

High ligation and stripping vs. endothermal ablation of the great saphenous vein: What can we learn from the latest long-term analyses?

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Keywords

Endothermal ablation, high ligation and stripping, randomised controlled trial, recurrence

Summary

Background: Saphenous vein incompetence is globally treated in different ways, by endovenous ablation, predominantly by endothermal ablation, sclerotherapy or by open surgery. The choice of the respective method seems thereby to depend more on national regulatory requirements e.g. in the British NHS, or on the preference of the particular medical practitioner, than on individual patients' factors. As some more evidence from randomised long-term clinical trials is currently available, it is reasonable to reevaluate the different techniques, especially endothermal ablation vs. open surgery. **Methods:** Selective literature analysis based on a systematic PubMed search focussed on long-term clinical trials (randomised controlled trials (RCT) and systematic reviews/meta-analyses) with a follow-up of at least 5 years comparing endovenous thermal ablation with high ligation and stripping of the great saphenous vein. Descriptive analysis of long-term results, especially due to recurrence and quality of

life. **Results:** The search terms „surgery“, „endovenous“, „varicose vein“, filtered by RCT, systematic review, and meta-analysis resulted in 74 publications since 01-Jan-2014, hereof 7 long-term RCTs and 2 meta-analyses comparing open surgery with endovenous techniques. In these studies, endovenous ablation was mostly performed by 810–980 nm wavelength lasers using a bare fibre. No differences between treatments were found with respect to venous severity scoring, patients' quality of life, and clinical overall recurrence due to REVAS classification. However, duplex and clinical recurrence from the groin were significantly more frequent after endovenous thermal ablation. **Conclusions:** Open surgery is more effective than endothermal ablation in the long term warranting lower rates of duplex and clinical same site recurrence. Therefore, rating open surgery as a treatment of second or third choice in current European guidelines seems currently to be no longer justified. However, there is a considerable paucity of randomised trials comparing open surgery with novel endovenous laser (e. g. laser with higher wavelengths and radial fibre) and radiofrequency techniques, which are mandatory by now.

Schlüsselwörter

Crossektomie/Stripping, Endothermische Ablation, randomisierte kontrollierte Studien, Rezidiv

Zusammenfassung

Hintergrund: Die Therapie der Stammvarikose erfolgt weltweit mit unterschiedlicher Präferenz endovenös, überwiegend thermoablativ, oder offen-chirurgisch. Aktuell liegt jedoch eine Evidenz aus Langzeitstudien (Nachbeobachtungszeit ≥ 5 Jahre) vor, die eine erneute Betrachtung der Wertigkeit der Therapieverfahren notwendig macht. **Methoden:** Systematische Literaturrecherche zu Langzeitstudien, in denen endovenös thermische Ablationsverfahren mit Crossektomie und Stripping der V. saphena magna verglichen werden. Deskriptive Auswertung der Ergebnisse. **Ergebnisse:** Langzeitstudien liegen nahezu ausschließlich für den Vergleich mit endovenöser Laserablation und Lichtwellenleitern der 1. Generation (810–980 nm) vor. Während hinsichtlich der Krankheitsschwere und der postoperativen Lebensqualität keine Unterschiede zu beobachten sind, ist die Rate duplexsonographischer und klinischer Crossenrezidive nach Crossektomie signifikant geringer. **Schlussfolgerungen:** Valide Langzeitstudien zu den heute überwiegend verwendeten endothermischen Ablationstechniken im Vergleich zur offenen Operation fehlen, sind aber angesichts der Befunde aus Studien mit Lasern der 1. Generation dringend geboten.

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Crossektomie und Stripping vs. endothermische Ablation der V. saphena magna: Was können wir aus aktuellen Langzeitanalysen lernen?

