1 (0.6) <sup>c</sup>	0	
Ecchymosis and/or bruising	169 (91)	145 (90)	.71
VAS score, mean (SD), (range, 1-5) <sup>d</sup>	1.9 (1.0)	1.8 (0.8)	.22
Phlebitis and/or periphlebitis	20 (11)	4 (3)	.003
Induration	70 (39)	13 (8)	<.001
VAS score, mean (SD), (range, 1-5) <sup>d</sup>	1.9 (1.0)	2.2 (1.2)	.32
Pain			
First postoperative week	118 (64)	91 (57)	.19
VAS score, mean (SD), (range, 1-5) <sup>d</sup>	1.6 (0.8)	1.3 (0.6)	.005
Retrospectively evaluated	139 (77)	88 (57)	<.001
VAS score, mean (SD), (range, 1-5) <sup>d,e</sup>	2.4 (1.0)	2.1 (1.0)	.10
Pain duration, mean (SD), d	8 (6)	17 (20)	.03
Dysesthesia			
At 3-mo follow-up	17 (9)	22 (14)	.18
At 1-y follow-up	11 (6)	11 (8)	.66
At 2-y follow-up	7 (4)	11 (8)	.23
Dyspigmentation			
At 3-mo follow-up	57 (32)	19 (12)	<.001
At 1-y follow-up	31 (18)	8 (6)	.002
At 2-y follow-up	12 (7)	4 (3)	.12

Abbreviations: CFV, common femoral vein; EVLT, endovenous laser treatment; HLS, high ligation and stripping; VAS, visual analog scale.

<sup>a</sup>The VAS parameters and pain duration are expressed as mean (SD); all other parameters are expressed as number (percentage).

<sup>b</sup>Gastrocnemius vein.

<sup>c</sup>Superficial infection, phlebectomy area, resolved with oral antibiotics.

<sup>d</sup>Range, 1-5.

<sup>e</sup>At 3-month follow-up.

In the HLS group, we detected refluxive veins originating from the SFJ in 2 patients with diameters of 3.5 and 3.8 mm, defined as incompetent tributary and neovascularization in 1 case each, both connected with a clinical recurrence. A total of 32 patients of the EVLT group revealed a duplex recurrence; 26 of

them (81%) were clinically silent. We observed partial GSV recanalizations in 24 patients (75%) and incompetent groin tributaries, predominantly the anterior accessory saphenous vein, in 9 patients (28%). The mean reflux length in recanalized GSVs was 5.7 cm (range, 2-30 cm).

**Table 5. Clinical Outcome (Assessed by HVVSS and DPPG) and Health-Related Quality of Life (CIVIQ-2)**

Measure <sup>a</sup>	Treatment Group, Mean (SD)		P Value
	EVLТ	HLS	
HVVSS score (range, 0-33)			
At 3-mo follow-up	3.9 (3)	3.8 (3)	.65
At 1-y follow-up	2.0 (2)	2.1 (3)	>.99
At 2-y follow-up	2.1 (3)	1.9 (3)	.33
Limbs with venous RT>25s (DPPG), No. (%)			
At 3-mo follow-up	160 (88)	122 (79)	.02
At 1-y follow-up	146 (86)	103 (76)	.03
At 2-y follow-up	141 (82)	101 (71)	.02
CIVIQ-2 score <sup>b</sup>			
Range, 0-100; all components			
Preoperative (n = 47 [EVLТ group]; n = 37 [HLS group])	28.6 (19)	29.4 (16)	.66
At 3-mo follow-up (n = 43 [EVLТ group]; n = 37 [HLS group])	12.8 (14)	18.0 (16)	.11
At 1-y follow-up (n = 40 [EVLТ group]; n = 32 [HLS group])	10.5 (14)	11.1 (14)	.73
At 2-y follow-up (n = 41 [EVLТ group]; n = 33 [HLS group])	10.8 (13)	9.5 (11)	.55
Subscore items at 3-mo follow-up			
0-20; pain items	3.0 (3)	4.6 (4)	.07
0-20; physical items	2.4 (3)	3.4 (4)	.12
0-45; psychological items	5.1 (6)	7.3 (8)	.18
0-15; social items	2.3 (3)	2.7 (3)	.52

Abbreviations: CIVIQ-2, Chronic Venous Insufficiency Questionnaire; DPPG, digital photoplethysmography; EVLT, endovenous laser treatment; HLS, high ligation and stripping; HVVSS, Homburg Varicose Vein Severity Score; RT, refilling time; VAS, visual analog scale.

<sup>a</sup>Limbs with normalized venous RT are expressed as number (percentage); all other parameters are expressed as mean (SD).

<sup>b</sup>CIVIQ was assessed in the last 100 patients enrolled; the numbers of evaluable patients are given in parentheses.

