Phlebolymphology

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Editorial

Dear Readers,

In this new issue of Phlebolymphology, *you will find the articles as below:*

Chronic venous disease is multifactorial. **A. RAIKER** *and* **N. LABROPOULOS (USA)** *examine in depth some of the most important factors that impede venous return and explain their dynamics and association within the spectrum of chronic venous disease.*

In treatment of varicose veins, risk of recurrence has always been known and can have several origins. Currently, the most widely accepted cause is recurrence attributed to the anterior accessory saphenous vein. However, the anatomy of this vein varies greatly. **A. S. LENSEL** *and* **J. L. GERARD (FRANCE)** *discuss the pertinence of a preventive treatment for an accessory anterior vein when that vein is competent and when it's practically feasible.*

M. ENGIN (TURKEY) *presents the clinical results of various treatments, including sclerotherapy, laser therapy, thermocoagulation, and microphlebectomy for telangiectasias, which make up a heterogeneous group of diseases that can affect various parts of the body in humans.*

May-Thurner syndrome, known for decades as a unique pathology, has recently been included with other pelvic compression maladies in the S-V-P CEAP classification (symptoms-varices-pathophysiology, clinical-etiology-anatomy-pathophysiology)—sponsored by the American Venous and Lymphatic Society—as part of several anatomic lesions in the abdominopelvic region having variable clinical presentations. **R. ARMENTA-FLORES (MEXICO)** *provides an overview of the diagnosis and management of May-Thurner syndrome.*

Although both endovenous laser ablation (EVLA) and radiofrequency ablation (RFA) follow the principle of thermal ablation for varicose veins, there are fundamental differences in the mechanism of ablation, device used, procedure, outcomes, and complications. **S. DAHAL, R. M. KARMACHARYA,** *and* **colleagues (NEPAL)** *discuss the principles and differences between EVLA and RFA techniques for the treatment of varicose veins.*

Lastly, iliac vein stenosis is a commonly present lesion in the general population and remains silent in the majority of individuals. **S. RAJU (USA)** *provides an up-to-date review of investigations regarding identification and treatment of iliac venous stenosis.*

Enjoy reading this issue!
Editorial Manager
Dr. H. Pelin Yaltirik

Factors impeding venous return and their impact on the management of chronic venous disease

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Abstract

Chronic venous disease is multifactorial. Although the main pathology of chronic venous disease is reflux and obstruction, several other factors play a role as well. These include the duration, distribution, and extent of disease, but also additional factors such as obesity, and musculoskeletal and heart failure. This is especially important for those with advanced disease, as these factors that impede venous return may be more common. In fact, there are reports where people do not have evidence of venous disease but still experience "venous-like" symptoms. This paper examines in depth some of the most important factors that impede venous return and explains their dynamic and association within the spectrum of chronic venous disease. Other than recognizing such factors, it is critical to consider that despite appropriately treating reflux and obstruction, patient symptoms may not improve due to the continued presence of these contributing factors. This knowledge further sets the stage for modifying patient conversations. It is important to appropriately discuss expectations with patients for the predicted improvement of their disease. Lowering expectations when several comorbid factors are identified and focusing on the correctable ones such as diet and exercise will all go a long way in patient well-being and recovery.

Keywords:

chronic venous disease, heart failure, lymphedema, muscle pump function, obesity, venous return

Introduction

Chronic venous disease is a complex condition with multiple contributing factors. The effective diagnosis and treatment of this condition relies upon a systematic consideration of each and every one of them. The pathophysiology of the impediment of venous return is primarily obstruction and reflux related. Whereas these remain the primary culprits, there exist additional risk factors. It is necessary to account for them when treating patients with chronic venous disease, as they could be contributing factors exacerbating the patient's condition. On the other hand, at times, they could even be the major etiology for the patient's signs and symptoms, leaving obstruction and reflux as innocent bystanders.

