Comparing endovenous laser ablation, foam sclerotherapy, and conventional surgery for great saphenous varicose veins

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Background: **Many case series have been published on treatments of varicose veins, but comparative randomized controlled trials remain sparse.**
Objective: **To compare the anatomic success rate, frequency of major complications, and quality-of-life improvement of endovenous laser ablation (EVLA), ultrasound-guided foam sclerotherapy (UGFS), and conventional surgery (CS), after 1-year follow-up.**
Methods: **A total of 240 consecutive patients with primary symptomatic great saphenous vein reflux were randomized to EVLA, UGFS, or CS, consisting of high ligation and short stripping. Primary outcome was anatomic success defined as obliteration or absence of the treated vein on ultrasound examination after 1 year. Secondary outcomes were complications, improvement of the "C" class of the CEAP classification, and improvement of disease-specific (Chronic Venous Insufficiency Quality-of-Life Questionnaire) and general (EuroQol 5) quality-of-life scores.**
Results: **More than 80% of the study population was classified as C2 or C3 venous disease. After 1 year, the anatomic success rate was highest after EVLA (88.5%), followed by CS (88.2%) and UGFS (72.2%) ($P < .001$). The complication rate was low and comparable between treatment groups. All groups showed significant ($P < .001$) improvement of EuroQol 5 and Chronic Venous Insufficiency Quality-of-Life Questionnaire scores after therapy; 84.3% of all treated patients showed an improvement of the "C" of the CEAP classification.**
Conclusions: **After 1-year follow-up, EVLA is as effective as CS and superior to UGFS according to occlusion on ultrasound duplex. Quality of life improves after treatment in all groups significantly. (J Vasc Surg 2013;58:727-34.)**

Varicose veins of the legs affect approximately 25% of the population[1] and may have a substantial impact on patient's health-related quality of life (HRQoL). The treatment of varicose veins and its complications consume a relatively large proportion of the limited health care resources.[1,2] Until recently, conventional surgery (CS) of the great saphenous vein (GSV), consisting of high ligation at the saphenofemoral junction (SFJ) and stripping of the above knee GSV, was the standard of care. In the last decade, minimally invasive techniques such as endovenous laser ablation (EVLA), radiofrequency ablation (RFA), and ultrasound-guided foam sclerotherapy (UGFS) have challenged the position of CS for primary varicose veins.[3] These techniques are effective (occlusion rates of EVLA and RFA >90%) and safe.[4,5] CS associates stripping of the refluxing GSV trunk with high ligation at the SFJ, and this may induce neovascularization.[6-8] Endovenous treatment techniques are performed without high ligation, which may be an advantage. Additional advantages of EVLA, RFA, and UGFS over CS are that they can be easily performed in an ambulatory setting. A comparative meta-analysis of observational studies and randomized clinical trials (RCTs) demonstrated that both EVLA and RFA were superior to CS and UGFS.[5] In the last few years, several important RCTs comparing two different treatment modalities for varicose veins show that the minimally invasive techniques are at least as effective as CS and that they result in faster recovery time and less postoperative pain, and they are preferred by patients.[7-11] In 2011, Rasmussen et al were the first to compare more than two different treatments in a four-arm RCT.[12] This study showed that thermal ablation and CS, all performed under tumescent anesthesia, had better anatomic results than UGFS; however, patient-reported outcomes were better after in the UGFS and RFA.

A recent comparative study of UGFS and CS showed significantly higher efficacy rates 2 years after CS. However, there were no differences in patient-reported outcomes.[13]

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Registration number: NCT00529672.
Author conflict of interest: none.
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The editors and reviewers of this article have no relevant financial relationships to disclose per the JVS policy that requires reviewers to decline review of any manuscript for which they may have a conflict of interest.
0741-5214/$36.00

http://dx.doi.org/10.1016/j.jvs.2012.12.074

The objective of this study is to compare the anatomic success rate, frequency of complications, and HRQoL improvement of EVLA, UGFS, and CS for the treatment of primary incompetent GSV after 1 year.

METHODS

Our study was designed as a consecutive single-center RCT at the Departments of Dermatology and Vascular Surgery of Erasmus Medical Center Rotterdam, The Netherlands, starting in January 2007. Because of a decreasing inclusion rate, the same departments of Catharina Hospital Eindhoven were added as second center in May 2009. The last patient was treated in May 2010. The medical ethics committee of Erasmus Medical Center, Rotterdam approved our protocol (MEC2005-325).

In Latin, the GSV is called "vena saphena magna" and in The Netherlands, we use this name to indicate the GSV; therefore, we have chosen to call our study the MAGNA trial.

