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Article

The Management of Stasis Dermatitis and Chronic Venous Insufficiency in Patients Refractory to Conservative Therapies

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Synopsis: Chronic venous insufficiency (CVI) is a common problem in primary care clinics, characterized by poorly functioning veins, leading to edema, skin changes, and even ulceration of the affected limb. Though conservative measures are often helpful, many patients ultimately require further intervention.

Case

A 76-year-old woman with a lengthy smoking history has been managed conservatively over the last year for her lower extremity chronic venous insufficiency (CVI) with only modest symptomatic improvements. Many conservative therapies have been trialed, including compression, elevation, aerobic exercise, aspirin, as well as topical emollients and corticosteroids, all without resolution of her disease. Given her persistent stasis dermatitis and chronic swelling, she expresses an interest in pursuing a surgical intervention for her venous insufficiency but is concerned about complications such as deep vein thrombosis (DVT). The following review will address next steps in management for CVI in a 76-year-old woman with an inadequate response to conservative medical therapy.

Background

Lower extremity venous disease is a common problem in both primary care and specialist practices with wide ranging clinical consequences. In some studies, the prevalence of this disorder has been found to be nearly 50%, though variations exist depending on the population studied (Zahariev et al., 2009). Clinical consequences range from benign cosmetic changes to painful skin breakdown that predisposes patients to a great deal of morbidity from secondary infection, all with a significant impact on a patient's quality of life (Tsai et al., 2005). Fortunately, there have been highly effective treatments developed for the management of this disease. Because the underlying pathogenesis of venous disease is due to incompetent veins that then swell and cause edema and inflammation, the goal of all of the treatments described below is to sclerose the dysfunctional veins and prevent blood from pooling in them.

The patient described above carried a clinical diagnosis at the time of evaluation of CVI, which, according to nomenclature set forth by a 2009 article clarifying the terminology of lower extremity venous disorders, constitutes functional abnormalities of the venous system along with advanced signs and symptoms of disease, including moderate or severe edema, skin changes, or venous ulcers (Eklof et al., 2009). Though the patient lacked lower extremity ulcerations, her skin exam demonstrated evidence of significant stasis dermatitis and edema (Figure 1), while an ultrasound examination showed she had abnormal retrograde flow in her great saphenous Vein (GSV), confirming an anatomical basis to her CVI. Thus, by a widely used scoring criteria known as Clinical-Etiology-Anatomy-Pathophysiology (CEAP) (Table 1) classification, the patient was category C_{4b}-E_p-A_s-P_r (Eklöf et al., 2004). Though there are currently no official guidelines published by vascular societies in the US for the management of CVI, review articles published in *Circulation* in 2005 and in the *New England Journal of Medicine* in 2009 recommend CVI be managed medically initially, using measures such as leg elevation, exercise, and compression therapy along with wound care to keep the overlying skin moisturized (Raju and Neglén 2009; Eberhardt and Raffetto 2005). For patients with an unsatisfactory response or with advanced disease (CEAP 3-6), interventions may be warranted. Our patient had been managed using such therapies for a duration of several months.

