



TITLE: Endovenous Laser for Treatment of
Varicose Veins (EVLT)

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ENDOVENOUS LASER TREATMENT OF VARICOSE VEINS

INTRODUCTION

The California Assessment Technology Forum has received requests to review the published data regarding the efficacy and safety of endovenous laser treatment (EVLT) of varicose veins in clinical practice.

BACKGROUND

The major superficial veins in the lower extremity are composed of the greater (or long) saphenous vein (GSV) and the lesser (or short) saphenous vein (LSV). The superficial venous system is interconnected with the deep system via perforating veins so that dysfunction in one system often leads to dysfunction in the other. Veins in the superficial system contain one-way valves that allow the return of blood to the heart in spite of the effects of gravity (Min and Khilnani 2002).

Varicose veins are most commonly found in the legs as abnormally dilated, elongated, and tortuous alterations in the saphenous veins and their tributaries. Varicose veins that arise spontaneously in the absence of deep venous involvement are referred to as primary varicose veins. An inherited vein wall or valvular defect appears to play a role in the development of most primary varicosities (Messina and Tierney 2001). Secondary varicosities that result from conditions such as thrombophlebitis, trauma, deep venous thrombosis, arteriovenous fistula, or non-traumatic proximal venous obstruction (e.g. pregnancy) account for a minority of varicose veins (5-10%). Venous reflux secondary to valve incompetence occurs in primary and secondary varicose veins. As the pressure in the deep venous system is generally greater than that of the superficial system, valve incompetence where these two systems meet (e.g. the saphenofemoral junction or SFJ) permits bi-directional blood flow and eventual dilation of the superficial veins (Min and Khilnani 2002). Dysfunction of the venous system may present as clearly visible, dilated varicose veins when the patient is standing, or may manifest as telangectasias ("spider veins") or reticular veins (not connected to major trunk varices) (Wakefield and Greenfield 2000).

BACKGROUND, continued

Varicose veins of the lower extremities are common and frequently symptomatic. Approximately half of the adult population has minor stigmata of venous disease but fewer than half of these (20-25% of women and 10-15% of men) will have visible varicose veins (Callam 1994). Risk factors for the development of varicose veins include increasing age, parity, occupations that require prolonged standing, hypertension and smoking (in men) and obesity (in women). Symptoms include dull, aching heaviness or a feeling of fatigue brought on by prolonged standing. The pain may be worse during pregnancy or the menstrual cycle due to increased fluid volume and/or higher circulating levels of estrogen. Complications of varicose veins include secondary ulceration, bleeding from high-pressure venous blebs, chronic stasis dermatitis, superficial venous thrombosis and thrombophlebitis (Messina and Tierney 2001; Callum 1994).

Mechanical therapy is the mainstay of treatment for chronic varicosities. Elastic graduated compression stockings give external support to the superficial veins. Compression stockings are thought to improve venous hemodynamics by reducing venous reflux, increasing deep venous flow velocity, improving lymphatic flow and the cutaneous microcirculation, and decreasing ambulatory venous pressures (Wakefield & Greenfield 2000). Leg elevation 3-4 times daily has also been shown to reduce edema and can improve cutaneous microcirculation in patients with venous insufficiency. In many patients, these mechanical therapies may provide adequate symptom relief and prevent or postpone the need for more definitive treatment (Abu-Own et al. 1994). Indications for surgical treatment include persistent pain, recurrent thrombophlebitis, and erosion of the overlying skin with bleeding and ulceration. Surgery is thought to produce beneficial effects via reduction of venous reflux from the deep to the superficial veins by removing incompetent superficial veins, thereby modifying the effect of venous hypertension upon the cutaneous tissues. Surgical options include venous stripping, ligation, and valvular reconstruction. Surgery is directed to the underlying disease as defined by Doppler ultrasonography. Stripping of the entire saphenous system is rarely required. The risk of serious complications following surgery is low (less than 1%) but minor complications such as temporary saphenous or sural nerve neuralgia are common (Sarin et al. 1994). The reported risk of recurrence following surgery ranges from 7 - 65%; approximately 20% of varicose vein operations are performed for recurrent varicosities (Jones et al 1996).