Adult patients with a symptomatic primary incompetent GSV at least above the knee with a diameter of ≥0.5 cm and with an incompetent SFJ were eligible to participate. The incompetence of the GSV was defined as reflux of ≥0.5 seconds at color duplex ultrasound (HDI 4500, 10-MHz probe; Philips, Andover, Mass). Exclusion criteria were previous treatment of the ipsilateral GSV, deep venous incompetence or obstruction, agenesis of the deep system, vascular malformations, use of anticoagulation, pregnancy, heart failure, contraindication for one of the treatments, (eg, allergy for aethoxysclerol or lidocaine), immobility, arterial insufficiency (defined as an ankle-brachial index <0.6), age under 18 years, and inability to provide written informed consent to trial participation.

Treatment. In this study, only the GSV in the thigh (from just below or above knee level in most cases) was treated. Patients were allocated to one of the three treatments. After written informed consent, eligible patients were randomized using a computerized list by an independent research nurse. All treatments were performed by dermatologists or surgeons with more than 5 years of experience with the treatments (EVLA and UGFS, and CS and EVLA, respectively).

EVLA. EVLA was performed under ultrasound guidance with a 940-nm diode laser as previously described.[14] In brief, venous access was obtained by puncturing the vein at knee level, with a 16 or 18F needle under ultrasound guidance. After entrance to the varicose vein was established, a guidewire was passed through the hollow needle into the vein up to the level of the SFJ. The needle was removed and a small cutaneous incision of 3 mm was made; then, an introducer sheath was passed over the guidewire. Subsequently, the laser fiber was introduced after removing the guidewire. The laser fiber was positioned 1-2 cm below the SFJ. About 250-500 mL (depending on the length of treated vein) of tumescent anesthetic solution was administered into the saphenous compartment under ultrasound guidance using a mechanical infusion pump. Withdrawal of the laser fiber was performed in continuous mode, and it was attempted to deliver at least 60 J/cm.[15]

UGFS. Ultrasound-guided foam sclerotherapy was performed as reported previously.[14] The Tessari-method[16] was used to prepare foam (1 cc aethoxysclerol 3%: 3 cc air), which was injected directly under ultrasound guidance in the GSV with the patient in a horizontal position.[14,16] The volume of injected foam depended on the length and diameter of the vessel, with a maximum of 10 mL per session (as suggested by the Second European Consensus).[17] After injection, the patient remained in a prone position for at least 5 minutes. If considered necessary, UGFS of the included GSV could be repeated after 3 months.

CS. High ligation with short (above knee) stripping was performed under spinal or general anesthesia. Flush SFJ ligation was followed by ligation of all tributaries back to the second branch and invaginating stripping of the GSV to knee level. The cribriform fascia, superficial fascia, and skin were closed.

After all treatments, an ambulatory compressive bandage was applied for 48 hours, followed by therapeutic compression stockings for 2 weeks postprocedure. All patients were observed for at least one-half of an hour in the clinic after treatment. No specific analgesics were prescribed. Patients were encouraged to mobilize and to resume their usual activities as soon as possible.

Outcomes

Primary outcome. Patients were evaluated at 3 and 12 months for clinical examination and duplex ultrasound. The primary outcome was anatomic success according to duplex ultrasound evaluation. For EVLA and UGFS, this was defined as complete obliteration, without flow or reflux, of the GSV at the level of the midthigh. For CS, success was defined as absence of the GSV in the saphenous compartment at thigh level. We differentiated between obliteration, partial, or complete patency of the treated vein, with or without reflux.

Postoperative neovascularization was assessed at the level of the SFJ using the classification described by De Maeseneer et al. They state that "The degree of neovascularization was determined as 'grade 1 neovascularization' (tiny new vein(s) up to 3 mm diameter, not connecting with any superficial vein) and 'grade 2 neovascularization' (tortuous new vein[s] with a diameter ≥4 mm, with pathological reflux and connecting with thigh varicose veins)."[18]

Secondary outcomes. At all visits, the "C" of the CEAP classification was recorded. The basic CEAP classification as described by Eklöf was used, which means patients are classified according to their highest C score.[19] The type and frequency of complications of the different treatments were reported. The following complications were assessed: superficial vein thrombosis (related to site of treatment), hyperpigmentation (at treatment site), paresthesia (defined as abnormal skin sensations such as tingling, tickling, itching, burning, or numbness), scotoma, migraine, skin burns, skin necrosis, anaphylactic shock,

wound infection for which antibiotic therapy was needed, symptomatic deep venous thrombosis (DVT), based on history and confirmed by duplex examination, and symptomatic pulmonary embolism.

