Treatment of varicose great saphenous veins with saphenofemoral junction insufficiency – what is the evidence?*

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Treatment of varicose great saphenous veins with saphenofemoral junction insufficiency – what is the evidence?*

Behandlung der Varikose der Vena saphena magna mit Mündungsklappeninsuffizienz – Was ist die Evidenz?

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Key words

great saphenous vein, high ligation and continuous stripping, endovenous laser ablation, radiofrequency ablation, foam sclerotherapy

Schlüsselwörter

Vena saphena magna, Crossektomie mit Stripping, endovenöse Laserablation, Radiofrequenzablation, Schaumsklerosierung

Bibliography

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ZUSAMMENFASSUNG

Die Studienlage zur Behandlung der insuffizienten Vena saphena magna (VSM) mit Mündungsklappeninsuffizienz ist unklar. Leitlinien empfehlen die Behandlung der Vena saphena magna mit chirurgischer Therapie, endovenös thermischen Ablationsverfahren oder ultraschallgestützter Schaumsklerosierung. Es gibt zahlreiche Studien der Behandlung der Vena saphena magna, aber nur wenige Studien sind randomisiert und haben ein längeres Follow-up als 2 Jahre. Metaanalysen haben meist alle Studien eingeschlossen und sich nicht auf Studien mit einem Follow-up von mehr als 2 Jahren beschränkt.

Methodik In einer Literaturrecherche über Pubmed wurden die Keywords "great saphenous vein treatment", "large saphenous vein treatment", "varicosis therapy" in Verbindung mit "randomized controlled trial", "meta-analysis" und "systematic review" erfasst. Es wurden 128 Studien gefunden, davon 24 Studien seit 1990 zur Behandlung der Vena saphena magna mit offener Chirurgie, Crossektomie und Stripping, Hohe Ligatur plus Stripping (HL + CS), endovenöser Laserablation (EVLA), Radiofrequenzablation (RFA), flüssiger (LS) oder Schaumsklerosierung (FS) sowie ultraschallgestützter Schaumsklerosierung (UGFS) mit einem "Follow-up" von mehr als 2 Jahren. Die Studien wurden nach "Reflux" und "Rezidiv" hinsichtlich Therapietechnik, Patientenzahl, Länge des Follow-ups sowie der Angabe primärer und sekundärer Endpunkte ausgewertet.

Ergebnis Die meisten Studien mit einem längeren Follow-up (≥ 2 Jahre) liegen für chirurgische Verfahren "Hohe Ligatur und konventionelles Stripping" (HL + S), aus dem Englischen für Crossektomie, vor. HL + S ist die Referenzmethode gegenüber den anderen Therapietechniken. Es bestehen erhebliche Unterschiede in Technik, Ausführung der Behandlung, Definitionen, Ein- und Ausschlusskriterien sowie Studienendzielen. Die chirurgische Gruppe bestand aus 1915 behandelten Beinen in 19 Studien. In der EVLA-Gruppe wurden 1047 Beine mit EVLA-Monotherapie in 12 Studien und 240 Beine mit HL + EVLA in 3 Studien behandelt und ausgewertet. 299 Beine in 4 Studien wurden mit RFA behandelt. In der UGFS-Gruppe wurden 661 Beine in 5 Studien behandelt. 39 Beine wurden kombiniert mit UGFS + HL und 92 Beine kombiniert mit LS + HL in jeweils 1 Studie behandelt.

Im Vergleich zu HL + S weisen die Studien mit EVLA mehr Reflux und Rezidive auf, Studien mit RFA hingegen zeigen bei Reflux und Rezidiven kaum Unterschiede. Studien zur Flüssigsklerosierung (LS), Schaumsklerosierung und (FS) ultraschallgestützten Schaumsklerosierung (UGFS) weisen wesentlich schlechtere Ergebnisse als die Studien der chirurgischen und endovenösen Behandlung auf.

Schlussfolgerung Aufgrund der Heterogenität der aufgeführten Studien sind verlässliche Aussagen zu HL + S, EVLA, RFA und LS/UGFS unter den angegebenen Bedingungen nicht möglich. UIP oder ECOP sollten eine Kommission gründen, die für varizenausschaltende Eingriffe ein verbindliches Studien-

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design definiert, um für zukünftige Studien eine bessere Vergleichbarkeit der Ergebnisse zu ermöglichen.