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Introduction

With a prevalence in the adult population of approx. 30%, varicose veins and the associated chronic venous insufficiency (CVI) are among the most common diseases in Germany (18). Due to demographic changes and the high birth rate of the 1960's, venous diseases are assumed to be currently undergoing a marked increase. The typical, congestion-induced symptoms in the legs with varicose truncal veins, as well as the cosmetic impairment, cause a marked loss in the quality of life (4). In addition, the potential complications are of considerable medical and socioeconomic importance (8). For example, the risk of thrombosis in patients with primary varicose veins is increased more than 5-fold compared to unaffected patients of the same age (2). To avoid complications and advanced stages of CVI, the current guidelines recommend early invasive therapy of incompetent truncal veins (30).

The aim of such therapy is to remove reflux in the truncal, tributary and perforating veins. This can be achieved either by the surgical removal of the refluxing vein – in the case of an incompetent truncal vein by high ligation and stripping – or by thermal and non-thermal techniques of endovenous ablation. Although the classic operation is in principle universally applicable (10), endovenous procedures, especially endovenous laser treatment, are increasingly being used throughout the world (28). This is because of the advantages of minimally invasive techniques: lower rates of infection, better quality of life in the first postoperative weeks and faster recovery compared to open surgery (1, 3, 14, 16, 19). But for the affected patient, it is not only the immediate postoperative comfort that is important but, to an even greater extent, the long-term therapeutic benefits (23). There are indications in the studies published to date that long-term effectiveness, in terms of inguinal recurrences demonstrated by duplex ultrasound and clinical recurrences, is higher after high ligation and stripping than with laser ablation (22). The occurrence of refluxing veins detected by duplex ultrasound in the region of the treated saphenofemoral junction is a sur-

rogate parameter for a subsequent clinical recurrence (5).

Differences in national health policies, the question of reimbursement and/or personal preferences of the physician often determine which treatment method is used. However, evidence from randomised studies with 5-year follow-up is now available that necessitates a reconsideration of the value of high ligation and stripping vs. endothermal ablation.

Methods

Based on a PubMed search, a selective analysis of the literature was carried out, limited to randomised controlled studies (RCT), meta-analyses and systematic reviews comparing high ligation and stripping (HL/S) and endothermal ablation procedures [ETAP: endovenous laser ablation (EVLA), radiofrequency ablation (RFA), endovenous steam ablation], to treat truncal vein incompetence of the great saphenous vein (GSV). Only publications written in English or German, or for which at least an English abstract was available, were considered. Search terms were the following: “surgery”, “endovenous”, “varicose vein”. The search period was limited to the past five years (2014–2018). Studies with a follow-up period of less than five years and studies in which all treatment groups underwent high ligation (e.g. HL/S vs. HL/EVLA) were excluded.

The aims of this review were firstly a descriptive comparison of the techniques in respect of the study variables of long-term relevance: quality of life, severity of the disease (vein-scoring), duplex ultrasound and clinical recurrence and secondly to determine whether the study results suggest that further research is needed. If this is the case, then an attempt was to be made to develop worthwhile future approaches to research.

Results

The search terms “surgery”, “endovenous”, “varicose vein”, filtered according to the above-named types of article, produced 74 publications (01.01.2014 – 30.06.2018), of

which 36 were RCTs, 13 meta-analyses and 39 systematic reviews. 14 publications were classed as being more than one type of article. 68 publications were excluded from further analysis, for reasons of non-relevance to the question being addressed, inapplicable type of publication according to the search filter and studies with follow-up periods of less than 5 years. A total of 9 publications were included: 2 meta-analyses (11, 12), 4 RCTs (9, 13, 21, 27) according to the above-named search criteria, two other RCTs published before the search period that were cited in the above-mentioned meta-analyses (6, 20) and another recent study not yet listed in PubMed as an RCT (26). The system used in the PubMed search is shown in ► Figure 1.

The following treatments were compared in the RCTs with five-year follow-up (► Table 1):

- HL/S or HL/cryostripping (HL/Cs) vs. EVLA (810 – 980 nm, bare-tip fibre); n=4
- HL/S vs. EVLA (940 nm, bare-tip fibre) vs. foam sclerotherapy; n=1
- HL/S vs. EVLA (sometimes 940 nm bare-tip fibre, sometimes 1470 nm radial fibre) vs. foam sclerotherapy; n=1
- HL/S vs. EVLA (940 or 1470 nm, bare-tip fibre) vs. RFA vs. foam sclerotherapy; n=1

The proportion of patients followed-up relative to the patients treated per protocol in the RCTs was between 39% and 93%. The treatment protocols for endovenous laser ablation and the most important study results and limitations are summarised in ► Table 1.