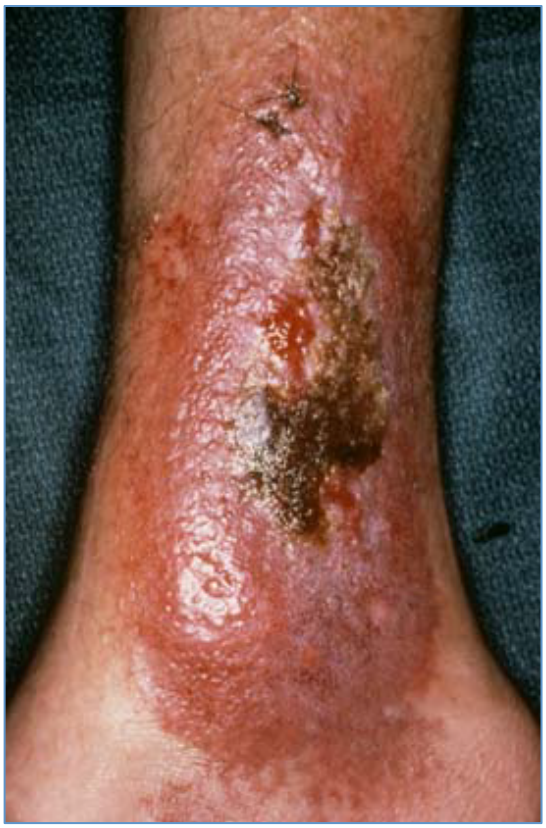

Figure 1. Ulcerated Lower Extremity Lesion

Classic appearance of advanced stasis dermatitis secondary to CVI, leading to central ulceration and necrosis. Note the characteristic presence hyperpigmentation of the overlying skin, ulceration, necrosis, and diffuse edema. Taken from CDC Public Health Image Library, Kraus 1981.

Should a patient be deemed clinically appropriate for intervention following a trial of conservative management, the interventional options are divided broadly into minimally invasive ablative therapy using either chemical (ultrasound-guided foam sclerotherapy [UGFS]), thermal (endovenous laser ablation [EVLA], endovenous steam ablation [EVSA], or radiofrequency ablation [RFA]), or mechanical (vein stripping or ligation). There are also three surgical techniques that aim to occlude perforator veins, repair an iliac vein obstruction, or reconstruct deep valves. However, these three latter surgical therapies are meant for patients in whom either the anatomical disturbance is in the perforator veins, have an obstruction in the iliac vein, or have failed other simpler therapy, respectively (Raju and Neglén 2009). Our patient has not met any of these criteria and thus is primarily a candidate for treatment by one of the four ablative techniques. However, in patients who are healthy enough for surgery and meet these criteria, a surgical approach might have been considered. A recent review article, however, demonstrated that endovenous approaches are at least as effective as surgical ones (Nesbitt et al., 2014).

Table 1. Breakdown of CEAP Classification System

Clinical	
C_0	No clinical signs of disease
C_1	Telangiectasia and reticular veins
C_2	Tortuous varicose veins
C_3	Edema
C_{4A}	Stasis dermatitis
C_{4B}	Lipodermatosclerosis
C_5	Skin changes with past ulceration
C_6	Skin changes with active ulceration
Etiological	
E_C	Congenital
E_P	Primary (most cases)
E_S	Secondary (to thrombosis, trauma)
E_N	Not identified
Anatomic	
A_S	Superficial veins
A_P	Perforator veins
A_D	Deep veins
A_N	Not identified
Pathophysiological	
P_R	Reflux
P_O	Obstruction
$P_{R,O}$	Reflux and obstruction
P_N	Not identified

Each category corresponds to a clinically determined score defining the disease severity, etiology, anatomic location, or underlying cause of the CVI. The goal of treatment is to modify and prevent disease progression through categories. Each limb may be further characterized as symptomatic or asymptomatic. Data from Eklof et al., 2004. Table modified from UpToDate, *Classification of Lower Extremity Chronic Venous Disorders.*

Table 2. Comparison of Percentage of Successful Outcomes at 3 Mo. and 5 Yr. by Ablation Method

	3 Months	**5 Years**
Stripping or ligation	80.4% (72.3%–86.5%)	75.7% (67.9%–82.1%)
UGFS	82.1% (72.5%–88.9%)	73.5% (62.8%–82.1%)
RFA	88.8% (83.6%–92.5%)	79.9% (59.5%–91.5%)
EVLA	92.9% (90.2%–94.8%)	95.4% (79.7%–99.1%)

These results show the highest rate of successful outcomes as assessed by ultrasound are seen with EVLA, both at 3 months and at 5 years. The 95% CI is given in parentheses. UGFS: ultrasound-guided foam sclerotherapy; RFA: radio frequency ablation; EVLA: endovenous laser ablation. Data is extracted from van den Bos et al. (2009).