The effect of the treatment on HRQoL was assessed using the disease-specific Chronic Venous Insufficiency Quality-of-Life Questionnaire (CIVIQ)[20] and the generic EuroQol 5D (EQ-5D) instrument[21] questionnaire. Health is a supplement of the EQ-5D. Patients can indicate on a visual analog scale what number they give at their general health. Additional phlebectomies performed during CS or EVLA of GSV or 3 months postoperative were noted. UGFS could be repeated after initial study treatment or could be used as an "escape" therapy in case of failure of the initially allocated treatment.

Statistical analysis. Sample size calculation indicated that 240 legs (80 in each group) were needed to detect a 10% difference in the proportion of patients with occlusion after 1 year between EVLA and UGFS and a 20% difference between EVLA and CS with a power of 90% and an alpha level of $P < .05$.

Data were analyzed on an intention-to-treat basis. Continuous data were first tested for normality using one-sample Kolmogorov-Smirnov Test. For normal distribution, data were presented as means with standard deviations (SDs), and analysis with one-way analysis of variance was done to compare it across three treatment groups.

Categorical data were analyzed by means of χ^2 test or, if appropriate, Fisher exact test. To gauge whether the treatment-related difference in CIVIQ scores was clinically relevant, we used Norman's rule of thumb when the change in score was more than one-half an SD of the distribution of the CIVIQ score prior to therapy, the change was considered clinically meaningful.[22] Patients with bilateral GSV insufficiency were randomized separately for each leg. For efficacy analysis, both GSVs were included, but for HRQoL analyses, these patients were excluded because patients are unable to differentiate the impact of varicose veins of each leg on HRQoL.[23]

A generalized estimating equation model with a logit link was used to model the odds ratio for total occlusion over time. To take the correlation into account between two legs of the same patient and multiple measurements over time, we chose an unstructured covariance matrix and used the patients as the independent subjects. For EQ-5D, CIVIQ, Health, and CEAP outcomes, we used a linear mixed model with empirical standard errors. For this model, we chose a direct product of an unstructured covariance matrix (for the covariance within a leg) and a compound symmetry correlation matrix (for the correlations within a patient between the legs). Thereby, we allow for an unstructured correlation matrix between measurements over time within one leg, and we assume that the unstructured correlation matrix is equal for the first and the second leg within one person.

Statistical analysis was performed using SPSS v. 20.0 (SPSS Inc, Chicago, Ill) and SAS 9.2 (SAS Institute, Cary, NC). All statistical tests were two-sided and considered significant at the $P < .05$ level.

RESULTS

Study population. In 223 eligible patients, 240 legs were randomized for one of the treatments between January 2007 and December 2009 (Fig 1). Seventeen patients were excluded from the analysis; 16 did not fulfill the inclusion criteria and one was lost to follow-up.

Five patients were treated with UGFS because initial treatment had failed: two patients from the EVLA group and three patients from the CS group. Data were analyzed on an "intention-to-treat" basis, according to randomization. "As-treated" analysis showed no significant difference from the intention-to-treat analysis.

In the study population, 82.3% suffered C2 and/or C3 venous insufficiency. The groups were well matched for the demographic data, CEAP classification, and GSV diameter and HRQoL impairment (Table I). The patients in the EVLA group were significantly younger than those in the CS and UGFS group. Patients in the EVLA group received on average 59.16 J/cm (SD, 15.20). Patients in the UGFS group received a mean of 4.7 cc (SD, 1.19) foam. The majority of patients were treated in one session of UGFS. Six patients with lasting complaints received a second treatment within the first year.

Anatomic success. EVLA and surgery were comparably effective (88.5%, n = 69; 88.2%, n = 60, respectively), after 1-year follow-up (Fig 2). However, in the CS group, 10% (n = 7) of patients had grade 1 neovascularization at ultrasound examination of the groin. After 1 year, the occlusion rate of UGFS was 72.7% (n = 56), which was significantly lower than EVLA and CS ($P < .02$). Twenty-one patients (27.3%) of the UGFS group had partial obliteration with reflux. In 11 of these patients, initial treatment resulted in complete relief of complaints despite persisting reflux after 1-year follow-up, and therefore they did not undergo any additional treatment.

Clinical improvement. In all groups, the C of the CEAP-classification decreased significantly after treatment, and there was no difference between groups. An improvement of the C score was seen in 79.4% of all treated patients at 3 months (Fig 3; Supplementary Table, online only). After 12 months, 47.6% of all patients showed improvement of at least two categories (Table II). However, the mean improvement in C score was not significantly different between the three groups. The clinical situation according to the CEAP deteriorated in one patient treated with EVLA; he developed hyperpigmentation at the treatment site and ankle after treatment.