Severity scores and quality of life

Disease severity was recorded in a validated manner in 3/7 RCTs. These studies demonstrated that disease severity measured with the Venous Clinical Severity Score (VCSS, n=2) (6, 20) or Homburg Varicose Vein Severity Score (HVVS, n=1) (21) significantly improved up to the 5th postoperative year compared with the preoperative value. In one study there was a slight (6), in another a significant deterio-

Tab. 1 Randomised long-term studies to compare endothermal ablation techniques with high ligation/stripping of the great saphenous vein. Abbreviations: AVVQ = Aberdeen Varicose Vein Questionnaire; HL/S = high ligation und stripping; CEAP = Clinical Etiologic Anatomic Pathophysiologic Classification; cm = centimetres; Cs = Cryostripping; cw = continuous; EVLA = endovenous laser ablation; FU = Follow-up; GSV = great saphenous vein; HVVSS = Homburg Varicose Vein Severity Score; J = joule; QL = quality of life; nm = nanometres; pw = pulse-wise; RFA = radiofrequency ablation; s = seconds; UGFS = ultrasound-guided foam sclerotherapy = foam sclerotherapy; VCSS = Venous Clinical Severity Score; W = watt

First author and year of publication	Study arms	Treatment parameters EVLA	Number (legs)	FU rate	Main results/limitations
Disselhoff (6) 2011	EVLA HL/Cs	810 nm / 14 W / cw 0.2 cm/s withdrawal speed Applied energy dose: 57 J/cm	60 60	63%	Results: No differences in primary study variables (incompetence shown by duplex ultrasound, VCSS, AVVQ) Limitations: Selection of patients: CEAP-C2; single-centre study, low FU rate
Rasmussen (20) 2013	EVLA HL/S	980 nm / 12 W / pw (1.5 s impulse / 1.5 s pause) Applied energy dose: 74 J/cm	69 68	67%	Results: No difference in primary (open refluxing segments of the GSV \geq 5 cm) or secondary study variables (clinical recurrence, reoperations, VCSS, AVVQ) Limitations: Selection of patients: CEAP-C2 (83%) to C4, low FU rate
Van der Velden (27) 2015	EVLA HL/S UGFS	940 nm / 10 W / cw 1/6 cm/s withdrawal speed Applied energy dose: 59 J/cm	78 69 77	86%	Results: In the comparison EVLA vs. HL/S no difference in primary study variables (obliteration or absence of GSV after EVLA or after HL/S); after EVLA significantly more frequent sapheno-femoral reflux; no differences in postop. QL (AVVQ) Limitations: Different anaesthetic techniques with EVLA and HL/S
Rass (21) 2015	EVLA HL/S	810 nm / 20 W / cw Intended energy dose: 20 J/cm ² Applied energy dose: 23 J/cm ² (49 J/cm)	185 161	81%	Results: No difference in primary study variables (clinical recurrence after REVAS); duplex-derived junctional recurrence and clinical recurrence originating in the sapheno-femoral region more often after EVLA vs. HL/S; no differences in terms of HVVSS and QL Limitations: EVLA and HL/S were exclusively performed at two different sites
Gauw (9) 2016	EVLA HL/S	980 nm / 12 W / cw Intended energy dose: 100 J/cm proximal 10 cm, then 50–80 J/cm depending on GSV diameter Applied energy dose: 65 J/cm	62 68	93%	Results: Clinical recurrence originating in the sapheno-femoral region and duplex-derived junctional recurrence more frequent after EVLA vs. HL/S; no difference in secondary study variables (CEAP-C, QL, reoperations) Limitations: Single-centre study
Lawaetz (13) 2017	EVLA HL/S RFA UGFS	980 nm (12% of legs) / 1470 nm (88%) 12 W / pw or cw (centre-dependent) Intended energy dose: 70 J/cm Applied energy dose: 77 J/cm	144 142 148 144	39%	Results: In the comparison EVLA and RFA vs. HL/S no difference in primary study variable (open refluxing GSV segments \geq 10 cm) Limitations: Very low FU rate, relevance of results unclear
Vähäaho (26) 2018	EVLA HL/S UGFS	980 nm / 1470 nm radial fibre 12 W / pw (1.5 s impulse) Intended energy dose: 70 J/cm	68 65 76	78%	Results: In the comparison EVLA vs. HL/S no difference in primary study variable (GSV occlusion rate) Limitations: Selection of patients: CEAP-C2 to C4, GSV diameter 5–10 mm; the patients of one centre (n=18) were excluded from the 5-year FU (single-centre study); different anaesthesia techniques with EVLA and HL/S