The first step involves an assessment of the symptoms presented by the patient.[1] The symptoms paint a picture. The frequency, position, duration, onset, and transforming

factors all need to be rigorously considered to evaluate their potential contributions to a chronic venous disease diagnosis.[1] This is especially true of chronic venous disease, since its symptoms have a low specificity.[1] Some of these include edema, muscle pain, tingling, varicose veins, and skin alterations.[2] They could have considerable overlap with other etiologies such as tendonitis, peripheral neuropathy, arterial pathologies, etc.[2] For example, edema could also be attributed to heart failure, or swollen legs with drug interactions.[1] A study evaluating the occurrence of "venous symptoms" in patients with venous disease versus other pathologies found the difference to be minimal.[3] Thus, whereas the symptoms of chronic venous disease alone are not sufficient to confirm chronic venous disease, they must be appropriately evaluated.[1]

Factors affecting venous return

Overall, the factors affecting venous return can be studied under 2 wings: vascular and other. The vascular etiologies include reflux, obstruction, vascular malformations, vein wall compliance, and lymphedema. Obstruction and reflux are typically accounted for in the diagnosis and treatment and are the major pathophysiology factors in the widely used CEAP classification system (Clinical-Etiology-Anatomy-Pathophysiology).[2] In a study evaluating the emergence of postthrombotic syndrome in patients with a prior deep venous thrombosis (DVT), obstruction and reflux together increased postthrombotic syndrome by a 3.5 times odds ratio.[4] Whereas these factors remain critical, it is essential to draw attention to the others that may play a role in the story as well.

Obesity
Obesity is one such player. It has been a rising epidemic in the United States with a 41.9% prevalence in 2017-2020.[5] With a definition of obesity as body mass index (BMI) $\geq$30 kg/m^2, it is projected that by 2030, about 50% of the population will be obese.[6] Obesity is not only a health crisis, but an economic predicament. This increase from 2010 levels will account for an additional $549.5 billion in medical expenses.[7] Obesity manifests as an inflammatory state and is a key contributor to the metabolic syndrome, one that can result in major pathologies from diabetes to cancer.[8] It is not surprising that it plays a role in chronic venous insufficiency as well.

Chronic venous disease patients who are also obese fall into a higher CEAP class than those who are not obese.[9] This correlation between obesity and chronic venous disease (CEAP C parameter) is independent of sex and age and stays true on accounting for metabolic-syndrome–related pathologies such as hypertension.[10] Obese patients also have

higher occurrences of varicose veins and venous leg ulcers.[9] Furthermore, in a study of morbidly obese patients with chronic-venous-insufficiency–like symptoms (BMI$\geq$40 kg/m^2) where obesity was associated with a higher CEAP class and increase in venous clinical severity score, two-thirds of legs lacked a venous pathology, suggesting obesity could even be an independent contributing factor to the symptoms.[11] Evidence has been growing on the pathophysiology of its contribution. Obesity has been linked to higher intra-abdominal pressures.[12] This creates a functional obstruction and environment for an alteration in venous physiology. For example, it has been found to heighten venous reflux, as quantified by venous filling index and venous filling time.[9] It has also been found to result in higher femoral vein diameters and vein pressures than in the nonobese.[9] Notably, this is seen across the postures sitting, standing, and laying down.[9] The increased femoral vein diameter is complemented by a decreased femoral vein velocity.[13] Ultimately, venous physiology alterations cause venous hypertension that can result in an inflammatory cycle, edema, and skin damage, which are the typical signs and symptoms observed.[14]

Its contributions are best illustrated through a case study (*Figure 1*). A 63-year-old female presented with bilateral lower extremity edema (C2-3). A superficial vein reflux on the left lower limb was identified via ultrasound. However, this alone could not explain the severity and extent of bilateral symptoms. She had bilateral pain, heaviness, itching, and edema, of equal intensity on both sides. The answer to her clinical presentation lay in her BMI: height, 162 cm; weight, 122 kg; BMI, 46.5.

Muscle pump function
Another player that cannot be discounted is musculoskeletal in nature: muscle pump ability. Interestingly, in obese patients, the calf muscle was found to be more effective with a higher ejection fraction and ejection volume.[9] This contradiction can be resolved when placed in its physiological context. In obese patients, there is also a drop in the amount of physical movement.[9] This would decrease its utilization, making it unable to make up for the higher reflux levels observed in obese patients.[9]