ABSTRACT

The results of studies on treatment of the great saphenous vein (GSV) with sapheno-femoral-junction (SFJ) insufficiency are unclear. Guidelines, however, recommend endovenous laser ablation (EVLA) and ultrasound-guided-foamsclerotherapy (UGFS) for symptomatic varicose large saphenous vein. There are numerous studies on GSV treatment but only a few randomized studies with a follow-up of two years and more. Meta-analyses in most instances included all studies and do not focus on studies with a follow-up of two years and longer.

Methods A literature research in Pubmed used the keyword "great saphenous vein treatment", "large saphenous vein treatment", "varicose therapy" in conjunction with "randomized controlled trial", "meta-analysis" and "systematic review". Of 128 studies only 24 randomized controlled studies investigated the effect of High Ligation and Continuous Stripping (HL + CS), Endovenous Laser Ablation (EVLA), Radiofrequency Ablation (RFA), Liquid Sclerotherapy (LS), and Ultrasound-Guided-Foam-Sclerotherapy (UGFS) and a follow-up of two and more years. Study evaluation included "reflux", "recurrence", "therapy technique", numbers of patients/legs treated, length of follow-up, and primary/secondary study endpoints.

Results Most of these studies investigated surgical High Ligation and Continuous Stripping (HL + CS) with a follow-up of two years and more. This technique served a reference technique for other techniques in randomized controlled studies. However, there are major differences in techniques, mode of treatment, definitions, criteria for exclusion and inclusion, and study endpoints.

The surgery study group included 1915 legs in 19 studies, the EVLA group 1047 legs in 12 studies and 240 legs in 3 studies with combined HL + EVLA treatment. RFA was used in 299 legs in 4 studies, UGFS in 661 legs in 5 studies, combined UGFS + HL in 39 legs and LS + HL in 92 legs in one study each.

EVLA is associated with more reflux and recurrence when compared to HL + CS. RFA shows similar reflux and recurrence rates as surgery. In most studies UGFS and LS is followed by more reflux and recurrence when compared to surgery.

Conclusion Due to heterogeneity of studies comparing study results of HL + CS, EVLA, RFA, LS and UGFS is not reliable. UIP or ECOP may form a commission to establish uniform, reliable and accepted study designs for varicose vein treatment to improve comparability of further randomized studies.

Introduction

Before the introduction of endovenous thermal procedures, the treatment of symptomatic reflux of the great saphenous vein (GSV) was mainly surgical (high ligation and conventional stripping (HL + S). Endovenous laser ablation (EVLA), radiofrequency ablation (RFA), liquid sclerotherapy (LS), foam sclerotherapy (FS) and ultrasound-guided foam sclerotherapy (UGFS) have become additional therapeutic options over the past 20 years.

There are only isolated reports on other treatment methods such as cyanoacrylate glue, steam ablation, CHIVA (from the French for 'haemodynamic correction of varicose veins in an ambulatory setting'), etc.

The study results in recent years have favoured EVLA, RFA and UGFS as the methods of choice for treating the GSV. The guidelines give preference to these three methods [1–3]. Differentiated assessment of clinical recurrence and the demonstration of venous reflux on duplex ultrasound (DUS) are important criteria in the evaluation of the treatment methods.

Recurrent varicose veins after interventions have been reported in up to 80 %. The saphenofemoral junction (SFJ) is involved in more than 50 % of cases [4]. Even so, the descriptions of SFJ incompetence are not precise and there is no information on the function of the preterminal and terminal valves [5]. Treatment of symptomatic trunk varicose veins [6] should take these individual changes in the development of recurrent varicose veins into consideration.

Methods

A systematic literature search of PubMed was based on the key words "great saphenous vein treatment", "large saphenous vein treatment", and "varicose vein therapy" in conjunction with "randomized controlled trial", "meta-analysis" and "systematic review".

Out of 128 studies, only those that treated the great saphenous vein (GSV) and had a follow-up of 2 years or more (n = 24) were included in the present review. The studies were evaluated on the basis of the types of intervention and specifics of the technique, total number of patients/ treated legs and number of patients/treated legs per treatment group, follow-up, primary and secondary endpoints, and results.

Results

Twenty-four randomised trials with a follow-up of two to eleven years were included in the evaluation [7–31].

Nineteen of the 24 studies investigated an open surgical procedure (HL + CS, HL, CS). EVLA as monotherapy was addressed in 12 studies, EVLA + HL in three studies, RFA in 4 studies, UGFS alone in five studies, UGFS + HL in one study, and LS + HL in one study. CHIVA and cryostripping were each investigated in a single study [7, 9].

The CONSORT criteria [32] were not mentioned in the relevant publications of eight of the 24 study reports [15–18, 23, 26, 27].

