

Comparison of traditional surgery and laser treatment of incompetent great saphenous vein.

Results of a meta-Analysis



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Comparison of traditional surgery and laser treatment of incompetent great saphenous vein. Result of a meta-analysis

AIM: *This paper aims to compare EVLA to traditional surgery, by evaluating the incidence of recurrences.*

MATERIAL OF STUDY: *We performed a meta-analysis to challenge both surgical and LASER treatment, using, as clinical outcome, the presence or the absence of reflux. A systematic review of literature about the treatment of varicose veins was performed, searching in the following databases: PUBMED-MEDLINE, Cochrane Library. Search terms considered were: stripping, HL/S, surgery, LASER, EVL*, varicose vein, GSV, saphenous vein. Only RCTs based at least on six-months follow-up were considered eligible in the study. Methodological quality of the included studies was evaluated using Cochrane Collaboration Bias Risk Assessment Tool. Effects of the dichotomous variables taken in consideration were evaluated using pooled risk-ratios with 95% C.I. Articles were evaluated initially from abstracts; eligible papers were full-text examined.*

RESULTS: *We have considered 2 groups, A and B. A Group: 756 legs treated with conventional surgical procedure; B Group: 755 legs treated with EVLA technique. A Group showed 175 post-procedure recurrences, while B showed 97 recurrences. The average O.R. was 1.72; minimum O.R. was of .497 while the maximum was of 8.064.*

DISCUSSION: *The obtained OR average value is 1.72 with a 95% C.I. of 0.94-3.12, which includes the value 1, contrary to the criteria for rejection of the null hypothesis. For this reason there is not a statistically significant difference between the results obtained by the two techniques.*

CONCLUSIONS: *The endovascular laser ablation (EVLA) does not prove to be superior in terms of recurrence, to the surgical technique. However, it remains a viable treatment option in patients with impaired great saphenous vein, reducing postoperative pain and hospital stay.*

KEY WORDS: Laser therapy, Meta-analysis, Saphenous vein, Surgery, Venous insufficiency

Introduction

The worldwide prevalence of Chronic Venous Disease (CVD) is 83.6%: 63.9% of the patients are classifiable

among CEAP category C1 and C6 while 19.7% of the subjects are CEAP C0¹. The gender-related difference in prevalence of lower limbs vein insufficiency is a topic of debate: the epidemiological studies that have dealt with the problem in the past are conflicting with each other. The Basle Study III² and the Edinburgh Vein Study³ reported a male preponderance, whilst in Patrick et al. 2004⁴, Franks et al. 1992⁵, Brand et al. 1988⁶, Novo et al. 1988⁷, Maffei et al. 1986⁸, is reported an higher prevalence in females than males. However, it is established that there is a prevalence of extra-saphenous vari-

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varicose veins in women, while males suffer from great saphenous vein insufficiency³⁻⁶. The most common symptoms are pain, heaviness in the legs, itching and night cramps. The chronicity of the varicose disease leads to a venous stasis, which favors reactive hyperpigmentation and ulcers^{9,10} in the lower segments of the leg. The conventional surgical therapy provides for ligation at the level of sapheno-femoral junction (SFJ) and stripping. Varicose recurrence occurs approximately in 30% of patients¹¹, probably caused by neo-vascularization¹². Moreover, apart from incorrect surgical procedures, some authors have found that in 11.6 % of the patients, lesions of suprafascial nerves occur during isolation and stripping of the great saphenous vein¹³.

Endovenous Laser Treatment (EVLA) of great saphenous vein is a minimally invasive technique that can be practiced in an outpatient setting. The advantages of its use include: less time of hospitalization, lower incidence of surgical complications, possibility of using tumescent anesthesia. It is a relatively recent technique and there is little data about long-term follow-up in order to evaluate the incidence of recurrences.

Our work consisted in a meta-analysis of randomized trials, comparing the endovascular laser ablation (EVLA) with the classical ligation and stripping using, as outcome variable, a duplex-US detectable reflux in presence of re-canalization (in case of EVLA) or neo-vascularization (in case of HL/S). The choice of this kind of set-up is slightly different from the other studies that have performed this evaluation. In fact, other Meta-analyses

perform a comparison between surgery and a set of endovascular techniques, such as EVLA itself, Radio-Frequency, Sclerotherapy, etc. Our goal is particularly to compare the medium/long-term efficacy of the great saphenous vein ablation which is obtained with the traditional intervention of stripping and the functional ablation obtained with the EVLA technique. For this reason we did not take into account other techniques, because we felt that there could be the possibility that they could act as confounding factors; for the same reason we chose not to consider any clinical scoring system as outcome variable.