Lymphedema
Returning to vascular-related factors, lymphedema is also one that must be explored. It was believed that the venous capillaries and venules were responsible for the majority of interstitial fluid returning to the vasculature, but it is now better appreciated that lymphatics play a much bigger role.[15,16] This can be fundamentally understood through the
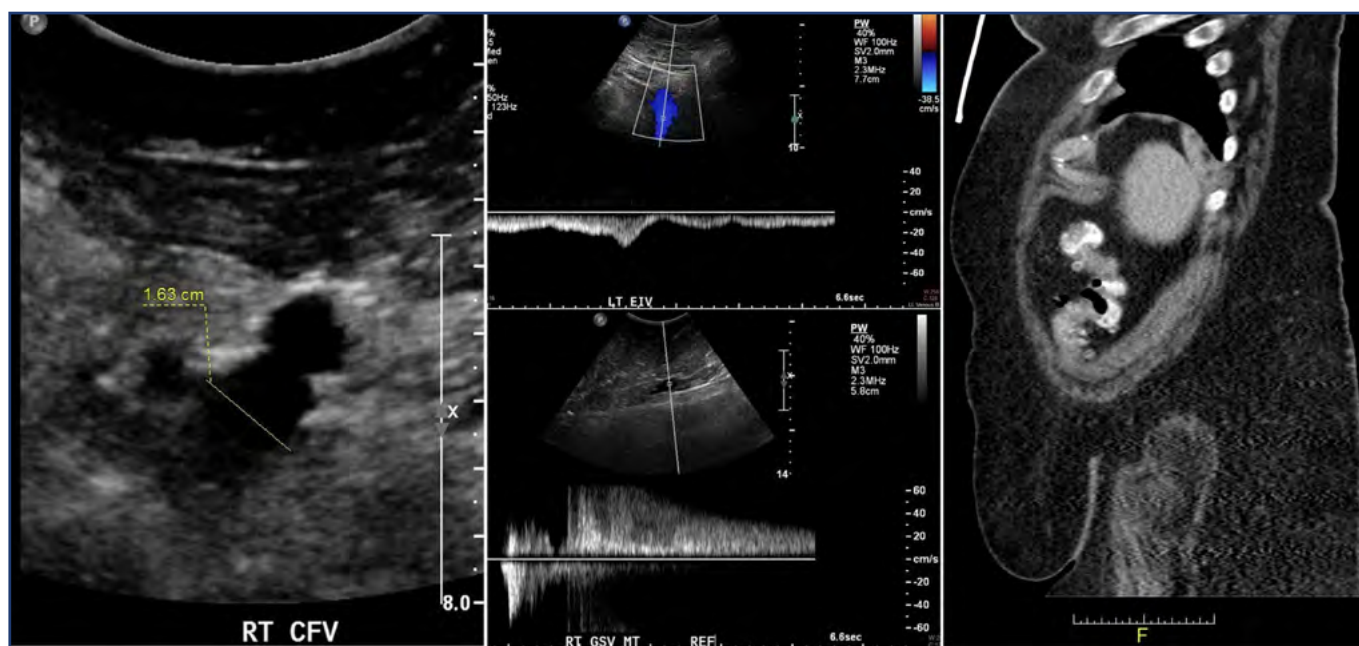
Figure 1. Case study of the contribution of obesity to chronic venous disease with bilateral signs and symptoms. A 63-year-old female patient presented with bilateral lower limb symptoms of equal intensity. Ultrasound evaluation demonstrated a dilated right common femoral vein (left), phasic flow in the left external iliac vein (middle top), and prolonged high velocity reflux in the right great saphenous vein (middle bottom). Computed tomography (CT) scan illustrating the patient's morbid obesity (right).

revised Starling pressure principle, which actually points to a small filtration at the venous end.[15,16] This shifts the burden of responsibility for chronic edema as it can occur when filtration is greater than lymphatic coverage as a result of increased filtration, decreased lymphatic coverage, or an amalgam of the two.[16] Thus, in a diagnosis of chronic venous disease, it is important to make the distinction between venous etiology or lymphatic attributions or an amalgam of the two for the signs and symptoms seen. Obesity and lymphedema can act synergistically as well. Recent evidence has accumulated linking lymphatic damage to increased adipose buildup and expression of adipocyte-related markers, and conversely, obesity with altered lymphatic drainage and less absorption of interstitial fluid.[17]