BACKGROUND, continued

Compression sclerotherapy or laser can be used for telangectasias, spider veins, and small (< 4 mm) varicosities. The goal of treatment is to obliterate the abnormal vein by inducing localized endothelial destruction and fibrosis (Bernstein et al. 1999).

More recently, there has been a surge of interest in endovenous techniques for the management of lower extremity varicosities, particularly GSV incompetence (Goldman 2000; Weiss and Weiss 2002; Rautio et al. 2002). The two most promising techniques to date are endoluminal radiofrequency and laser ablation of varicose veins. Radiofrequency ablation is performed by means of a specially designed catheter inserted through a small incision in the distal medial thigh to within 1-2 cm of the saphenofemoral junction. The catheter is slowly withdrawn as high frequency radiowaves are delivered through the catheter electrode and cause direct heating of the vessel wall leading to fibrosis and causing the vein to collapse, closing the vein. In a recent study, the time of procedure from access to completion of pullback averaged 52.3 minutes, with actual pullback time averaging 17.9 minutes (Weiss and Weiss 2002). The most common adverse effects of endoluminal radiofrequency are heat-induced paresthesias of the leg, clinical thrombophlebitis, thermal skin injury and propagation of thrombus at the site of the procedure (Chandler et al 2000). More recently, with the use of tumescent anesthesia, reported side effects include bruising and tenderness after the procedure in less than 1% of patients and long term paresthesia in only one patient. Complete disappearance of the treated saphenous vein persisted for two years in 90% of patients (Weiss and Weiss 2002).

Endovenous Laser Treatment

Endovenous Laser Treatment (EVLT) delivers heat in the form of laser energy into the vessel lumen. The presumed pathophysiological mechanism of action of EVLT is that laser-induced indirect local heat injury of the inner vein wall by steam bubbles originating from boiling blood leads to thrombotic occlusion and fibrosis of the vein (Proebstle et al. 2002). EVLT is an outpatient procedure that is performed in a minor procedure room with local anesthesia. To perform EVLT, the GSV is mapped with duplex ultrasound, and after local anesthesia is administered, the GSV is generally entered at or above knee level with a 5-Fr, 45 cm long introducer sheath over a guide wire.



BACKGROUND, continued

Endovenous Laser Treatment, continued

Position is confirmed by aspiration of venous blood and visualization with ultrasound. A sterile bare-tipped 600- μ m diameter laser fiber is then put into the vein and position just below the saphenofemoral junction is confirmed by direct visualization of the red aiming beam of the laser fiber through the skin. Perivenous local anesthesia is then administered along the GSV that serves to compress the vein around the laser tip and also absorbs heat and helps prevent damage to surrounding tissue. The laser is then slowly withdrawn at a rate of 3-5 mm/second as 810-nm wavelength diode laser energy is delivered endovenously along the course of the GSV. Following withdrawal of the fiber and sheath, the patient is dressed with a compression bandage worn for 3-7 days. Patients are instructed to walk immediately after the procedure and to continue with normal, low impact daily activities. Contraindications to EVLT include patients with thrombus in the vein segment to be treated, patients with an aneurysmal section in the vein segment to be treated and patients with peripheral arterial disease as determined by the Ankle-Brachial Index < 0.9 (Min and Khilnani 2002,; Diomed website: www.evlt.com/physicians/patient%20selection.htm).

TECHNOLOGY ASSESSMENT (TA)

TA Criterion 1: The technology must have final approval from the appropriate government regulatory bodies.

The equipment needed for EVLT consists of a portable Diomedplus 810nm Surgical Laser and handpiece and EVLT procedure kit (consisting of a disposable laser fiber, introducer sheath, and guide wire and entry needle). Diomed Inc. received FDA 510K clearance for the Diomed 810 nm Surgical Lasers and EVLT Procedure Kit on January 22, 2002. This device is intended for use in endovascular coagulation of the greater saphenous vein of the thigh in patients with superficial vein reflux. On December 2, 2002, Diomed Inc. received FDA 510K clearance for the EVLT Kit and D15plus and D30 plus Diode Lasers for use in the treatment of varicose veins and varicosities associated with superficial reflux of the Greater Saphenous Vein.