The total number of patients enrolled in the individual studies showed a large scatter (n = 42 to n = 500). The information on definitions and methods was very varied.

Information on exclusion criteria such as incompetent accessory saphenous veins [20], or additional procedures such as phlebectomy and ligation of perforators were not taken into account in the analysis.

All the studies investigated recurrent varicose veins both clinically and by means of duplex ultrasound scanning. Nine studies [8, 11, 12, 15, 16, 18, 26–28] gave no information on the published differentiated classifications of SFJ recurrence [33–38].

Different information on primary and secondary endpoints was given in 15 of the 24 studies:

- Occluded or absent GSV [8]
- Recurrent varicose veins in the groin, reflux in the GSV, scores, no recurrent varicose veins [10]
- Aberdeen Varicose Vein Questionnaire (AVVQ) [11]
- Recurrence at the SFJ confirmed on DUS, quality of life, technical success, subjective symptoms, lymphoedema, neurological complications [12]
- Recurrence of reflux around the SFJ [13]
- Venous reflux, length of occluded vein [16]
- Extent of haematoma one week after surgery and the Chronic Venous Insufficiency Questionnaire (CVIQ) [19]
- Recurrence of symptomatic reflux in the GSV, change in reflux in recurrent varicose veins [20]
- Occluded or absent GSV, presence of varicose veins according to the REVAS classification [21]
- Patent GSV with reflux, recurrent varicose veins, frequency of repeat surgery, scores [24]
- Clinical recurrent varicose veins, SFJ recurrent varicose veins on duplex ultrasound, scores [25]
- Reflux eliminated on duplex ultrasound, scores, pain, complications, recurrence [27]
- Rate of occluded or absent GSV on duplex ultrasound after one year and Aberdeen Varicose Vein Severity Score (AVVSS) [28]
- Obliteration or absence of the GSV, absence of reflux in the GSV, scores [29]
- Visible clinical recurrence, presence of neovascularisation on duplex ultrasound [31]

Even within the treatment groups themselves (surgery, EVLA, RFA, FS), the actual methods differed.

Surgical treatment showed the following differences:

- Classical stripping alone
- Stripping with or without high ligation
- Pin stripping
- Maintenance of the GSV (CHIVA)
- Phlebectomy of the tributary veins at the same time or in a second session
- Sclerotherapy at different times
- Ligation of perforators at different times
- Different lengths of stripping the GSV (thigh, knee, lateral malleolus)
- High ligation and removal of the small saphenous vein
- [7, 15, 26, 30, 31] (▶ **Table 1**).

The outcomes of treatment with open surgery HL + CS, EVLA, RFA, UGFS are presented summarised into one group each.

Results of surgical treatment

In the 19 studies that included an open surgery arm, 1915 legs were treated surgically.

The DUS recurrence rate was 18 % after CHIVA + HL versus 35 % after HL + CS ($p < 0.04$) [7].

Recurrence with demonstration of the GSV was not seen in any of the 100 legs treated with HL + CS. Reopening of the GSV occurred in 7 out of 104 legs treated with EVLA ($p < 0.051$) [8].

EVLA came out worse than HL + CS with respect to DUS reflux ($p < 0.0001$) [12].

Neoreflux in incompetent tributary veins at the SFJ was found in 19/61 (31 %) legs treated with EVLA versus 4/60 (7 %) of the legs treated with HL + CS ($p < 0.01$). Neovascularisation in visible recurrences was seen only in the HL + CS group (6/60). Clinically visible recurrences connected around the SFJ occurred in 22/61 (33 %) in the EVLA group and in 10/60 (17 %) in the HL + CS group ($p < 0.04$). Recurrence on DUS was found in 49 % after EVLA and in 23 % after HL + CS ($p = 0.02$) [13].

There was no difference in the clinical recurrence rate between HL (11 %) and HL + CS (12 %) [15].

Primary occlusion rates were given as 94.5 % after RFA and 100 % after HL + CS. There was no difference in the DUS recurrence rates between RFA (12/90) and HL + CS (9/90) [17].

Obliteration of the GSV above the knee was confirmed in 14 legs (53.8 %) after HL + CS and in 19 (57.6 %) after HL + UGFS [18].

The recurrence rates (clinical and DUS) after HL + CS (55 %) and EVLA + HL (40 %) did not differ ($p = 0.217$). Nor was the DUS recurrence rate of 67 % after HL + CS different from that of EVLA + HL ($p = 0.49$). The same applied to the findings on recanalisation of the GSV and incompetent tributary veins at the SFJ [19].