Complications. Complications were recorded in the first year after initial treatment (Table III). The frequency of adverse events was low and not significantly different between the three treatment groups ($P = .64$). Ten patients were seen earlier than 3 months after treatment with complaints of pain. All these patients had a superficial vein thrombosis of a tributary of the GSV, and duplex ultrasound excluded additional DVT in all cases. No

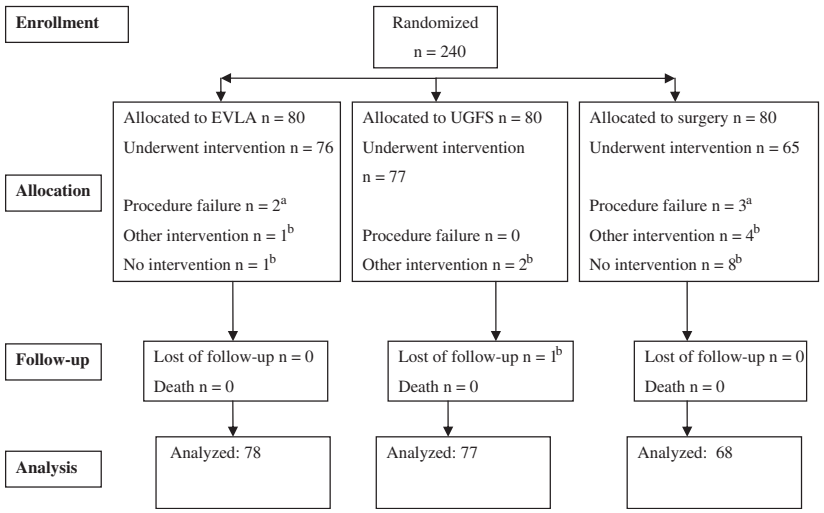

Fig 1. Consort flow. [a]If there was a procedure failure, patients were treated with ultrasound-guided foam sclerotherapy (*UGFS*), and data analysis was on an intention-to-treat basis. [b]Patients who did not receive treatment or received another treatment or were lost to follow-up in the first year were excluded from the analysis. *EVLA*, Endovenous laser ablation.

Table I. The distribution of baseline characteristics for each of the three treatment groups

	EVLA (n = 78)	*UGFS (n = 77)*	*CS (n = 68)*	P *value*
Age, years (SD)	49 (15.03)	56 (13.30)	52 (15.59)	.005[a]
Sex, No. (%)				
Women	54 (69.2)	52 (67.5)	46 (67.6)	.89[b]
Men	24 (30.8)	25 (32.5)	22 (32.4)	
Side, No. (%)				
Left	48 (61.5)	45 (58.4)	34 (50)	.36[b]
Right	30 (38.5)	32 (41.6)	34 (50)	
Unilateral, No. (%)	62 (79.5)	58 (75.3)	51 (75)	.74[b]
Bilateral (same treatment)	6 (7.7)	11 (14.3)	8 (11.7)	
Bilateral (different treatment)	10 (12.8)	8 (10.4)	9 (13.3)	
Mean GSV diameter				
Left, cm (SD)	0.64 (0.15)	0.58 (0.14)	0.62 (0.14)	.08[a]
Right, cm (SD)	0.59 (0.11)	0.62 (0.14)	0.59(0.16)	.65[a]
CEAP, No. (%)				
C1	0	0	0	.64[c]
C2	37 (47.4)	33 (42.9)	28 (41.2)	
C3	29 (37.2)	30 (39.0)	21 (30.9)	
C4	8 (10.3)	8 (10.4)	14 (20.6)	
C5	0	1 (1.3)	1 (1.5)	
C6	0	0	0	
Unknown	4 (5.1)	5 (6.5)	4 (5.8)	
CIVIQ				
Mean score (SD)	25.21 (20.73)	23.96 (17.97)	25.13 (19.15)	.91[a]
EQ-5D				
Mean score (SD)	0.85 (0.16)	0.83 (0.20)	0.86 (0.11)	.65[a]
General health score, % (SD)	79.4 (14.6)	78.8 (12.5)	79.1 (12.7)	.96[a]

CIVIQ, Chronic Venous Insufficiency Quality-of-Life Questionnaire; *CS*, conventional surgery; *EQ-5D*, EuroQol 5D; *EVLA*, endovenous laser ablation; *GSV*, great saphenous vein; *IQR*, interquartile range; *SD*, standard deviation; *UGFS*, ultrasound-guided foam sclerotherapy.
[a]Analysis of variance.
[b]χ^2.
[c]Fisher exact.

symptomatic DVT, pulmonary embolus, or scotoma occurred. No procedure-related mortality was observed. Three patients received antibiotics because of wound infection in the groin after CS; there were no wound infections after EVLA nor after UGFS ($P = .023$). Most of the milder adverse events were transient and disappeared after 3 months. Overall, 11 CS, seven EVLA, and five UGFS patients reported any adverse events.