TA Criterion 1, continued

Dornier Medtech America, Inc (Kennesaw, GA) received 510K clearance on October 25, 2002 for the Medilas D Fibertom Laser ("Medilas D"), Medilas D SkinPulse ("SkinPulse") and Medilas D SkinPulse S ("SkinPulse S") for use in endovascular coagulation of the greater saphenous vein of the thigh in patients with superficial vein reflux.

Biolitec, Inc. (East Longmeadow, MA) received 510K clearance on January 2, 2003 for the Ceralas D Diode Laser System with Endo Laser Vein System Kit for endovascular coagulation of the greater saphenous vein of the thigh in patients with superficial vein reflux.

TA criterion 1 is met

TA Criterion 2: The scientific evidence must permit conclusions concerning the effectiveness of the technology regarding health outcomes.

To date, the scientific literature assessing the use of EVLT in clinical practice is quite limited consisting exclusively of case series (Navarro et al 2001, Min et al 2001; Proebstle et al 2002; Chang and Chua 2002) and abstracts (e.g. Min RJ. 2002) The major outcomes evaluated in these studies are the rate of post-procedure vein occlusion as evaluated by duplex ultrasound and/or color doppler, and the rate of recurrence of saphenous vein reflux and venous varicosities. Other outcomes include relief of preoperative symptoms, prevention and treatment of complications of venous varicosities, patient satisfaction, and side effects and complications of the procedure.

There have been no randomized controlled trials comparing outcomes of EVLT with the standard surgical approach of vein ligation and stripping or with endoluminal radiofrequency ablation. Previous research regarding treatment of varicose veins has documented that clinical reports (case series) have described better results than more rigorous randomized controlled trials (Baccaglini et al 1996). Therefore, the published evidence is insufficient for drawing firm conclusions regarding the efficacy or safety of this procedure.

Level of evidence: 5 (case series)

TA criterion 2 is not met.

TA Criterion 3: The technology must improve net health outcomes.

Benefits and Risks

Min et al (2001) report the results of a prospective, non-randomized, consecutive enrollment multicenter trial of 84 patients with SJF incompetence and GSV reflux. Exclusion criteria included nonpalpable pedal pulses, inability to ambulate, deep vein thrombosis, and "general poor health". Ninety GSVs in 84 patients (63 women and 21 men) were examined with bi-directional continuous wave doppler examination and duplex US to identify sources of venous incompetence and map out abnormal venous pathways. The GSV was entered at knee level and a 600- μ m diameter laser fiber was introduced into the vein through the sheath and the distal tip of the laser fiber was positioned 1-2 cm below the SJF with sonographic and visual guidance. Perivenous local anesthesia was administered along the GSV and manual compression was used to compress the vein wall around the fiber tip of the laser. Energy from the Diomed D15 Surgical Laser (Diomed, Andover, MA) was delivered endovenously as the laser fiber was withdrawn in 1-2 mm increments (see figure 1 in Min et al 2001). Patients were instructed to wear medium weight (30-40 mm/Hg) compression stockings for one week following the procedure and to engage in normal but not vigorous exercise. Patients were followed-up at 1 week, 4 weeks, 3 months and 6 months after EVLT. Tributary veins were treated with compression sclerotherapy as needed beginning 4 weeks after EVLT. Transverse measurements of the GSV diameter were made 2-3 cm below the SFJ in the standing position at each follow up. At 1 week follow-up, 87 of 90 (97%) GSV segments were closed with no flow detected by color Doppler. The open GSVs were retreated and successfully closed. At 1-9 months of follow-up (mean=6months) 89 of 90 (99%) of GSVs remained closed. The procedure was generally well tolerated with most patients experiencing ecchymoses and mild discomfort along the treated GSV resolving in 1-2 weeks. One patient had paresthesia in the medial calf that resolved over 6 weeks. The authors conclude that although early results with EVLT have been impressive they await longer-term follow-up results from patients already treated with EVLT and additional studies of patients wishing to "avoid surgery".