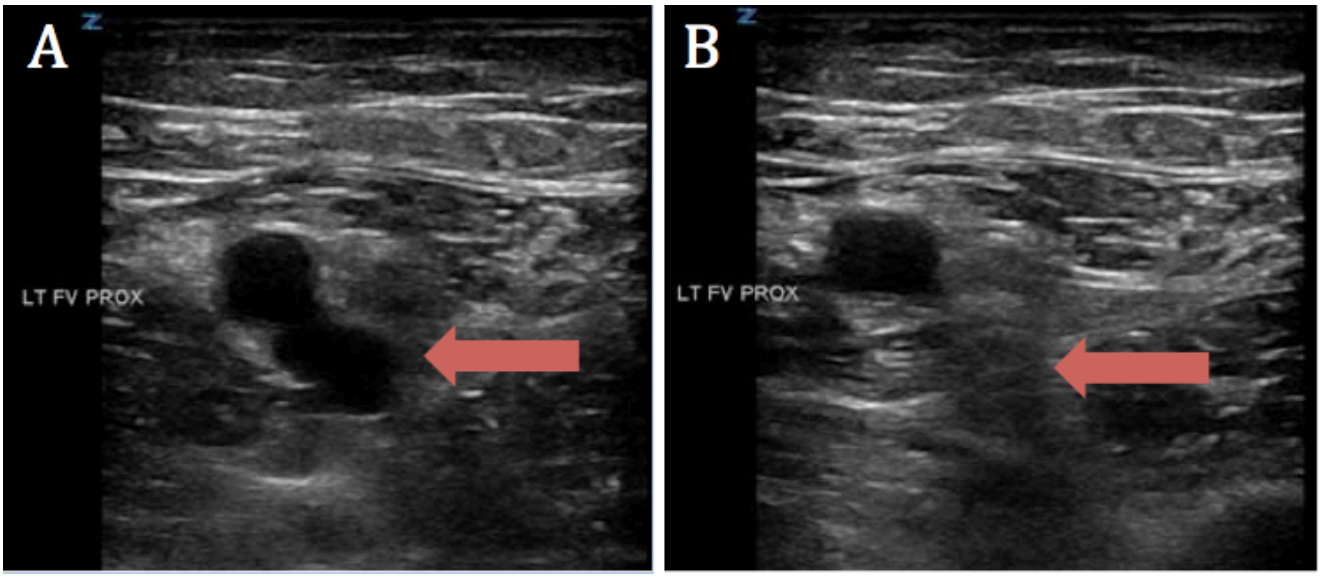

Figure 2. Normal Compressibility of the Popliteal Vein as Assessed by Ultrasound

The image on the left (A) shows the proximal portion of the left femoral artery (superior) and vein (inferior, red arrow), and the image on the right (B) shows the same femoral artery and vein under compression. Because of the relatively low intraluminal pressure in the vein, it is compressible and occluded and therefore disappears from ultrasound. If the vein were found not to be compressible, it would be suggestive of a thrombus within the lumen. When this occurs in the deep veins of an extremity, it is known as a DVT. CVI is not usually caused by DVT.

Review

There are two seminal studies in the literature that seek to compare the efficacy of the ablational methods for which our patient is a candidate. *Endovenous Therapies Of Lower Extremity Varicosities: A Meta-Analysis* was published in 2008 and investigated 119 retrieved studies, of which the authors ultimately included 64 that assessed a total of 12,320 limbs. They included any randomized controlled trial (RCT), clinical trials, or case series of human lower extremity varicosities treated by EVLA, UGFS, RFA, or surgical stripping/ligation and that used post-procedural ultrasound to determine whether the intervention was successful. After a mean follow-up period of 32.2 months, the authors compared the success rates at different time points up to 5 years to assess the percent of successful outcomes (summarized below and in Table 2). It was found that for surgical stripping or ligation was 80.4% successful at 3 months and 75.7% successful at 5 years. The rate of success increased incrementally between UGFS, then RFA, and appears to be highest for EVLA with a 92.9% and 95.4% at 3 months and 5 years, respectively. When the results were compared, the higher success rate of EVLA was statistically significant ($p < 0.05$) (van den Bos et al., 2009).