ration of the scores from the 2nd to the 5th postoperative year (21). However, in none of the studies was a difference found between HL/S and endothermal ablation at long-term follow-up, as was investigated and confirmed in one of the two meta-analyses (11).

Disease-related quality of life was systematically recorded in 5/7 RCTs using

AVVQ (n=3) (6, 20, 26) or CIVIQ (n=2) (21, 27), and again in one of the two meta-analyses (11). No significant differences were found in the long-term analysis between the open surgery and the endothermal techniques either for the disease-specific or the general quality of life.

Duplex ultrasound inguinal junctional recurrence (DJR)

The inguinal recurrence pattern after endothermal ablation procedures (ETAP) and after HL/S showed fundamental differences. After ETAP, recanalisation of ablated veins and neoreflux through previously competent junctional tributaries can occur

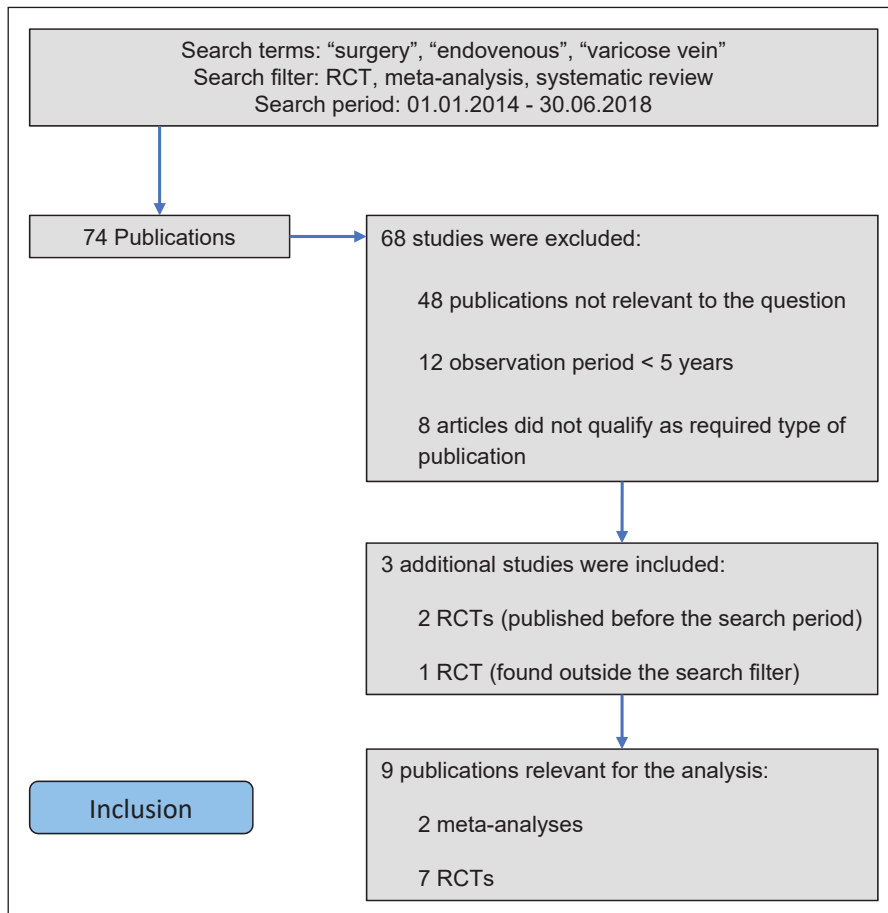


Fig. 1 Flow diagram of the PubMed search system.

in the groin area, especially via the anterior accessory saphenous vein (AASV), whereas after correctly performed high ligation, neovascularisation and/or neoreflux through junctional tributaries not connected to the common femoral vein, e.g. the superficial epigastric vein into the AASV, can develop (25). Under the assumption that the two phenomena can lead to clinical recurrences with comparable frequency, these are here combined as DJR.