Symptomatic reflux of the GSV was found in 55.1 % after UGFS and in 72.1 % after HL + CS ($p = 0.024$). SFJ insufficiency was seen in 65.8 % after UGFS and in 41.7 % after HL + CS ($p = 0.001$). Recurrent reflux above the knee occurred more often after UGFS (72.55 %) than after HL + CS (20.4 %) ($p = 0.001$) [20].

Clinical recurrence was more frequent after HL + CS (27 %) than after RFA (13 %) and about the same following EVLA (29 %) and UGFS (19 %) ($p = 0.0032$). The same frequency of reflux in the groin was demonstrated after RFA, EVLA and HL + CS, but was significantly greater after UGFS ($p < 0.0001$). While virtually no neovascularisation developed after UGFS, there was no difference between RFA, EVLA and HL + CS. The number of repeat interventions was higher after UGFS in comparison with RFA, EVLA and HL + CS ($p < 0.001$) [21].

The cumulative recurrence rate was 14.3 % after RFA and 20.9 % after HL + CS (not significant) [22].

Treatment with RFA and HL + CS did not differ in the assessment of clinical recurrence (33 % versus 15 % as assessed by the surgeon) ($p = 0.4$). Occlusion or no evidence of the GSV on DUS was complete. The DUS and clinical results did not differ ($p = 0.68$) [23].

▶ **Table 1.** Randomised clinical trials on the treatment of trunk varicose veins with a follow-up of at least 2 years.

author	year	treatment	M/F	age	patients	legs	follow-up	clinical recurrence	duplex U/S	primary/ secondary endpoints	consort	REVAS stonebridge/ turton/de maesener	outcome
Carandina	2008	HL + CS (75) HL + CHIVA (75)	33/91	50/48	150	150	10	+	+	–	+	+	recurrence CHIVA < HL + CS
Christenson	2010	HL + CS (100) EVLA (104)	29/71 37/67	46.3 44.6	204	204	2	+	+	+	+	–	reflux HL + CS = EVLA recanalisation rate EVLA > HL + CS.
Disselhoff	2011	EVLA (60) cryostripping (60)	19/41 18/42	48 49	120	120	5	+	+	–	+	+	EVLA = cryostripping
Disselhoff	2011	EVLA (43) EVLA + HL (43)	7/36	45	43	86	5	+	+	+	+	+	recurrence EVLA = EVLA + HL neovascularisation EVLA < EVLA + HL recanalisation EVLA > EVLA + HL
El-Sheikha	2014	EVLTAP (25) EVLA (25)	8/17 4/21	51.1 52.5	50	50	5	+	+	+	–	–	EVLA = EVLA + phlebectomy
Flessenkämper	2015	HL + CS (159) EVLA (142) EVLA + HL (148)	47/112 45/97 37/111	47.7 47.7 48.7	449	449	2	*	*	+	+	–	recurrence EVLA = HL + CS reflux EVLA > HL + CS.
Gauw	2016	HL + CS (68) EVLA (62)	15/53 16/46	50 49	121	68 62	5	+	+	+	+	+	recurrence EVLA > HL + CS
Gibson	2018	CAC (108) RFA (114)	25/83 21/93	49 50.5	222	98 114	3	+	+	+	*	*	obliteration CAC = RFA
Hammarsten	1990	HL (18) CS (24)	18/24	52	42	42	4	+	Phlebography US	–	–	–	HL = CS
Hamel-Desnos	2007	1 % FS (74) 3 % FS (74)	15/59 16/58	53 56	148	148	2	+	+	+	–	–	1 % = 3 % GSV <= 8 mm
Helmy Elkaffas	2011	RFA (90) HL + CS (90)	42/48 45/45	33.1 34.9	180	180	2	+	+	–	–	+	occlusion RFA < HL + CS Recurrence RFA = HL + CS
Kalodiki	2012	HL + CS (43) HL + UGFS (39)	16/23 11/32	47 49	73	82	5	+	+	–	–	–	HL + CS = UGFS
Kalteis	2015	HL + EVLA (50) HL + CS (50)	21/79 29/71	46 46.5	100	100	5	+	+	+	+	+ (not cited)	HL + CS = EVLA + HL
Lam	2018	UGFS (233) HL + CS (227)	58/175 65/162	55.8 54.6	460	460	8	+	+	+	+	+	recurrence HL + CS < UGFS reflux HL + CS < UGFS