Methods

A systematic search of studies on interventions on saphenous vein was carried out. The literature search was performed in February 2014 using the search engine PUBMED-MEDLINE entering the following query: (stripping[Title/Abstract] OR hl/s[Title/Abstract]) OR surgery[Title/Abstract]) AND laser[Title/Abstract]) OR (evl[Title/Abstract] OR evl'[Title/Abstract] OR evl's[Title/Abstract] OR evl1[Title/Abstract] OR evla[Title/Abstract] OR evla1470[Title/Abstract] OR evla810[Title/Abstract] OR evla980[Title/Abstract]) AND ("varicose veins"[MeSH Terms] OR ("varicose"[All Fields] AND "veins"[All Fields]) OR "varicose veins"[All Fields] OR ("varicose"[All Fields] AND "vein"[All Fields])

TABLE I - Literature search criteria

Time limit for literature search	February 2014
Searched Databases	PUBMED-MEDLINE OVID, EMBASE, CINAHL, ClinicalTrials.gov, Cochrane Central Register of controlled Trials Cochrane Database of Systematic Review
Searched journals	The International Journal of Angiology Phlebology, Journal of Vascular Surgery, Acta Phlebologica
Inclusion Criteria	Articles based on retrospective or prospective studies and RCTs comparing HL/S and EVLA Articles based on studies that used duplex U.S. examination to determine the absence/presence of reflux as an outcome variable.
Exclusion Criteria	Studies that performed isolated ligation, radiofrequency, sclerotherapy, cryostripping, foam sclerotherapy. Studies based on analysis of questionnaires about pre- and/or post-procedure quality of life. Studies based on a follow-up of less than six months Studies based on mid-term results

OR “varicose vein”[All Fields])) AND gsv[All Fields]) AND (great[All Fields] AND (“saphenous vein”[MeSH Terms])
 OR (“saphenous”[All Fields] AND “vein”[All Fields])
 OR “saphenous vein”[All Fields])).
 OVID, EMBASE, CINAHL.
 ClinicalTrials.gov, the Cochrane Central Register of controlled Trials and the Cochrane Database of Systematic Reviews were also consulted. The results were considered in all languages. In addition, relevant articles were searched in journals such as *The International Journal of Angiology*, *Phlebology*, *Journal of Vascular Surgery*, *Acta Phlebologica*. Publication bias was evaluated using Cochrane Collaboration Bias Risk Assessment Tool.

Inclusion Criteria. Our meta-analysis included articles based on retrospective or prospective studies and RCTs that compared the traditional surgical technique (high ligation and saphenous stripping) with the EVLA technique. We considered eligible only studies that used U.S. examination in order to determine the absence/presence of reflux as an outcome variable.

Exclusion Criteria. Several studies, particularly the American ones, included under the category of surgical treatments¹⁴, a wide repertoire of techniques, such as cryostripping, phlebectomies, simple high ligation, isolated crossectomy and conservative techniques¹⁵, such as C.H.I.V.A. (Cure Conservatrice et Hémodynamique de l’Insuffisance Veineuse en Ambulatoire)¹⁶ and A.S.V.A.L. (Ablation Sélective des Varices sous Anesthésie Locale)¹⁷. In our meta-analysis we considered, as “surgery”, only HL/S (high ligation with stripping) and isolated stripping. Studies that performed isolated ligation, radiofrequency, sclerotherapy¹⁸, cryostripping, foam sclerotherapy were excluded. Studies that have based their findings on an analysis of questionnaires about the pre- and/or post-procedure quality of life had not been included. In addition, studies based on a follow-up of less than six months were excluded, because this range of time was considered, the shortest follow-up compatible with recurrence of varices. Finally, we discarded publications based on the mid-term results of RCTs of which long-term results were published (Table I).

Data Extraction. Articles, in first instance, were analyzed according to their titles and their abstracts. Successively an examination of full-text reports suitable for the study was performed. Data was extracted from the texts, tables and graphs and analyzed by 2 different authors (E.F. and E.G.) independently.