These results established for the first time in a large study the suggestion that EVLA is superior in achieving a successful outcome as measured by ultrasound compared with other methods. However, while this ameta-analysis successfully summarizes much of the existing evidence and directly compares the different methods, it also has several limitations. The study participants, like our patient, are limited to patients under treatment for venous reflux of either the GSV or SSV. However, our patient is CEAP 4b, and there is no mention of the patient characteristics in this study, particularly with regard to their CEAP score, making it difficult to apply these results to particular patient groups. Further, this study limits its outcome measures to the ultrasound occlusion of the vein (Figure 2). While this is the gold standard in the field for determining a successful intervention, it will not necessarily correlate with improvement in a patient's symptoms. The authors point this out, noting that the correlation with scores such as the Health-Related Quality of Life and complication rates should be considered particularly when multiple interventions are highly effective (such as for instance HVLA and RFA) in distinguishing between them. In addition, when interventions are comparatively effective, cost analysis is also warranted to guide recommendations on a national level.

Fortunately, there is a recently published RCT comparing EVLA, UGFS, and ligation/stripping by Biemans et al., (2013). This study was conducted between 2009 and 2010 in the Netherlands, and it enrolled 240 consecutive patient legs (223 patients) during this study period. The patients had to have ultrasonographic evidence of GSV reflux that was reported to be symptomatic. It randomized these eligible patients to one of the three treatment arms (either EVLA, UGFS, or ligation stripping). Over the course of the 1 year of follow-up in this study, the primary

outcome measure was again the rate of anatomic success on follow-up ultrasound. However, this study was comprehensive in that it also tracked changes in CEAP score, the frequency and nature of complications, and subjective quality of life improvements in patients as secondary outcomes. Primary outcome results showed a high success rate by ultrasound, demonstrating total occlusion in 88.5% of EVLA patients, 88.2% in the stripping/ligation group, and 72.7% of the UGFS group, which was lower than the EVLA and stripping/ligation group ($p < 0.02$) (Biemans et al., 2013). Notably, 10% of the stripping/ligation group demonstrated neovascularization at 1 year, an undesirable consequence that may compromise the long-term success of the procedure. All three groups were found to have significant improvement of their CEAP score; however, none of these changes were statistically significant ($p < 0.05$) between any of the groups. Similarly, while quality-of-life scores improved in all three groups, no statistically significant differences were found between any of the groups. Complication rates were low overall, with 7, 5, and 11 patients experiencing post-operative complications in the EVLA, UGFS, and stripping/ligation groups, respectively (Table 2). The stripping/ligation group specifically had a significantly higher rate of wound infections ($p = 0.03$). Superficial vein thrombosis accounted for 10 of the 23 total complications. Notably, there were no DVTs reported.

EVSA is the newest ablational technique, and the LAST trial (van den Bos et al., 2014) is the only major studying the efficacy of this new therapy. Because of previous findings suggesting the high success rate of EVLA, they compared EVSA only to EVSA by enrolling 227 legs and observing them for 1 year. Primary outcomes were vein ablation at 1 year and a validated measured of CVI severity (venous clinical severity score [VCSS]). Secondary outcomes were pain, satisfaction, duration of analgesia use, complication rates, and others. From an efficacy standpoint, EVSA was shown to be non-inferior to EVLA, and many of the secondary outcomes were in favor of EVSA (though notably, complication rates were comparable) (van den Bos et al., 2014), though this is the highest quality evidence currently available, there are again several potential limitations in using the data to recommend EVLA or EVSA to patients. In the Biemans et al., (2013) trial, EVLA patients are significantly younger than either the UGFS or stripping/ligation, which may falsely introduce healthier patients into this cohort. Another major shortcoming of both studies is that there is only 1 year of follow-up, which is significant considering that previous studies have suggested the surgical techniques do not have equivalent long-term success rates. The studies also have only a small number of total complications, which may suggest it is not powered to detect differences between the rate of complications between these methods. This is important given the theoretical risk of very clinically important complications such as DVT. Finally, despite the promise of EVSA, it is a new technique that has not been studied in the long-term, and not all clinicians may be comfortable adopting it immediately.