TA Criterion 3, continued

Navarro et al (2001) describe treatment of 40 greater saphenous veins in 33 patients with SFJ reflux associated with GSV incompetence. Mean pre-treatment GSV measurements were 10.2 mm X 10.6 mm. Patients were examined with Doppler and color duplex ultrasound and patients with anatomic malformations of the GSV and/or reflux and dilation of several saphenofemoral branch tributaries beyond the GSV were excluded and other treatments recommended. Using local anesthesia and ultrasound guidance, the GSV was entered on the lower thigh or a knee level via a percutaneous needle puncture or a stab wound-Mueller hook approach. A wavelength of 810 nm diode laser energy was delivered endovenously 1-2 cm below the SFJ and along the course of the GSV as the laser fiber and catheter were slowly withdrawn in 3-5 mm increments. All 40 treated GSV segments were closed following initial treatment and remained closed with up to 14 months of follow-up (mean follow-up 4.2 months). No patients required re-treatment. The authors report that the procedure was "well tolerated" by all patients. At 24 hour and 7 day follow-up "most" patients had mild ecchymoses and "occasional" mild induration in the area of anesthetic infiltration. There were no heat-related complications reported. The authors acknowledge the limitations of this trial concluding, ". . . long-term follow-up results are needed to further define the role of endovenous laser as a minimally invasive alternative treatment to ligation and stripping for those patients wishing to avoid surgery."

Proebstle et al (2002) evaluated EVLT of the incompetent greater saphenous for efficacy, treatment related adverse effects, and putative mechanisms of action. Twenty-six patients (31 total limbs) treated at University of Mainz, Germany were evaluated with duplex scanning and prepped in the usual manner. They were treated endovenously with 940 nm wavelength and evaluated clinical and biological outcomes 30 minutes and 1 day following the procedure. On days 1,7 and 28, all but one limb (97%) showed a thrombotically occluded GSV. Adverse events in all 26 patients were ecchymoses and palpable induration along the thrombotically occluded GSV that lasted 2-3 weeks. Two limbs developed thrombophlebitis of a varicose tributary treated with non-steroidal antiinflammatory medication.

TA Criterion 3, continued

Chang and Chua (2002) report on the results of an endovenous laser treatment they call endovenous laser photocoagulation (EVLV) from Singapore. This technique is not considered to be generally applicable (personal communication Robert Min, MD). In this technique, patients underwent spinal or general anesthesia and a Nd:YAG laser system was used to deliver laser pulses at a wavelength of 1,064 nm with 10-15 W of energy and pulse duration of 10 seconds. They treated 149 patients with 252 varicose GSVs. Mean follow-up period was 19 months. One hundred forty one patients with 244 legs (96.8%) demonstrated eradication of their varices within 6 months. Eight legs total (3.2%) developed recurrent varices and were treated by sclerotherapy. Patients seemed to experience more complications than described in other studies. Paresthesia was experienced by 36.5%, ecchymosis and dyschromia in 23%, superficial burns in 4.8% and superficial phlebitis in 1.6%. The authors report that these problems resolved by 28 months.

Pending Trials

TA Criterion 3 is not met.

TA Criterion 4: The technology must be as beneficial as any established alternatives.

The established alternatives to endovenous laser treatment are medical therapy (compression or sclerotherapy), surgical therapy (saphenous vein stripping, saphenofemoral junction ligation) and endoluminal radiofrequency ablation. To date, there are no published studies that randomize patients into these different treatment modalities to directly compare efficacy and safety. The reported rate of recurrence of superficial varicosities following surgery reportedly ranges from 7 - 65 percent (Sarin et al 2002), though well done studies report recurrence as low as 5-15% (Min and Navarro 2000). The reasons for this wide variability include lack of agreement on the definition of recurrence, inadequate length of follow-up, progression of the disease process, inaccurate initial diagnosis and other surgeon related variables (Sarin et al 1992). About 20% of varicose vein operations are for recurrence (Darke 1992). The exact mechanism of recurrence is not clear, though some authorities believe that it is primarily due to neovascularization (Dwerryhouse et al 1999).

TA Criterion 4, continued

In addition to recurrence, the other draw-backs of surgery include potential complications such as paresthesia, bleeding, infection and scarring; risks of anesthesia; longer recovery time and higher costs. The incidence of major complications following vein stripping operations is low (0.8%) but the rate of minor complications is 17% (Rautio et al 2002).