▶ **Table 1.** (Continuation)

author	year	treatment	M/F	age	patients	legs	follow-up	clinical recurrence	duplex U/S	primary/ secondary endpoints	consort	REVAS stonebridge/ turton/de maesener	outcome
Lawaetz	2017	RFA (148) EVLA (144) UGFS (144) HL + CS (142)	55/70 53/72 49/76 47/77	51 52 51 50	500	580	5	+	+	+	+	+	recanalisation UGFS > HL + CS, EVLA, RFA recurrence EVLA, HL + CS > UGFS reoperation UGFS > HL + CS, RFA, EVLA
Lurie	2005	RFA (46) HL + CS (40)	13/32 14/26	49 47	85	86	2	+	+	+	+	+	recurrence RFA = HL + CS neovascularisation RFA = HL + CS obliteration RFA = HL + CS
Perälä	2005	RFA (15) HL + CS (13)	1/14 1/12	33 38	28	28	3	+	+	–	–	+ (not cited)	RFA = HL + CS
Rasmussen	2013	HL + CS (68) EVLA (69)	16/43 21/41	54 53	121	137	5	+	+	+	+	+	HL + CS = EVLA
Rass	2015	EVLA (185) HL + CS (161)	61/124 48/113	48 50	400	400	5	+	+	+	+	+	recurrence EVLA > HL + CS reflux EVLA > HL + CS
Rutgers	1994	HL + CS (89) HL + LS (92)	22/67 23/69	–	156	181	3	+	+	–	–	–	recurrence HL + CS < HL + LS
Samuel	2013	EVLA 12 W (48) EVLA 14 W (38)	17/31 13/25	52 54	76	76	5	+	+	+	–	–	recurrence EVLA 14 W < EVLA 12 W
Vähäaho	2018	HL + CS (50) EVLA (57) UGFS (56)	–	48.5 47.7 59	196	233	5	*	*	–	+	–	GSV occlusion rate HL + CS = EVLA > UGFS
Van der Velden	2015	HL + CS (80) EVLA (80) UGFS (80)	20/45 21/49 220/44	52.5 50.2 56.4	199	240	5	+	+	+	+	+	obliteration UGFS > EVLA, HL + S reflux UGFS > EVLA, HL + CS
Winterborn	2004	HL + CS (64) CS (69)	33/67	49	100	133	11	+	+	–	+	+	reoperation CS < HL + CS
Winterborn	2008	HL + CS (114) flush ligation + CS (96)	26/69 31/56	47.3 52.6	182	210	2	+	+	+	+	+	HL + CS = flush ligation + CS

HL + CS high ligation + continuous stripping; HL high ligation; CS continuous stripping; EVLA endovenous laser ablation; RFA radiofrequency ablation; UGFS ultrasound-guided foam sclerotherapy; LS liquid sclerotherapy.

The outcomes after EVLA and HL + CS were not different (open segments of the GSV 9 vs 4, clinical recurrence 24 vs 25, reoperation 17 vs 15) [24].

In the overall analysis of REVAS [34], treatment with HL + CS and EVLA did not differ, but the origin of recurrence after EVLA was more often found at the SFJ (39 % EVLA versus 3 % HL + CS, $p < 0.001$) and was more often on the same side (39 % EVLA versus 10 % HL + CS, $p < 0.002$), while recurrent reflux at the SFJ was more often seen on DUS (28 % EVLA versus 5 % HL + CS, $p < 0.001$) [25].

Clinical recurrence after HL + CS (10 %) occurred less often than after HL + LS (47 %) ($p < 0.001$). The recurrence rate seen on DUS was likewise different [26].

The occlusion rate of the GSV after HL + CS with and without additional treatment (96 %/96 %), EVLA (89 %/89 %) and UGFS (51 %/41 %) showed significant differences between UGFS and HL + CS or EVLA (these last two giving similar results) ($p < 0.001$). UGFS without further treatment of the GSV was successful in only 16/59 (27 %) [28].

After HL + CS, EVLA, and UGFS, obliteration or absence of the GSV was determined in 85 %, 77 %, and 23 % respectively ($p < 0.001$), with absence of any reflux above the knee in 85 %, 82 %, and 41 % respectively ($p < 0.001$) [29].

The risk of repeat surgery was reduced after HL + CS compared with HL (freedom from reoperation 70 % after HL and 86 % after HL + CS, $p = 0.01$) [30].

Standard high ligation (SHL) was no different from flush high ligation (FHL) with respect to recurrence (33 % versus 32 %, $p = 0.9$) and neovascularisation (22 % versus 19 %, $p = 0.57$) [31].