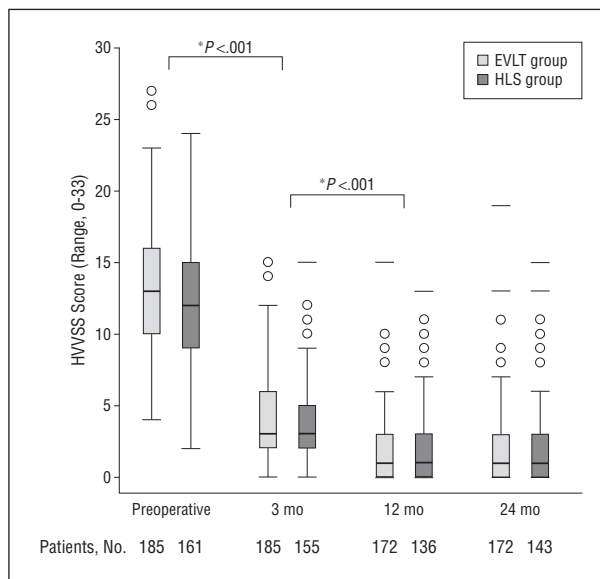
### Treatment-Related Adverse Effects

There were no significant differences of major complications between the groups. We observed 1 case of gastrointestinal tract bleeding 5 days after EVLT that was associated with low molecular weight heparin and ibuprofen intake. This patient presented with an asymptomatic gastrocnemius vein thrombosis at the 3-month follow-up. Two additional patients developed thrombus propagations of less than 5 mm into the common femoral vein after EVLT (complication rate, 1.1%). Both events resolved without complications after 3 and 5 weeks of treatment with low molecular weight heparin. One patient in the HLS group was diagnosed as having a gastrocnemius vein thrombosis 2 weeks after surgery. One 62-year-old female patient in the EVLT group died during the study follow-up from a cerebral hemorrhage in conjunction with a hypertensive crisis. This event occurred 11 months after study treatment and was considered not to be study related.

Minor adverse effects were frequent but were mild in most cases. Phlebitic reactions, indurations, dyspigmentations, and pain incidence and intensity were more pronounced in the EVLT group. Pain persisted longer after HLS. Skin burns did not occur. No significant differences were found concerning bruising and dysesthesia. The detailed results and P values are given in **Table 4**.

### Clinical and Functional Outcome

HVVSS significantly decreased from baseline to 3 months ( $P < .001$ ), further decreased from 3 months to 12 months ( $P < .001$ ), and remained stable 12 to 24 months without differences between the groups (**Table 5** and **Figure 3**). No differences in the relative HVVSS changes could be observed. A normalized venous refilling time (assessed by



**Figure 3.** Box plots demonstrating preoperative and postoperative values of the Homburg Varicose Vein Severity Score (HVVSS). The responses from before surgery to 3 months after surgery and from 3 to 12 months after surgery were significant ( $P < .001$ ) without differences between the treatment groups. EVLT indicates endovenous laser treatment; HLS, high ligation and stripping. The whiskers represent the data distribution outside the interquartile range (IQR) and are limited to 1.5 times the IQR. Circles and dashes are outliers outside the  $\times 1.5$  and 3 IQR ranges, respectively.

DPPG) was achieved by more patients of the EVLT group (**Table 5**).

### Disease-Specific QOL

The CIVIQ-2 scores improved significantly in both groups from before surgery to 3 months after surgery ( $P < .001$ )

and further improved in the HLS group from 3 to 12 months after surgery ( $P = .01$ ). There were no significant differences between groups either in the overall score or in the subscore items (pain, physical, psychological, social well-being) (see Table 5 for  $P$  values). However, we observed a trend toward a better QOL 3 months after EVLT, particularly concerning pain ( $P = .07$ ) (Table 5).

#### Patients' Satisfaction, Cosmetic Outcome, and Recovery

All patients were asked to evaluate their satisfaction with each treatment and with the cosmetic results by VAS-based questionnaires (scale, 1-5). Cosmetic outcome was rated significantly better by the EVLT group at the 2-year follow-up (1.5 vs 1.7;  $P = .02$ ). We detected no other differences between the treatments. At the 2-year follow-up, 98% of all patients stated that they would undergo each treatment again if medically necessary.

Furthermore, the patients were asked to indicate how long the recovery took until they could resume basic physical activities (eg, walking around without discomfort, doing housework) and capacity to work. Basic activity was achieved after 4.8 days (EVLT group) and 4.0 days (HLS group) ( $P = .13$ ), and the ability to work or to perform comparable tasks was achieved after 10.4 and 11.8 days ( $P = .02$ ).

#### COMMENT

This is, to our knowledge, the largest and most powerful RCT comparing an endovenous technique with conventional surgery at this time. Both methods—EVLT and HLS of the GSV—are equivalent in terms of the primary objective of clinical recurrence and most of the secondary objectives at 2-year follow-up. This major finding is in accordance with those of all the RCTs published so far comparing EVLT and HLS.<sup>11,16-21</sup> The patients were remarkably satisfied with the treatment results of both procedures. Ninety-eight percent of the study population would undergo each treatment once again. In addition, the clinical outcome did not differ. However, some findings were surprising and contradictory to those in the corresponding literature.