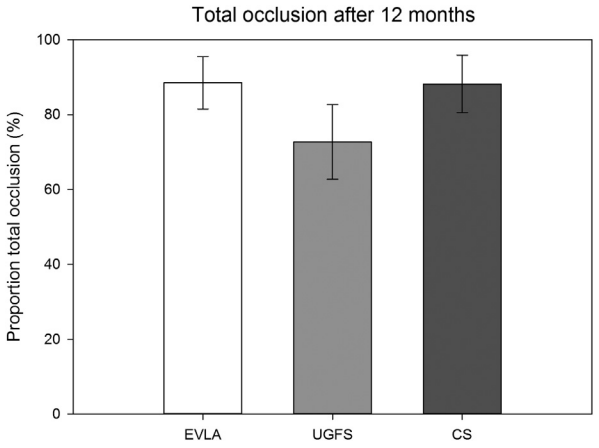

Fig 2. Complete obliteration after 12 months. The proportion of legs that had complete obliteration or absence of the great saphenous vein (GSV) after treatment was significantly different between endovenous laser ablation (*EVLA*), ultrasound-guided foam sclerotherapy (*UGFS*), and conventional surgery (*CS*) ($P < .02$).

Quality of life. Seventeen patients with bilateral GSV insufficiency were excluded from all QoL analysis. Eight of these patients were allocated for the same treatment in both legs and nine patients for different treatments. The CIVIQ and EQ-5D score improved in all groups at 3 months and remained relatively stable until 1 year (Fig 3, *B-D*; Supplementary Table, online only) CIVIQ score and EQ-5D showed no significant differences between the three groups. Additional analysis adjusted for age and sex showed no significant differences for CIVIQ, EQ-5D, and Health score.

It is remarkable that the CIVIQ scores improved in 11 patients (14%) of the UGFS group despite their remaining (segmental) reflux on ultrasound examination and without performing additional injections.

Additional interventions. Phlebectomies were permitted during initial treatment with the intention of removing all varicosities in the same procedure, but because of practical issues, this was not possible in all cases. In 15 patients (19.2%) in the EVLA group and 18 (25.7%) in the CS group, phlebectomy was performed during initial treatment. In 12 (15.3%), 15 (19.5%), and 11 (15.7%) of the EVLA, UGFS, and CS group respectively, phlebectomies were performed after 3 months. In the UGFS group, six patients (4.6%) with lasting reflux and complaints received a second injection with foam.

Subgroup analysis. Subgroup analysis did not show any significant differences between anatomic success, clinical improvement, complications, or quality of life improvements between the two centers.

There were no significant differences of CIVIQ and EQ-5D scores between unilateral and bilateral treatments (n = 52) nor between groups with or without additional treatments. There were no significant differences in anatomic success, CEAP classification, or HRQoL scores between patients who received additional treatments and those who did not. The group that received additional treatments reported more adverse events than the patients who had only GSV treatment (12.7% vs 6.7%; $P = .228$).

DISCUSSION

In the last decade, EVLA and RFA were introduced and UGFS has been optimized. These minimal invasive interventions are increasingly used as an alternative to CS for treating saphenous veins.[4,5] The MAGNA trial shows that EVLA and CS are comparably effective (almost 90%) and that both are significantly more effective than UGFS (72.7%) using ultrasound-based anatomic outcomes. Complications are rare and quality of life (CIVIQ and EQ-5D) improved after each treatment. Using a repeated-measure analysis, there were no significant differences in CIVIQ and EQ-5D scores between the groups. Applying the Norman's rule of thumb on the unadjusted data, none of the improvements in the CIVIQ and EQ-5D appeared to be clinically relevant.[22]

The results of this RCT are strikingly similar to other clinical studies, meta-analysis, and two recent RCTs that included UGFS increasing the validity of the findings.[5,12,13,24] One year after treatment, remaining (segmental) flow with reflux was observed in more than one-quarter of the patients treated with UGFS, which is in line with other observational studies and RCTs.[12,13,25,26] Neovascularization occurs in 10% of the patients in the CS group 1 year postoperatively, which corresponds with results of a previous study focusing on the effect of closing the cribriform fascia to contain postoperative neovascularization at the SFJ.[18]

Despite randomization, EVLA-treated patients were significantly younger than those in the other two treatment arms. Adjusting for age and sex in a logistic model, there were no differences in CIVIQ scores or in CEAP classification between the three groups.