Results of EVLA therapy

Four studies (499 legs treated with EVLA) reported disadvantages of EVLA therapy in comparison with surgery. Four studies (350 legs treated with EVLA) found similar results with surgical and EVLA treatment. Three studies (432 legs treated with EVLA) looked at EVLA in comparison with EVLA + HL [10, 12, 18]. One study (50 legs treated with EVLA) compared EVLA and the simultaneous removal of tributary veins with EVLA and the subsequent removal of tributary veins [11]. One study (60 legs treated with EVLA) compared EVLA therapy with cryostripping; the outcomes were the same with respect to recurrence, reflux, neovascularisation, and tributary veins [9]. In the case of reflux and tributary veins, the results of EVLA + HL were better than those of EVLA monotherapy [12]. Two further studies found no differences in reflux, recurrence, neovascularisation, or tributary veins between treatment with EVLA + HL and EVLA alone [10, 19]. Phlebectomy of tributary veins at the same time as EVLA therapy did not hold any advantage with respect to reflux, recurrence or tributary veins [11].

Different laser techniques were used in the EVLA group, which makes it difficult to compare the study results:

- EVLA 810 nm [11, 19, 25]
- EVLA 940 nm [29]
- EVLA 980 nm [8, 12, 13, 24]
- EVLA 980 nm and 1470 nm [21]
- EVLA 12 W [28]
- EVLA 12 W and 14 W [10, 27] (▶ **Table 2**).

Results of RFA therapy

RFA therapy (299 legs treated with RFA) showed similar results regarding recurrence, neovascularisation, and obliteration in two studies [22, 23], and with respect to recurrence in one study [17] compared with HL + CS. RFA therapy came out worse with respect to occlusion in one study [17] but better with respect to clinical recurrence and neovascularisation in another [21].

Different techniques were used in the RFA groups:

- RFA VNUS closure [17, 22, 23]
- RFA closure fast [21] (▶ **Table 3**).

Results of treatment with UGFS/LS

Four studies [20, 21, 28, 29] addressed the effects of UGFS as monotherapy (507 legs treated with UGFS); one study [17] looked at a combination of UGFS + HL (39 legs treated with UGFS) and one study [25] at the combination of LS + HL (92 legs treated with LS). Treatment with UGFS gave poorer therapeutic results throughout (obliteration, reflux, recurrence, reoperation) in comparison with HL + CS [18, 21, 28, 29]. A poorer outcome for HL + CS was seen only for clinical recurrence in one study [21]. Combining UGFS with HL [18] or LS with HL [26] did not bring about any improvement.

There were considerable differences in the quantity and strength of the sclerosant used in the sclerotherapy groups. This may have affected the results, even though a randomised trial found no difference between the use of 1 % and 3 % polidocanol [16]:

- 40 % of the legs in the surgery group were given 25 additional treatments with foam (mean volume 11 mL, 3 % sodium tetradecylsulfate (STS)), 47.5 % of the legs received 33 treatments (mean volume 9 mL) [18]
- 3 % Aethoxysklerol [20]
- 3 % Aethoxysklerol (1:4), one further treatment was allowed within the first month [21]
- 3 % Aethoxysklerol (1:4) [21]
- 3 % Aethoxysklerol (1:4), the majority of patients received 5 mL or more, 48 patients less than 5 mL [20]
- 1 % Aethoxysklerol or 1 % STS or 3 % STS [28]
- 3 % Aethoxysklerol (1:3), quantity of foam appropriate to the length and diameter of the GSV, maximum 10 mL, treatment of tributary veins only if symptomatic, repeat therapy possible once in the period between 3 months and 1 year after the start of treatment [29] (▶ **Table 4**).

One randomised trial, which compared occlusion of the great saphenous vein using cyanoacrylate (CAC) with radiofrequency ablation (RFA) – but not with surgical treatment – determined that 94.4 % of the veins in the CAC group and 91.9 % in der RFA group were occluded after 3 years [14].

Discussion

One limitation of this article is that we carried out a review rather than a meta-analysis. We restricted ourselves to presenting the study aims and outcomes as well as the qualitative and quantita-

▶ **Table 2.** Long-term comparison of EVLA with surgical treatment (– inferior; = comparable).