Statistical Analysis

The statistical analysis of the results was performed using MIX 2.0™¹⁹ and S.P.S.S. 21™²⁰ for Windows™

software. Variables were tested using the Odds Ratio (OR), calculated by pooled R.Rs. with 95% C.I., as summary statistic. An OR>1 favored the EVLA group and the point estimate of the OR was considered statistically significant at p<0.05 if the 95% confidence interval (CI) did not include the value 1. The statistical heterogeneity was calculated using I₂ and Q parameters. A Fixed-Effects model was preferred to a Random-Effects model because it has been not considered recruited studies samples as a random one of a larger population.

Results

Literature research, carried out according to the above-mentioned query, has resulted in 72 articles. 59 items were rejected due to the title and the content of the abstracts. Of the remaining 13 studies, 3 did not meet the eligibility criteria, 1 was excluded being a review and 1 was excluded because it was based on mid-term results of an already included study. (Fig. 1).

8 studies²¹⁻²⁸ were enrolled, for a total of 1511 legs. Of these, 755 were subjected to laser therapy and 756 to conventional surgery. The average follow-up was of 94,12 ± 73.59 weeks (Table II). The average age of the patients was of 51.4 ys. CEAP classification is indefinite, but all patients were considered eligible for curative surgery. Rasmussen²¹ reported the longest follow up amounting to 260 weeks (five years); the shortest follow up was 25 weeks in Van Groenendal’s study²². The evaluation of clinical outcome has been carried out verifying the lack of reflux, detected by using Duplex U.S., and/or the appearance of new varicose veins. There were no differences in patient demographics, etiology and race, between EVLA and Surgery groups. Duplex frequency used for instrumental assessment is variable. Laser frequency, delivered energy and modality of wave delivering (single dose v/s pulsed-dose), used for EVLA, in the analyzed studies is variable. 95 LASER recurrences were

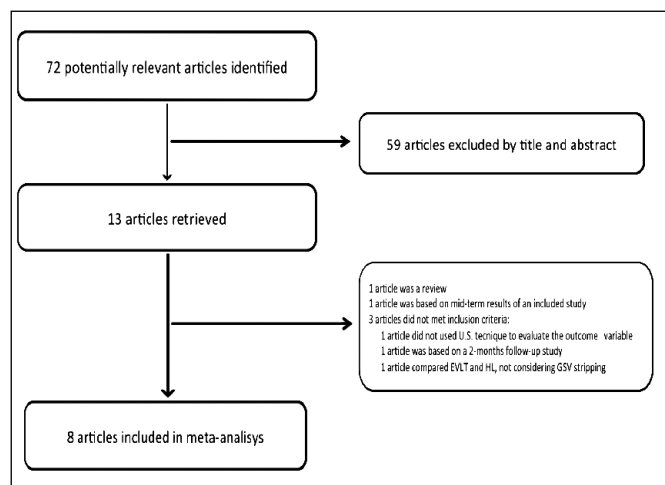


Fig. 1: Literature research methodology.

TABLE II - Distribution of treatment modalities

	Author	Surgery	Post-surgery recurrence	EVLA	Post-EVLA recurrence	Total Legs	OR	C.I. Lower	C.I. Upper
1	Rasmussen (DB) 2013 ¹³	68	24	69	25	137	.960	.48	1.93
2	Van Groenendael ¹⁴	149	43	67	13	216	1.685	.84	3.40
3	Darwood ¹⁵	32	4	71	4	103	2.392	.56	10.25
4	Rass ¹⁶	161	37	185	30	346	1.541	.90	2.64
5	Christenson ¹⁷	100	1	99	2	199	.497	.04	5.48
6	Theivacumar ¹⁸	60	4	69	5	129	.914	.23	3.57
7	Carradice (DB) ¹⁹	137	56	139	11	276	8.044	3.98	16.26
8	Pronk ²⁰	49	5	56	5	105	1.159	.31	4.27
	TOTAL	756	175	755	95	1511	1.72	.94	3.12

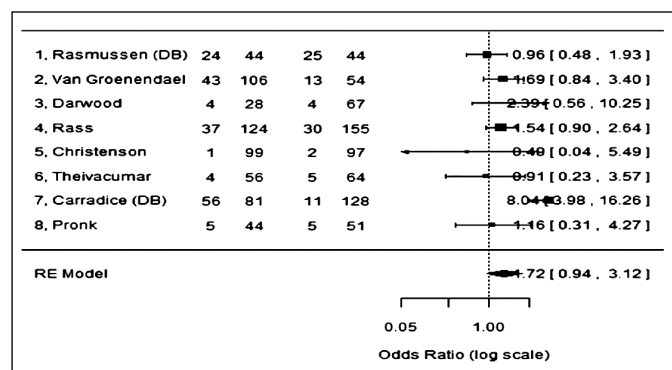


Fig. 2: Forrest plot.