With sclerotherapy, a sclerosing agent is injected into the vein with the goal being to cause endothelial and vein wall damage, resulting in a fibrous cord that is ultimately resorbed (Min and Khilnani 2002). The risk of recurrence following this procedure is estimated at 20-25%. Potential complications include anaphylaxis and intra-arterial injection.

Endoluminal radiofrequency also may be considered an alternative to EVLT, but in most ways they are quite similar. To date, there have been approximately 20,000 radiofrequency procedures done world wide and about 5,000 laser procedures (R. Weiss personal communication). Recent studies with radiofrequency closure of the GSV have shown recurrence rates similar to EVLT of around 10% (Weiss and Weiss 2002). Complications of radiofrequency including paresthesias and skin burns have lessened with the use of tumescent anesthesia.

TA criterion 4 is not met.

TA Criterion 5: The improvement must be attainable outside of the investigational setting.

The published data are not sufficient to conclude that the efficacy and safety of EVLT have been established under conditions of usual medical practice.

TA criterion 5 is not met.



RECOMMENDATIONS OF OTHERS

Blue Cross Blue Shield Association (BCBSA)

The Blue Cross Blue Shield Association reviewed this topic in March 2002 and concluded that: "Laser ablation of the saphenous vein is considered investigational as an alternative to saphenous vein ligation and stripping."

Centers for Medicare and Medicaid Services (CMS)

CMS does not have a national or local policy specific to this treatment modality. Nationally CMS recognizes the use of lasers for medical purposes. If the laser is approved by the FDA for medical use and the procedure performed with a laser is reasonable and necessary it is considered for coverage at the local level. Coverage is restricted to practitioners with training.

American College of Phlebology

The College provided the following position statement and representation at the meeting.

Position statement from the American College of Phlebology on Endovenous Laser for Treatment of Varicose Veins

The American College of Phlebology does not endorse or seek to promote any particular diagnostic or treatment procedure. The mission of the ACP is to improve the standards of practice and patient care related to venous disorders. The ACP sponsors international congresses, regional symposia, fellowship grants; research awards, maintains an online phlebology primer and supports the publication of phlebology papers in Dermatologic Surgery.

A chapter on endovenous laser treatment will soon be added to the ACP online phlebology primer. Educational sessions on endovenous laser have been included in the annual congress of the ACP for the last several years and will be presented at the upcoming World Congress meeting this coming August in San Diego.

Studies available and in press suggest that Radiofrequency Ablation and Endovenous Laser Treatment of the incompetent greater saphenous vein yield similar levels of efficacy and risk. We do not believe there is evidence that would support the California Technology Forum to distinguish between these two treatment modalities.



RECOMMENDATIONS OF OTHERS, continued

American College of Surgeons and Southern California Chapter

The College chapter does not provide position/opinion statements and was not able to provide representation at the meeting.

The Society for Interventional Radiology

The Society indicated that they are supportive of the use of this technology. A representative was not able to attend the meeting.

The American Society for Dermatologic Surgery

The Society representative was unable to attend the meeting.

California Dermatology Society & Dermatologic Surgery

The Society has been asked to provide a position statement or opinion and to provide representation at the meeting.

CONCLUSION

Endovenous laser treatment appears to be a promising non-invasive treatment for lower extremity varicose veins. In uncontrolled case series, recurrence rates have been quite low, comparable to that seen for radiofrequency, and generally better than that reported for surgery. In studies to date, recurrence has been documented with the use of duplex ultrasound which may demonstrate flow in a vein that is clinically undetectable. Endovenous laser treatment has several potential advantages over existing technologies. The small diameter flexible fiber used permits treatment of a wider range of veins and the shallow depth of penetration of laser energy and faster withdrawal time results in less damage to the vessel wall and surrounding tissue. Patients with pacemakers are excluded from treatment with radiofrequency.

However, these potential advantages of EVLT have not yet been shown in prospective, randomized controlled studies. Since non-randomized series may tend to overstate the efficacy of a new procedure, there is a need for well designed studies that compare EVLT to existing treatments of varicose veins before it can be endorsed for widespread use.

TA criteria 2-5 are not met.



RECOMMENDATION

It is recommended that EVLT for the treatment of varicose veins does not meet California Technology Assessment Forum criteria.

The California Technology Assessment Forum voted to accept the recommendation as stated.

June 11, 2003



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