author	year	treatment group/legs	surgery versus EVLA
Christenson	2010	HL + CS 100 EVLA 104	reflux EVLA = HL + CS recanalisation EVLA –
Disselhoff	2011	EVLA 60 cryostripping 60	no GSV insufficiency, tributary veins on DUS, neovascularisation EVLA = cryostripping
Disselhoff	2011	EVLA 43 EVLA + HL 43	recurrence EVLA = EVLA + HL neovascularisation EVLA – recanalisation EVLA –
Rasmussen	2013	HL + CS 68 EVLA 69	reflux, recurrence, reoperation HL + S = EVLA
Samuel	2013	EVLA 12 W 48 EVLA 14 W 38	recurrence, SFJ reflux EVLA 12 W –
El Sheikha	2014	EVLTAP 25 EVLA 25	recurrence, reflux, tributary veins EVLTAP = EVLA
Rass	2015	EVLA 185 HL + CS 161	recurrence and reflux EVLA –
Van der Velden	2015	HL + CS 80 EVLA 80	obliteration, reflux HL + CS = EVLA
Kalteis	2015	HL + CS 50 EVLA + HL 50	recurrence, reflux, tributary veins HL + CS = EVLA + HL
Flessenkämper	2015	HL + CS 159 EVLA 142 EVLA + HL 148	reflux EVLA – clinical and DUS recurrence EVLA – reflux, tributary veins EVLA + HL < EVLA
Gauw	2016	EVLA 68 HL + CS 62	recurrence EVLA –
Lawaetz	2017	EVLA 144 HL + CS 142	recanalisation, recurrence reoperation HL + S = EVLA
Vähäaho	2018	EVLA 57 HL + CS 50	occlusion rate EVLA = HL + CS

HL + CS high ligation + continuous stripping; HL high ligation; CS continuous stripping; EVLA endovenous laser ablation; RFA radiofrequency ablation; UGFS ultrasound-guided foam sclerotherapy; LS liquid sclerotherapy.

▶ **Table 3.** Long-term comparison of RFA treatment with surgery (– inferior; = comparable).

author	year	treatment group/legs	surgery versus RFA
Lurie	2005	RFA 46 HL + CS 40	recurrence, neovascularisation, obliteration HL + CS = RFA
Perälä	2005	RFA 15 HL + CS 13	reflux, recurrence, occlusion, RFA = HL + CS
Helmy Elkaffas	2011	RFA 90 HL + CS 90	occlusion RFA – recurrence RFA = HL + CS
Lawaetz	2017	RFA 148 HL + CS 142	neovascularisation HL + CS – clinical recurrence HL + CS –

HL + CS high ligation + continuous stripping; RFA radiofrequency ablation.

▶ **Table 4.** Long-term comparison of UGFS or FS with surgery (– inferior; = comparable).

author	year	treatment group / legs	surgery versus UGFS, FS, LS
Rutgers	1994	HL + CS 89 HL + LS 92	recurrence, reflux HL + LS –
Kalodiki	2012	UGFS + HL 39 HL + CS 43	obliteration UGFS = HL + S
Van der Velden	2015	HL + CS 80 UGFS 80	obliteration, reflux UGFS –
Lawaetz	2017	UGFS 144 HL + CS 142	reoperation, reflux, recanalisation UGFS – recurrence HL + S –
Lam	2018	UGFS 233 HL + CS 227	recurrence, reflux, SFJ insufficiency UGFS –
Vähäaho	2018	UGFS 56 HL + CS 50	GSV obliteration, reoperation UGFS –

HL + CS High ligation + continuous stripping; HL High ligation; UGFS ultrasound-guided foam sclerotherapy; LS liquid sclerotherapy.

tive criteria of the 24 randomised trials that we found on the treatment of trunk varicose veins affecting the GSV with saphenofemoral junction incompetence and a follow-up of two years or more. The reduced number of patients at follow-up after several years may have affected the results. Our review did not include a report on secondary data from a randomised trial one year after the presentation of the two-year follow-up data [12], as only 27 %, 26.7 % and 39 % of the original patients in the study arms could still be examined; the results were published without comment on the limitations of their statistical power [39].

Overall, the available studies are not homogeneous. They report over different data collection periods, with different definitions, and a very wide range of study populations and numbers of patients. The combinations of different techniques – surgical methods with endovenous techniques or endovenous techniques with phlebectomy – hardly allow any sort of comparison.

The CONSORT criteria to improve the reporting of randomised trials [32] were not to be found or were inadequately observed in eight of the 24 studies.

Several study groups have reported on the classification of SFJ recurrence [33–38]. Nine of the randomised trials analysed gave insufficient information in this respect, or none at all. They therefore did not take into account whether the underlying disease had progressed, whether there was neovascularisation, or whether a technical error had occurred [8, 11, 12, 15, 16, 18, 26–28].

Definitions of the anatomical success of treatment included occlusion, obliteration, competence of the vein, no reflux, no recanalisation, and partial obliteration with antegrade flow [40, 41].