5/7 studies comparing ETAP and HL/S reported DJR as a defined study variable. The rates of 22% (EVLA) vs. 28% (C/Cs) found by Disselhoff et al. were not significantly different (6). Rasmussen et al. did not show any significant differences between EVLA and HL/S either, although the data of this study cannot be clearly quantified (20). The DJR rates reported by Van der Velden et al. were 22% (EVLA) vs. 13% (HL/S) and were significantly different (27), as was the case with Rass/Frings et al. with 28% vs. 5% (21) and Gauw et al. with

49% vs. 23% (9). In the meta-analysis of Hamann et al. the difference in terms of recurrent reflex at the SFJ/groin were described as significant with 22% (EVLA) vs. 12% (HL/S) (11). Neovascularisation and recanalisation of the GSV were considered separately in the meta-analysis of Kheirel-seid et al. (12). A conclusion regarding the DJR rate was not possible in this study.

Clinical recurrence

According to the REVAS classification (REVAS classification: recurrent varices after surgery), clinical recurrence is defined as the presence of varices in the lower extremities that had previously undergone surgery for varicose veins. This clinical definition covers the “true recurrence” that develops in the area operated upon, but also residual varices diagnosed preoperatively as well as newly occurring varices caused by progression of the disease pro-

cess (17). On the other hand, to enable the effectiveness of different treatment methods to be compared, a differentiation between a recurrence associated with the treatment undertaken and the natural disease progression is useful.

In terms of the recurrence of varices on the operated leg (progression and recurrence) no difference between EVLA and HL/S was detected in 4/5 RCTs and in one of the two meta-analyses (9, 12, 20, 21, 27). One RCT showed a significantly lower rate of clinical recurrence after RFA compared with HL/S and EVLA in the Kaplan-Meier analysis (13). However, the relevance of this finding is unclear because of the low follow-up rate in this study (► Table 1).

An analysis of clinical recurrence with varicosis originating in the previously operated area (REVAS „same site“ or “clinical groin recurrence“) was undertaken in 3 RCTs. In two studies, there was a significant difference in recurrence rates with 18% (EVLA) vs. 5% (HL/S), and 33% vs. 17% (9, 21). In the third study no difference was found between RFA, EVLA and HL/S (13). This parameter was not considered in the meta-analyses.

Discussion

Until a few years ago, open surgery with high ligation and stripping was the standard therapy for treatment-requiring incompetent truncal veins. The operation has recently lost this status to endothermal ablation techniques on the basis of the guidelines of the European Society of Vascular Surgery and the British National Institute for Health and Care Excellence (NICE) in which HL/S is classed as the 2nd or 3rd choice of treatment following endothermal ablation (15, 30) [NICE 2013, Wittens 2015]. The recommendations of these guidelines are based on many studies that were analysed as part of an updated (2014) systematic Cochrane Review (14). This found no inferiority of endovenous radiofrequency and laser ablation compared to open surgery with regard to effectiveness, and their lower invasiveness was reflected, among other things, in a better postoperative quality of life. However, the only randomised studies available at the time of the

Cochrane analysis in 2014 were almost exclusively those with a short follow-up of not more than 2 years, so that the long-term effectiveness of the techniques was not included in the final assessment and thus could not be considered in the above-mentioned guidelines either. The data has since changed fundamentally to provide the highest level of evidence. What conclusions can be drawn from the most recent RCTs with long-term follow-up and from the two meta-analyses now available?