In accordance with other RCTs comparing CS to new minimally invasive treatment methods, we had difficulty enrolling the required number of patients in the RCT because of the reluctance among patients to undergo CS. Therefore, an additional center was added during the study period. No differences in outcomes were noted between the two centers. Of the 17 included patients that withdrew from the trial, 10 were assigned to CS suggesting that informed patients preferred minimally invasive treatments.

The primary outcome of this study was total occlusion and/or absence of the treated GSV according to ultrasound. This outcome has the advantage to be objective and reproducible and is possibly a proxy of symptom reduction and future clinical relevant recurrence. These latter assumptions will be tested when the 5-year results become available. Also, defining the outcome as total occlusion may have been too strict, because "remodeling" of the insufficient vein, as is often seen after UGFS, may be associated with alleviation of symptoms while persisting flow with or without reflux is present in the treated vein. Eleven patients with residual reflux after UGFS did decline an additional

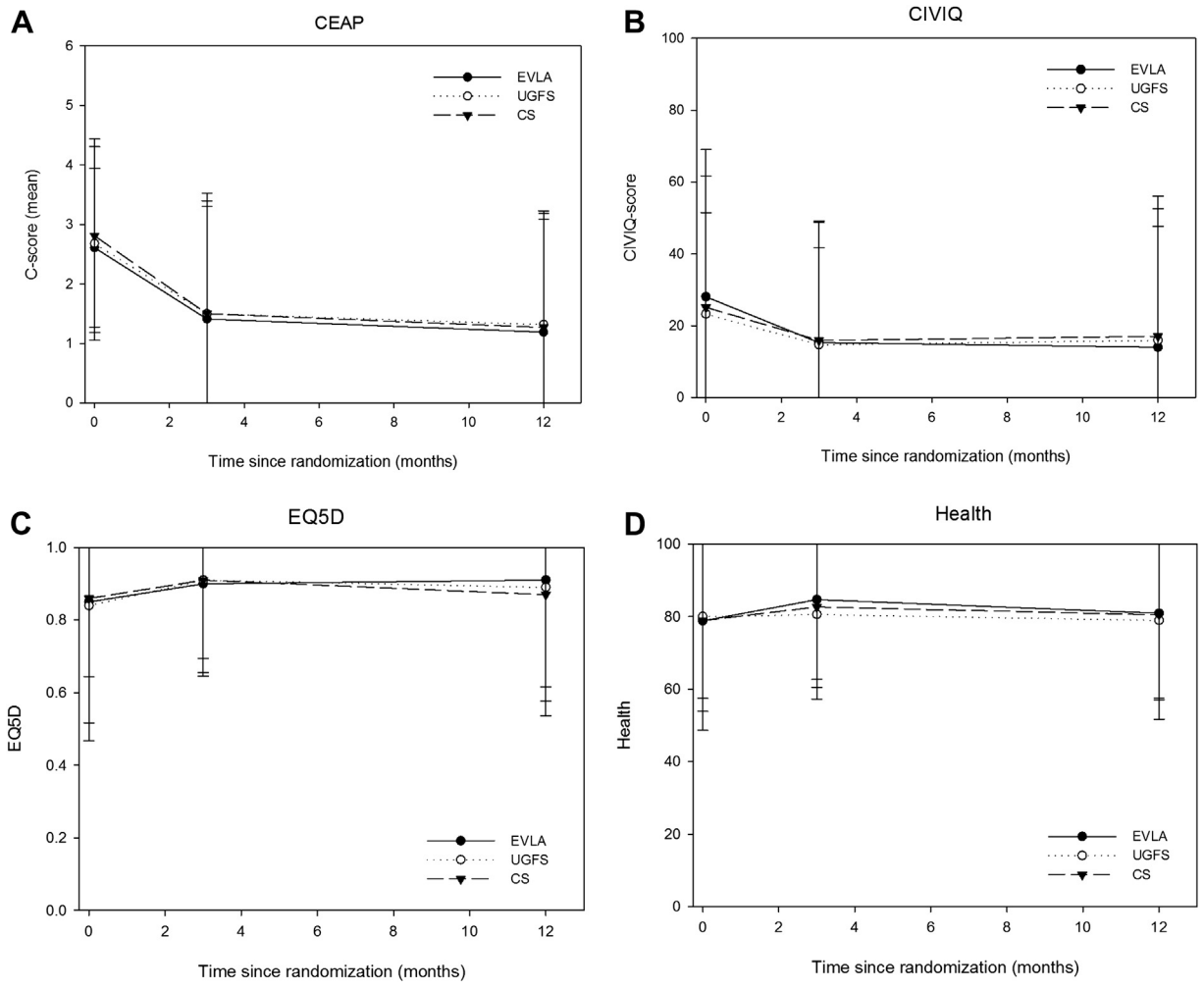

Fig 3. Repeated measurement analysis for CEAP and quality-of-life scores **A,** Thirteen patients with missing CEAP scores were excluded. **B,** Fourteen patients with missing Chronic Venous Insufficiency Quality-of-Life Questionnaire (*CIVIQ*) scores and 24 patients with different bilateral randomized treatment were excluded. **C** and **D,** Twenty-four patients with missing EuroQol 5D (*EQ-5D*)/health scores and 24 patients with different bilateral randomized treatment were excluded. *CS,* Conventional surgery; *EVLA,* endovenous laser ablation; *UGFS,* ultrasound-guided foam sclerotherapy.

UGFS session because of absence of venous symptoms. This observation challenges the strict definition of primary outcome criteria such as "total occlusion" and "absence of reflux" used as the gold standard for evaluation after GSV treatment in RCTs. Moreover, it emphasizes the conviction that we treat patients and not ultrasound findings.[27] Recently, the Union Internationale de Phlébologie has proposed a new classification to describe the fate of the junction and the treated trunk after endovenous ablation.