The studies gave different definitions of recurrent reflux: reflux around the SFJ or in the groin, reflux at a distance of 2 cm from the opening of the great saphenous vein, reflux in tributaries of the common femoral vein measuring more than 2 mm in diameter, and retrograde flow for more than 1 second [41].

Most of the studies did not take the haemodynamic closure functions of the terminal and preterminal valves in the vein into consideration (Valsalva positive and negative reflux and/or diastolic reflux), especially with respect to the anterior accessory vein [5, 42]. This aspect is, however, critical in the evaluation of treatment.

The cause of reflux included reconnection of the GSV stump (24.5 %), a pelvic vein network (17.8 %), neovascularisation (15.5 %), and newly incompetent tributaries of the GSV (42.2 %). A valve in the femoral vein that was already incompetent before surgery was the cause of saphenofemoral junction recurrence (found in 26.9 % with SFJ recurrence versus 7 % without SFJ recurrence) [4]. In recent studies, ligation of SFJ tributary veins has been shown to be the cause of SFJ recurrence [43]. The terminal valve was not responsible for reflux at the SFJ in 24.8 %, so that HL did not have to be performed in every case [44]. Reflux is not always a question of technique.

In comparison with the endovenous procedures, the surgical treatment of trunk varicose veins has been studied more often and over a longer period of time. It cannot be ignored, however, that the study groups show considerable differences in the surgical treatment of trunk varicose veins with respect to technique, extent of the intervention, and combinations with or without high ligation and endovenous techniques. Despite these weaknesses, surgical treatment is accepted as the gold standard against which endovenous interventions are to be assessed.

In studies with a follow-up of more than 2 years, the results of surgical treatment are better than those in patients treated with EVLA and UGFS, with respect to clinical recurrence and reflux. RFA-treated veins show approximately the same results as surgical treatment. Given this similarity, the comparison of cyanoacrylate (CAC) with RFA showing an occlusion rate of 94.4 % (CAC) versus 91.9 % (RFA) may also be relevant to future studies in view of the lower rate of side effects [14]. Hamann et al. also showed an increased rate of reflux around the SFJ or groin after EVLA. RFA was not investigated [40]. The differences in neovascularisation, which frequently occurs after high ligation and stripping, and reflux in tributary veins and accessory veins after EVLA are not clinically relevant to the results after 5 years as, according to Hamann [40],

even the best treatment method is not completely free of recurrence. Other factors such as genetics, body weight, and occupational stress may have an effect [45–47].

Despite these differences, meta-analyses try to make it possible to compare the study results. Hamann et al. (2017), for example, took anatomical success to be the lack of reflux in a treated vein on duplex ultrasound, as not all studies reported an occlusion rate [40].

Meta-analyses have compared HL + CS and EVLA or RFA with respect to reflux and recurrence [48–55]. Regarding clinical recurrence, FS comes out similar to EVLA and worse than HL + S [56]. FS is presented as an effective treatment but the evidence base is not adequate [49, 57, 58].

Mentioned as an aside, treatment with CHIVA has less recurrence than HL + CS although the quality of the studies is rated as low to moderate [59].

Some authors go as far as claiming that, all studies being similar, it is merely a question of treatment costs [60].

In a Cochrane review, Nesbit states that incompatibilities and different points in time make it more difficult to compare the results [49].

Many studies are not clear how to present or evaluate bias. The study population is often small in size [40]. Different exclusion and inclusion criteria may affect the results [61].

Over the years, there have been changes in technique in the two endovenous techniques (EVLA, RFA) – including the type of energy application, power, vein diameter, pullback velocity – which may have had an effect on the results [62].

Thakur reported that a CEAP classification was given in only 17 out of 28 studies. The frequency of CEAP grade 2 varied between 6.3 % and 83.5 %, depending on the study. There were 31 different categories of results, 13 different questionnaires used to assess the results of treatment, 38 different points in time to determine clinical recurrence, and at least 30 different categories of complications [63].

Summary

The available studies on the treatment of great saphenous varicose veins with valve incompetence exhibit differences that make comparison almost impossible. At the present time, there is no best treatment method without recurrence. Recurrent varicose veins seem to occur irrespective of the technique used. Treatment of a varicose GSV should be multimodal and adapted to the individual case. The International Union of Phlebology (UIP) or the European College of Phlebology (ECOP) should set up a commission to establish a uniform, reliable and accepted study design for varicose vein treatment to improve the comparability of future randomised trials. In these circumstances, however, the question arises as to whether randomised studies are still meaningful or whether it would be better to establish a vein treatment registry.

Conflict of Interest

PD Dr. Thomas Noppeney Vorträge und Honorare von Medtronic.

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