Complication Rates

Given the above studies, it would seem EVLA or EVSA is a suitable option for patients, given its high success rate and improvement in CEAP and quality of life scores, which are at least comparable to stripping/ligation and UGFS. However, the question of the risk of complications in these patients, specifically DVT, remains largely unanswered. For this, there are several studies devoted to this question. First, a Mayo Clinic study enrolled 130 limbs in 92 patients in a non-randomized protocol. Of the 130 limbs, 124 were CEAP 2–4. DVT was assessed for in 70% of the EVLA group by ultrasound, with the finding of three thrombi (2.4% of cohort) in the common femoral vein (CFV), one requiring IVC filter placement, all of which were treated with heparin and were without further complication such as extension of the clot or pulmonary embolus (Puggioni et al., 2005). There was no significant difference between the overall rate of complications between EVLA and RFA in this study. In another larger retrospective study published this year comparing RFA and EVLA, both EVLA and RFA again demonstrated low (<1%) rates of DVT and no significant differences in the rate of complications between the two therapies (Marsh et al., 2010). One case of pulmonary embolus was reported in the RFA group. In addition, two new studies from UC Davis and Rush Medical Center suggested that age >66, female gender, and tobacco use were all associated with increased post-procedure DVT risk, perhaps suggesting some patient's risk is higher than even those in the earlier cited studies (Chi and Woods, 2013; Jacobs et al., 2013).

Conclusions

In consulting the literature in search of a therapeutic recommendation for CVI, it is apparent the treatment options are rapidly evolving as new technologies emerge. The first RCT comparing the new minimally invasive techniques gave preliminary evidence that EVLA and EVSA have among the highest rates of success in terms of correcting the underlying anatomical abnormalities of CVI while maintaining at least equivalent rates of subjective improvement with other therapies. In preliminary studies, EVSA has had a high success rate while simultaneously decreasing pain and analgesic use and improving patient satisfaction. These findings should be interpreted with caution until they have been duplicated in larger patient cohorts over more extended periods of time, and this research is of particular importance moving forward. Additional studies cited above have demonstrated a low rate of complications and

DVTs in EVLA patients, with the caveat that the study populations in the available literature may not reflect a given patient's comorbidities, CEAP score, or age.

Besides ablational therapies, the other alternative for patients to consider is ongoing medical management, in consideration of the fact that even a low risk of complications may not be acceptable in an otherwise frail patient for whom a DVT leading to a pulmonary embolus could be fatal. Conversely, equally threatening are the complications and debilitating symptoms from further progression of her CVI that include ulceration and secondary infection, or immobilization leading to DVT. Perhaps the next area of endeavor in CVI will be in preventing the venous anomalies from developing years prior to the onset of symptomatic CVI.

The management of CVI patients was previously challenging given the lack of data or therapeutic options. However, for patients who have had an insufficient response to medical therapy and/or clinically severe disease, there are now several interventional options available. Following a thorough review of this data, the patient described earlier was referred for consultation with a vascular surgeon, who concurred with the findings above and recommended EVLA as the best therapeutic option and one with among the lowest risk profile, which was deemed clinically acceptable in our patient. Therefore, this patient underwent an uncomplicated EVLA procedure and has since seen significant clinical and symptomatic improvement in her lower extremity venous disease as a result.

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