[28] This classification allows to describe postoperative findings more detailed, distinguishing between obliteration, partial or complete patency of the treated vein, and segmental obliteration or patency of the treated trunk, with or without reflux. Apart from these duplex ultrasound findings, clinical outcome parameters as well as other outcome measures such as patient-reported outcomes (eg, HRQoL, symptoms, satisfaction, and preference) should be considered.[13,28,29] In contrast to HRQoL, symptom reduction was not maximally assessed in this study, which in retrospect is a missed opportunity.[13] At time of the study design, we overlooked the problem of including bilateral GSV. For the HRQoL outcomes, patients with two different study treatments were excluded from the HRQoL analysis because patients may not differentiate HRQoL impairment between both legs. Patients with the same treatment for both legs were included for HRQoL analysis by taking the correlation between HRQoL scores of the same patient into account. All patients were included in the efficacy analysis, which was adjustment for bilateral GSV treatments.

Because of the scarring after CS and in a lesser extent EVLA having a blinded outcome assessor was not feasible.

Table II. Changes in "C" from CEAP classification 12 months after therapy

	C improvement					
	−3.00	*−2.00*	*−1.00*	*0*	*2.00*	*Total*
Type of treatment, No. (%)						
EVLA	10 (13.5)	26 (35.1)	25 (33.8)	12 (16.2)	1 (0.4)	74
UGFS	7 (9.7)	22 (30.6)	33 (45.8)	10 (13.9)	0	72
CS	8 (12.5)	27 (42.2)	19 (29.7)	10 (15.6)	0	64
Total	25 (11.9)	75 (35.7)	77 (36.7)	32 (15.2)	1 (0.48)	210

CS, Conventional surgery; *EVLA*, endovenous laser ablation; *UGFS*, ultrasound-guided foam sclerotherapy.

Table III. Distribution of the complications for each of the three therapies at 3 and 12 months after therapy

		EVLA (n = 78)	*UGFS (n = 77)*	*CS (n = 68)*	P *value*[a]
3 months	Hyperpigmentation	2	1	0	.78
	Paresthesia	2	1	4	.30
	Superficial vein thrombosis	3	3	4	.85
	Wound infection[b]	0	0	3	.03
	DVT	0	0	0	1.00
	Pulmonary emboli	0	0	0	1.00
	Death due to therapy	0	0	0	1.00
	Total number of patients with complications	7	5	11	.64
12 months	Hyperpigmentation	1	1	0	1.00
	Paresthesia	0	1	1	1.00

CS, Conventional surgery; *DVT*, deep vein thrombosis; *EVLA*, endovenous laser ablation; *UGFS*, ultrasound-guided foam sclerotherapy.
[a]Fisher exact.
[b]Requiring systemic antibiotics.

The ultrasound investigations were done by physicians not necessarily part of the research team, hopefully limiting the impact of this limitation.