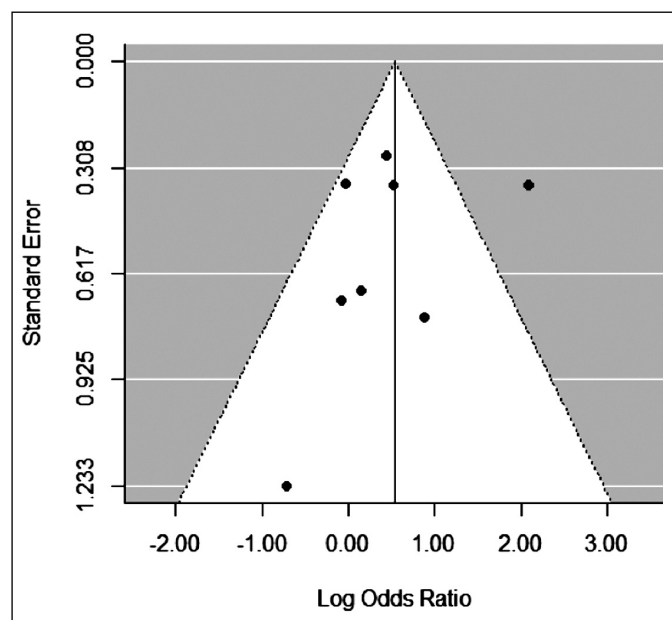


Fig. 3: Funnel plot.

observed in total, while the Surgical ones were 175. The range of ORs varies from Carradice's²⁷ 8.044 (2013) to Christenson's²⁵ .497 (2010), with an average value of

TABLE III - Leavout analysis: the elimination of Carradice's trial (nr 7) makes other trials uniform.

	Q	τ^2	I ²	H ²
1	19.282	.469	67.804	3.106
2	23.368	.578	72.236	3.602
3	23.335	.526	74.255	3.884
4	22.792	.581	69.702	3.301
5	22.272	.455	72.177	3.594
6	22.368	.467	72.557	3.644
7	3.171	0	0	1.00
8	22.928	.515	73.542	3.378

.9141 (Fig. 2). The obtained ORs were tabulated. The Q test is not statistically significant but I² is < 75% (= 69.38) (Fig. 3). The Leavout analysis shows that the elimination of Carradice's trial reduces the parameters of heterogeneity: in fact, Carradice's trial is the only one that increases the values of I₂ and Q (Table III).

Discussion

From our meta-analytic assessment, the obtained OR average value is 1.72 with a 95% C.I. of 0.94-3.12, which includes the value 1. For this reason we can say that there is not a statistically significant difference between the results obtained by the two techniques. However, it is right to point out that the average odds ratio is slightly shifted to a value in favor of the laser technique, mainly due to the odds ratio calculated in the Carradice's trial which is the only one non-aligned with the others. Carradice reported a change of procedure in the course of the trial. In fact, at first, in his study protocol, it was planned that both stripping and EVLA procedures had to stop to the knee, for the prevention of post-procedure neuropathies. However, during the study, it was decided to extend the EVLA, but not the stripping, below the knee, cannulating at the

lowest point of demonstrable reflux, up to medial malleolus. This, in our opinion, may constitute a bias: when Carradice perform traditional surgery, leaves "in situ" a segment of saphenous vein longer than the one left in course of EVLA; this could give rise to the suspicion that the disproportion between surgical recurrences and EVLA ones is due to treatments that are not completely overlapping.

Other considerations are due. Data could be affected by the overall shortness of follow-ups, as the endovenous LASER ablation is a more recent technique introduced into the therapeutic baggage for the therapy of incontinence of the great saphenous vein. The importance of a reasonably long follow-up is that the EVLA leaves in situ the treated vein; its ablation is only functional and is due to the thermal damage induced by the LASER fiber. We found that the various studies are not homogeneous: nor for delivered energy (in recent years it was used an increase of energy and consequently of the temperatures and it has been demonstrated that the obliteration is a direct function of the temperature²⁹⁻³⁰, nor of wavelength, nor of modality of energy delivering (single dose v/s pulsed-dose). Moreover, it has recently been demonstrated that the new radial fibers³¹ are more effective in creating thermal damage. For this reason we are unable to know, in the short term, if there were sections of the vein only partially obliterated, neither do we know if the U.S. assessment has scanned the entire course of the treated vein, without skipping. Moreover, post-surgical recurrences (both clinical, morpho-functional and instrumental) may occur even after several years from surgical procedure; for this reason it is evident that more trials with prolonged follow-ups (at least 5 years) are required and only the study of Rasmussen reaches such a long follow-up.

