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REVIEW ARTICLE

Richard P. Cambria, MD, Section Editor

Recurrence of varicose veins after endovenous ablation of the great saphenous vein in randomized trials

Thomas F. O'Donnell, MD,[a] Ethan M. Balk, MD, MPH,[b] Meghan Dermody, MD, MS,[a] Erica Tangney, BA,[a] and Mark D. Iafrati, MD,[a] *Boston, Mass*

Background: **Recurrence of varicose veins after surgery (REVAS) for saphenous incompetence has been well described after ligation and stripping (L&S) but not after the now most frequently performed method of saphenous ablation, endovenous ablation (EVA). The purpose of this study was to define the overall incidence of REVAS as well as both the sites of reflux and the causes of REVAS through a systematic review and meta-analysis of randomized controlled trials (RCTs) for EVA. These studies have the advantage of prospectively collected data and a uniform duplex follow-up.**

Methods: **We searched databases (January 1, 2000 through July 1, 2014) for published RCTs evaluating EVA treatment of great saphenous vein (GSV) incompetence that employed endovenous laser ablation or radiofrequency ablation. RCTs were eliminated that (1) did not have follow-up of at least 2 years, (2) did not obtain postoperative duplex scans, (3) did not clearly report the incidence of recurrent varicosities after GSV ablation, and (4) treated the small saphenous or anterior accessory saphenous veins.**

Results: **Of the 68 studies screened, 20 RCTs that employed EVA of the GSV were identified. Eight had a follow-up of at least 2 years, but one was eliminated because of lack of information on both the site and cause of REVAS. The resultant seven RCTs provided eight comparisons (one study compared both types of EVA to a comparator arm): three used radiofrequency ablation, and five employed endovenous laser ablation. Overall recurrent varicose veins developed in 125 limbs after EVA (22%), with no difference in the incidence vs the L&S group (22%) based on the number of limbs available at the time of the development of recurrence for both groups, but this incidence is dependent on the length of follow-up after the initial treatment. The two studies with serial follow-up showed an approximate doubling of REVAS over time for both EVA and L&S. By contrast, the cause of REVAS was different between the two methods. Neovascularization occurred in only two limbs (2%) after EVA vs 18 (18%) in the L&S group. Recanalization was the most common cause of REVAS for EVA (32%; 40 of 125 limbs), followed by the development of anterior accessory saphenous vein incompetence (19%; 23 of 125 limbs). In contrast to other reports, incompetent calf perforating veins were an infrequent cause of REVAS (7%; eight of 125).**

Conclusions: **There is no difference in the incidence of REVAS for EVA vs L&S, but the causes of REVAS are different with L&S, which has important implications for treatment. (J Vasc Surg: Venous and Lym Dis 2016;4:97-105.)**

Symptomatic varicose veins (VVs) negatively affect a patient's quality of life, but this altered quality of life can be improved by intervention on the axial reflux and tributary varicosities.[1] Thermal endovenous ablation (EVA) of the great saphenous vein (GSV) or small saphenous vein by laser (EVLA) or radiofrequency (RFA) has progressively become the principal therapy for VVs in the United States. EVA has increased in volume 450-fold to 300,000 procedures during the last decade.[2] Both the Society for Vascular Surgery/American Venous Forum guidelines for venous disease[3] and the National Institute for Health and Care Excellence guidelines for VVs of the leg[4] have recommended EVA as the first line of therapy for symptomatic VVs.

Durability is an important long-term characteristic of any vascular procedure, so that recurrence of VVs is a key outcome measure for any procedure to treat VVs. Recurrence of VVs with ligation and stripping (L&S) of the GSV has been well described, ranging from 20% to 80%. Its incidence increases with the length of time after the procedure.[5-7] Like the definition of chronic venous insufficiency before the Clinical, Etiologic, Anatomic, and Pathophysiologic (CEAP) classification, the classification of recurrent VVs after surgery (REVAS) lacked a consistent reporting standard. Perrin, however, led a consensus conference that provided standard definitions and a classification system for REVAS: "the existence of varicose veins in a lower limb

From the CardioVascular Center[a] and the Institute for Clinical Research and Health Policy Studies,[b] Tufts Medical Center.

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Correspondence: Thomas F. O'Donnell, MD, Tufts Medical Center, 800 Washington St, Boston, MA 02111 (e-mail: todonnell@tuftsmedicalcenter.org).