The duplex-detected saphenofemoral recurrence rates were the opposite of what we expected according to available publications at the study initiation, which were predominantly single center case series. Concerning EVLT, the 2-year rate of 17.8% was in the upper range of RCT data published to date (7.4%-17.5%).<sup>10,16,17,20</sup> This rate might be improvable by modifying the treatment protocol with less power but with a higher linear endovenous energy dose (LEED) as recently recommended ( $>60$  J/cm),<sup>32</sup> although pullback velocity and LEED, at least concerning the larger GSVs, were within the recommended ranges.<sup>33</sup> However, these recommendations are not proved by RCTs, and we could actually not find a negative correlation between LEED and duplex recurrence (data not shown).

More striking is the low saphenofemoral recurrence rate after HLS after 2 years (1.3%) that is warranted by cross-

over follow-up investigations at both centers. This finding confirms the study of Frings et al,<sup>7</sup> who significantly reduced saphenofemoral recurrence by invaginating the GSV stump with a nonresorbable suture. In contrast, comparable studies using silicon or polytetrafluoroethylene patch barriers revealed duplex-detected recurrent reflux rates of 6% to 21% after 1 to 3 years.<sup>6,8</sup> Besides the suture technique and neoreflux protection with nonresorbable material that we used in this study, an additional important detail might be that surgery was performed under tumescent local anesthesia (TLA), which allows for a gentle bloodless preparation, thus minimizing the surgical trauma and hypothetically alleviating the risk of neovascularization.<sup>12</sup> To our knowledge, the role of TLA as a protective factor in neoangiogenesis has not been investigated so far. However, Christenson et al<sup>20</sup> reported a similarly low saphenofemoral recurrence rate 2 years after HLS, which they performed under general or spinal anesthesia.

The significant difference of saphenofemoral recurrence was, however, not mirrored by the clinical and functional outcome at the 2-year follow-up. Eight-one percent of the refluxes after EVLT were clinically irrelevant as shown by REVAS N<sub>ss</sub> (Figure 2B). Currently, it remains speculative as to if, when, and to what extent the duplex-detected refluxes at the SFJ evolve to a clinical recurrence. While correlations between neovascularization and the subsequent development of clinical recurrence have been shown for HLS from 1 to 5 years postoperatively,<sup>28</sup> studies concerning EVLT are missing. We assume that recanalization after EVLT is an early but limited recurrence event, whereas neovascularization due to HLS might increasingly occur several years after surgery, as very recently shown.<sup>10,11</sup> Further follow-up to 5 years after treatment is scheduled for this study and will probably provide more evidence on this topic.

The superiority of EVLT concerning clinical recurrence at distant sites (REVAS N<sub>ds</sub>) and venous refilling time (assessed by DPPG) can be explained by a different hemodynamic situation after EVLT with physiological antegrade flow via groin tributaries. Nevertheless, a center bias caused by different intensities in performing the phlebectomies cannot be excluded. However, the recurrent varicose veins observed in both groups at the 2-year follow-up had no notable impact on venous severity scoring and QOL and can therefore be considered as more aesthetically than clinically relevant.

The observed adverse effects after EVLT were in the range of published reviews focusing this topic.<sup>34</sup> It is noteworthy that EVLT induced more pain in a higher percentage of patients compared with HLS in the early postoperative phase, confirming the data of a recent RCT.<sup>21</sup> Use of TLA and more analgesodatives in the HLS group (data not shown) as well as phlebotic reactions of the GSV after EVLT might both account for this. Of additional importance is the fact that in this study EVLT was performed using a bare fiber and 810-nm wavelength. Novel laser devices (eg, radial fiber, devices with 1320- and 1470-nm wavelength) probably warrant less adverse effects.<sup>35</sup> However, we found advantages for EVLT in terms of disease-related QOL, particularly the pain section, at the 3-month follow-up, which might have become significant if the whole study population had been as-

sessed for CIVIQ-2. Although we observed significantly more dyspigmentations after EVLT up to 1 year after treatment, this did not impair QOL and satisfaction with cosmetic outcome, which actually was superior after EVLT.

Endovenous laser treatment was advantageous in terms of how soon a patient could return to work, but the difference of 1.4 days was smaller, and the recovery time of 10 days was longer than expected from the literature. However, because recovery is a highly variable parameter depending on multiple factors (eg, the extent of varicose veins, simultaneously performed phlebectomies), the studies published so far are utterly not comparable owing to different approaches and study populations.<sup>36</sup>

In conclusion, in our study EVLT and HLS were equally effective and safe approaches to treat GSV incompetence, with minor advantages for the EVLT group in a patient's evaluation of cosmetic outcome and reconvalescence at the 2-year follow-up. The significantly higher rate and the course of duplex-detected saphenofemoral recurrences after EVLT will remain a matter of further investigations.

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