In addition, even if the analyzed works are the most significant and useful to a meta-analytical evaluation, for setting, number of patients and homogeneity, they do not perform, at least a greater number of them, a comparison between LASER treatment and a specific surgical technique (only HL/S or only isolated stripping).

In fact, in Johnes 2011³² it is reported that the most important cause of recurrence is an incomplete primary surgery (such as an un-adequated ostial ligation – Savel'ev 2007³³) and that it leads to neo-vascularization in a large part of cases. Moreover, we must consider that ostial valvular incontinence, pre-ostial, or mixed ostial + pre-ostial valvular incontinence, combined with a complete saphenous vein insufficiency may lead to different incidences of clinical-instrumental recurrence; moreover the incidence of recurrence of an incontinent great saphenous vein varies according to the association with the incontinence of deep venous system³⁴ and the type of surgical treatment performed: for these reasons, it is clear that there are many variables that should be considered to evaluate the results of a great saphenous vein incontinence treatment. For the same reasons, we consider a

lack of all the examined trials the fact that a subdivision, within the groups, considering gender and age as variables, was not carried out.

Conclusions

In conclusion, after all the above considerations, our meta-analytic assessment states that LASER treatment, at the moment and with the actual follow-ups, is an equally effective procedure than the surgical one. Its usefulness lies in reducing time of hospitalization and, ultimately, the functional recovery of the patient, which is definitely faster confronting the surgical procedure, regardless if the latter is done under local anesthesia or loco-regional spinal anesthesia.

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Riassunto

OBIETTIVI: Questo lavoro si propone di confrontare la tecnica ablativa della vena safena interna con Laser Endovascolare alla chirurgia tradizionale, valutando l'incidenza di recidive.

MATERIALE DI STUDIO: È stata eseguita una meta-analisi per confrontare la validità della tecnica endovascolare Laser con il trattamento chirurgico, utilizzando, come risultato clinico, la presenza o l'assenza di reflusso. È stata effettuata una revisione sistematica della letteratura sul trattamento delle vene varicose, con ricerca nei seguenti database: PUBMED-MEDLINE, Cochrane. I termini di ricerca considerati sono stati: *stripping*, *HL / S*, *surgery*, *laser*, *EVLA**, *varicose vein**, *GSV*, *saphenous vein*. Sono stati considerati ammissibili nello studio Trials Randomizzati e Controllati (RCT) basati almeno su sei mesi di follow-up. La qualità metodologica degli studi inclusi è stata valutata utilizzando il *Cochrane Collaboration Bias Risk Assessment Tool*. Gli effetti delle variabili dicotomiche prese in considerazione sono state valutate calcolando il rischio relativo con un intervallo di confidenza al 95%. Gli articoli sono stati valutati inizialmente dagli abstracts; i documenti idonei sono stati esaminati full-text.

RISULTATI: Abbiamo considerato due gruppi, A e B. Gruppo A: 756 arti trattati con intervento chirurgico convenzionale; Gruppo B: 755 arti trattati con la tecnica EVLA. Il gruppo A ha mostrato 175 recidive post-procedura, mentre B ha mostrato 97 recidive. L'ODDS Ratio (O.R.) medio è 1,72; O.R. minimo è di 0,497, mentre il massimo è stato di 8,064.

DISCUSSIONE: Il valore OR medio ottenuto è di 1,72 con un Indice di Confidenza al 95% di 0,94-3,12, che com-

prende il valore 1, contrariamente ai criteri di rifiuto dell'ipotesi nulla. Per questo motivo non vi è una differenza statisticamente significativa tra i risultati ottenuti con le due tecniche.

CONCLUSIONI: L'ablazione endovascolare laser (EVLA) non dimostra di essere superiore, in termini di recidive, alla tecnica chirurgica. Tuttavia resta una valida opzione terapeutica nei pazienti con insufficienza della safena interna, riducendo la sintomatologia dolorosa postoperatoria e i tempi di degenza.

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