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previously operated on for varicosities, with or without adjuvant therapies."[8] REVAS was further subdivided into *anatomic recurrence*, frequently asymptomatic and defined by duplex ultrasound, and *clinical*, symptomatic REVAS. Finally, REVAS was classified by site, cause (source), and anatomy. As opposed to numerous studies of REVAS after L&S, there are few studies that specifically focus on REVAS after EVA. Moreover, the difference in techniques between L&S, in which the GSV is removed, usually to the knee, and EVA, in which components of the GSV are thermally denatured to above or preferably just below the knee without an inguinal incision and left in situ, may result in alternative mechanisms of recurrence. For L&S, neovascularization assumes importance, whereas for EVA, recanalization of the GSV could be a major source of recurrent axial reflux.[9]

An older systematic review and meta-analysis of EVA, which in part reported on recurrence, was based on (1) a mixture of observational case series and randomized controlled trials (RCTs), (2) many studies with short follow-up periods (1 year or less), and (3) series published up to 2007.[10] This review showed a 20% better anatomic success rate for EVLA (95%) for REVAS over RFA (76%). No details of additional causes of recurrence other than GSV recanalization were presented. A recent retrospective cohort review of 164 patients with REVAS after EVA, the Recurrent Veins After Thermal Ablation (REVATA) study, with a median follow-up of 3 years, demonstrated that recanalization of the GSV occurred in 29% of limbs, but "perforator pathology" was found in 64%.[11] The calculation of the "true" overall REVAS rate, however, was hampered by a lack of the actual number of original limbs at risk after EVA, no minimum length of follow-up, no differentiation of the types of RFA devices (first generation vs second), and no direct prospective comparison to L&S. Therefore, we conducted a review of EVA RCTs with a minimum of 2 years of follow-up to determine the incidence, the anatomic sites, and the various causes of REVAS. These RCTs have the benefits of standardized and prospective data collection and duplex ultrasound examinations, specified adjunctive procedures, and direct comparison to L&S or an alternative form of stripping, such as cryostripping.

METHODS

As described in the methods of a previous publication,[12] we searched MEDLINE, EMBASE, Cochrane, and Clinical Trials Registry databases (January 1, 2000 through July 1, 2014) for published RCTs evaluating EVA treatment of GSV incompetence that employed EVLA or RFA (using either the Closure PLUS catheter [VNUS, San Jose, Calif] or the ClosureFast catheter [Covidien, Mansfield, Mass]). We combined search terms for saphenous vein, varicose vein, laser, radiofrequency, endovenous, ligation and stripping, and recurrent varicose veins. We also manually searched the following journals: *Journal of Vascular Surgery, European Journal of Vascular and Endovascular Surgery, Phlebology,* and *Dermatologic Surgery.* We included only peer-reviewed, published RCTs that compared EVLA with RFA, L&S, or cryoablation for treatment of GSV incompetence. Because this review was focused on EVA, we excluded foam sclerotherapy. Repeated GSV surgery and the addition of a high GSV ligation to an EVA procedure were also reasons for initial exclusion. After examination of the individual studies, we further excluded RCTs that (1) did not have follow-up of at least 2 years, (2) did not obtain postoperative duplex scans, (3) did not clearly report the incidence of recurrent varicosities after GSV ablation, and (4) treated the small saphenous or anterior accessory saphenous veins.

Data extraction and statistical analysis. Each eligible study was extracted by two reviewers (T.F.O., M.D.) and validated by a third (E.M.B.). For each study, the following data were extracted as available: number of patients and limbs treated; patient demographics, including age and sex; disease severity (CEAP classification); details of the procedure; and particularly concomitant or delayed phlebectomies of varicose branch veins and treatment of perforators. In our analysis of the studies, we attempted to follow the REVAS classification system.[8] Recurrence was categorized as duplex-detected reflux—anatomic; clinical; and, where possible, as detected by physician or patient. We based our calculation of incidence on the number of limbs at risk in follow-up at the time of the analysis, not those limbs initially entered into the study. We detailed the specific anatomic sites of reflux as well as the cause of reflux and whether the same site or different sites were involved. Because ablation (EVA) or removal (L&S) of the GSV is the prime goal of abolishing axial reflux, we defined failure to abolish GSV reflux into three types: (1) technical, in which the GSV could not be cannulated for EVA or the stripper malfunctioned for L&S; (2) open, in which the GSV remained open after EVA; and (3) recanalized, in which an initially ablated GSV segment reopened with reflux. Finally, the proportion of patients undergoing treatment for REVAS was detailed. The causes of REVAS, as defined by Perrin,[8] were classified into (1) tactical error: persistence of reflux due to inadequate preoperative evaluation and inappropriate surgery; (2) technical error: persistence of reflux due to inadequate technique; (3) neovascularization: reflux in a previously ligated or ablated saphenofemoral junction, which is associated with thin serpentine veins, usually in the inguinal area; and (4) disease progression: a result of the "natural history" and evolution of the disease.

The incidence of reflux at each site and the cause of REVAS were expressed as a percentage of the total limbs at risk for that characteristic at the time of follow-up. We performed meta-analyses of the overall recurrence, site, and cause of recurrence in each treatment arm. For the percentages of limbs with recurrence after each treatment, we used random-effects model meta-analyses of the arcsine transformed proportions.[13] The summary percentages were compared across interventions by meta-regression for statistical significance.[14] Our data are organized by RFA catheter type (RFA with Closure PLUS [RFA-CP] vs RFA with ClosureFast [RFA-CF]) vs EVLA vs L&S in an attempt to elucidate differences among the various catheters and techniques. Finally, each study was graded by the