In this study, phlebectomies were allowed during initial treatment of the study, GSV in patients allocated to EVLA or CS, or after 3 months for all included patients. Phlebectomies were proposed to all study patients with residual superficial varicose veins as additional treatment after 3 months regardless of the study treatment. The MAGNA trial includes the three treatments most frequently used in The Netherlands in 2007 explaining the exclusion of segmental RFA. In this study, CS was performed using spinal or general anesthesia, which is still common practice in The Netherlands. It is anticipated that the long-term results of the minimally invasive interventions will stimulate surgeons to switch to minimally invasive procedures and/or use of tumescent anesthesia when CS is indicated.[27] Using tumescent instead of general anesthesia will improve patient satisfaction and will lead to shorter down time after intervention.[30] The 5-year follow-up of the MAGNA trial and other similar ongoing RCTs will further clarify whether the observed results of EVLA, UGFS, and CS persist over time.

CONCLUSIONS

The 1-year results of the MAGNA trial show that the short-term efficacy, defined as anatomic success according to duplex ultrasound, is equally high for EVLA and CS and lower for UGFS. The treatments are equally safe; no severe adverse events were seen. Wound infections and neovascularization were more common after CS. All therapies resulted in significant clinical and HRQoL improvement. Long-term efficacy of these three intervention methods needs to be established and will be available in 4 years.

The authors thank Jaap Buth (vascular surgeon), Marjon de Jong (research nurse), Loes Hollestein (statistics), Olga van Beuningen (vascular technologist), and all participating vascular surgeons and dermatologists from Catharina Hospital Eindhoven and Erasmus MC Rotterdam for their assistance.

AUTHOR CONTRIBUTIONS

Conception and design: MK, MN, TN
Analysis and interpretation: AB, RB, TN, TS
Data collection: AB, MK, GA, MM, PC
Writing the article: AB, RB, TN
Critical revision of the article: AB, RB, GA, MM, TS, TN
Final approval of the article: AB, MK, RB, GA, PC, MM, TS, MN, TN
Statistical analysis: AB, TS, TN
Obtained funding: Not applicable
Overall responsibility: AB, TN

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Submitted Jun 9, 2012; accepted Dec 22, 2012.

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Supplementary Table (online only). Repeated measurement analyses for all outcome measures

			EVLA		*UGFS*		
	No.	*CS*	*OR for total occlusion*	*95% CI*	*OR for total occlusion*	*95% CI*	P *value*
Anatomic success							
Occlusion	223						
Unadjusted[a]		Reference	1.24	(0.56-2.77)	0.34	(0.17-0.67)	.02
Adjusted[a,b]		Reference	1.22	(0.55-2.69)	0.35	(0.17-0.67)	.02
	No.		*Difference mean change in score*	*95% CI*	*Difference mean change in score*	*95% CI*	P *value*
CEAP							
C score	210[d]						
Unadjusted[c]		Reference	0.00	(−0.24 to 0.24)	0.09	(−0.14 to 0.33)	.61
Adjusted[c,b]		Reference	0.00	(−0.24 to 0.24)	0.10	(−0.12 to 0.33)	.55
Quality of life							
CIVIQ	185[e]						
Unadjusted[c]		Reference	−2.01	(−6.43 to 2.41)	−0.63	(−4.91 to 3.65)	.63
Adjusted[c,b]		Reference	−1.93	(−6.36 to 2.49)	−0.66	(−4.89 to 3.57)	.67
EQ-5D	175[f]						
Unadjusted[c]		Reference	0.01	(−0.02 to 0.04)	0.01	(−0.03 to 0.04)	.86
Adjusted[c,b]		Reference	0.01	(−0.02 to 0.04)	0.01	(−0.02 to 0.04)	.81
Health	175[f]						
Unadjusted[c]		Reference	1.73	(−1.55 to 5.01)	−2.03	(−4.79 to 0.73)	.04
Adjusted[c,b]		Reference	1.61	(−1.67 to 4.89)	−1.97	(−4.78 to 0.84)	.07

CI, Confidence interval; *CIVIQ,* Chronic Venous Insufficiency Quality-of-Life Questionnaire; *CS,* conventional surgery; *EQ-5D,* EuroQol 5D; *EVLA,* endovenous laser ablation; *OR,* odds ratio; *UGFS,* ultrasound-guided foam sclerotherapy.

[a]Time since randomization was included in the model.

[b]Adjusted for age and sex.

[c]Time since randomization and baseline score were included in the model.

[d]Thirteen patients with missing CEAP scores at all time points were excluded.

[e]Fourteen patients with missing CIVIQ scores and 24 patients with different bilateral randomized treatment were excluded.

[f]Twenty-four patients with missing EQ-5D/Health scores and 24 patients with different bilateral randomized treatment were excluded.