1. Open surgery and endothermal techniques – the latter almost exclusively for laser ablation with wavelengths of 810 to 980 nm using a bare-tip fibre – are of equal value in terms of quality of life, clinical recurrence according to REVAS (recurrence and disease progression) and hence closely connected to the disease severity (VCSS, HVVSS) up to 5 years postoperatively.
2. Duplex ultrasound recurrences at the groin/SFJ occur after endothermal ablation (and this also applied almost exclusively to laser ablation with wavelengths of 810 to 980 nm and use of a bare-tip fibre) significantly more often than after high ligation and stripping. It is to be expected that clinically relevant recurrences, originating in the treated groin region, will develop. This was shown in 2 of the 3 RCTs where this clinical parameter was recorded. In addition, the study by de Maeseneer et al. confirmed that the duplex ultrasound result at the operated inguinal SFJ is positively correlated with the later occurrence of clinical recurrence from this region (5).

Assuming that patients want the longest possible freedom from recurrence as the top priority of their treatment for truncal vein incompetence, for example above postoperative comfort or even the side effect profile (23), then the present data has to be interpreted as showing that, in an international context, the classic operation was abandoned as the treatment standard too soon. The argument – that newer lasers with longer wavelengths and modified fibre optics are a technical advance and not comparable with the long-term studies that were overwhelmingly undertaken with the

first generation of lasers – may be true but carries no weight in view of the stated data. In the past ten years, hardly any more randomised studies with high ligation and stripping as the control arm have been undertaken. It is therefore simply not possible to compare the latest endothermal techniques with open surgery.

However, it should not be dismissed out of hand that, due to the lower invasiveness and good standardisation, the latest laser and radiofrequency technologies offer a considerable therapeutic potential – as has been impressively demonstrated for radial emitting fibre optics compared to bare-tip fibre (7). However, the question of treatment selection for an individual patient remains unclear and – in view of the long-term studies now available comparing them with the open surgery – regains its importance. There are some indications in the literature that a prognostic estimation of the success or failure of endothermal ablation with respect to the risk of recurrence can be undertaken on the basis of individual parameters (22). Van der Velden et al. showed that GSV diameter and the C class of the CEAP classification are strong prognostic factors for recanalisation after endovenous thermoablation and hence behave in reverse proportion to the therapeutic effectiveness (29). In addition Spreafico et al. found that a diameter of ≥ 9 mm at the mean confluence of the superficial inguinal veins in patients with GSV incompetence and a C class of $\geq C4$ were independent predictors for recanalisation of the truncal veins ablated using a 1470 nm radial fibre laser (24).

Hence future research should follow at least two important approaches:

1. It is essential that studies to assess the therapeutic benefit of endovenous thermal ablation techniques contain a control arm with high ligation and stripping.
2. Such studies should undertake stratifications that enable a statement to be made about patient selection based on parameters of prognostic importance (vein diameter, CEAP classification).

It has already been pointed out that the quality of the available RCTs displays certain deficiencies (12, 14), for instance in the

proportion of patients followed up, which should definitely be as high as possible (at least 80%) and the choice of validated and/or recommended study endpoints that should enable the studies to be compared and high-quality meta-analyses carried out. Furthermore, RCTs should be multi-centre and the centres should undergo qualification to standardise the surgical techniques and the recording of study variables. This is amply demonstrated by the observation that 5 years postoperatively, duplex ultrasound recurrence rates vary considerably both with endothermal ablation (22–49%) and also with high ligation and stripping (5–28%). Finally, it would be desirable if, as a minimum, an independent investigator recorded the primary study variable.

Further studies are inevitably needed with regard to the optimum treatment of patients and an effective and economic use of the available resources. The responsibility for these studies now lies with the specialist societies and the research community. The interest of the industry in supporting such clinical research projects may be aroused by the fact that in the long term, as part of individualised treatment, it is highly likely that defined indications will be developed that will enable the introduction of reimbursement for endothermal ablation techniques for which evidence is available.

Conflict of interest

The author declares that no financial contributions have been received in the last 5 years.

Ethical guidelines

No studies in humans or animals were conducted for the manuscript.

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