Anatomical factors

Next, we move our attention to anatomical dispositions and look at the contributions of static foot disorders. Whereas these disorders have a prevalence of about 8% to 26% in the general population, they were found in 31% of limbs in a group of patients with chronic venous disease, warranting an exploration of the role they play.[18] These disorders can be described by the Dijan-Annonier angle, the angle created by the medial sesamoid, talus navicular joint, and calcaneus bones.[18] Normally, as we walk, the foot acts as a pump, directing the blood from the distal veins of the foot to more proximal veins.[18] However, in a static foot disorder, the angle

with which the foot touches the ground deviates either in the flat foot or hollow foot direction, and this negatively affects venous return.[18] On evaluating the odds ratios for chronic venous insufficiency, the hollow foot yielded 4.2, whereas a flat foot yielded a 3.1.[18] Not only did this study correlate static foot disorders to chronic venous disease, but also intertwined other critical risk factors such as obesity and the impact of position. Obese patients (BMI>30) were found to disproportionately have hollow feet, potentially increasing their risk for chronic venous disease.[18] Position also had an impact, with standing being significantly correlated to hollow feet.[18] Thus, factors such as the morphology of the foot and position must also be accounted for in the assessment of chronic venous disease.

Dynamic factors

Complementing the anatomical factors are dynamic ones. The ankle's range of movement and calf muscle ability have both been linked to chronic venous disease as well.[19] Range of movement was quantified in terms of dorsiflexion and plantarflexion, and calf muscle efficiency by the ejection fraction and residual volume fraction.[19] Both were more impaired in chronic venous insufficiency patient groups with ulcerations than in the group with normal limbs.[19] The limited-range-of-motion factor itself was also associated with the presence of impaired calf muscles.[19] A potential mechanism suggested has been that venous disease, complicated by risk factors affecting ankle movement such as trauma, arthritis,

or physical inactivity, could limit the range of motion and subsequently impact activation of calf muscles.[19] Ultimately, this would explain the ulcerations associated with these 2 factors.[19]

This is further illustrated with the case of a 61-year-old female presenting with bilateral venous disease (*Figure 2*). Her right extremity had a mild ache and itching, whereas her left experienced more pain, swelling, and heaviness, as well as discoloration of her skin. She was a mother of 3 with a

maternal history of varicose veins. Her BMI was 26.4, with no prior venous treatment or procedures. Her chronic venous disease dated >20 years on the right and about 10 years on the left. On comparing her right vs left ultrasound findings further, from distal to proximal, her right vein diameters were 3.2 mm to 8.4 mm with a reflux duration of 2.2 seconds to 4.7 seconds. Her left vein diameters were 3.3 mm to 4.9 mm with a reflux duration of 1.3 seconds to 2.7 seconds. However, despite the right leg presenting a worse venous pathology, her left limb experienced more severe signs and symptoms. The key to explaining her presentation was that she had restricted motion on her left limb due to degenerative knee disease. It had affected her muscle pump functioning and explained the discrepancy in venous pathology versus symptom severity.

Congestive heart failure

Finally, the venous implications of congestive heart failure will be considered. The phenomena occurring in the heart can be reflected in the veins. Pulsations in the basilic veins have been identified as an indicator of congestive heart failure and tricuspid regurgitation, with their intensity correlating with the disease progression.[20] An account reported pulsation of varicose veins in both limbs for a man with both tricuspid regurgitation and heart failure.[21] In that case, it was successfully treated with digitalis and diuretics.[21] Thus, heart failure can also be a contributing factor for venous pathology, beyond valvular incompetence or obstruction. In treating venous-related symptoms in patients with heart failure, it is important to optimize treatment of heart failure first. Other systemic diseases such as renal failure, retroperitoneal fibrosis, or intestinal malabsorption should also be accounted for.

Figure 2. Case study of the contribution of musculoskeletal factors to chronic venous disease. Schematic representation of the venous reflux pattern of a 61-year-old female, including venous diameter and CEAP classification in both lower limbs. Venous disease was more pronounced on the right limb; however, the left limb was more symptomatic. This can be attributed to the knee issues on the left side.

Figure 3. Case study of heart failure contributing to pulsatile vein flow and advanced chronic venous disease. A 65-year-old male patient presented with bilateral skin damage. Ultrasound evaluation in the standing position demonstrated pulsatile flow in the lower extremity veins as shown in left common femoral (left) and right great saphenous vein (right).

This was seen in the case of a 65-year-old male patient who presented with bilateral lower extremity edema and skin discoloration (C2-4) (*Figure 3*). He was found to have pulsatile flow bilaterally in the deep and superficial veins, even in the standing position. Superficial and deep vein reflux were absent, and thus could not account for the severity and extent of his signs and symptoms. However, he was found to have a long-standing history of right heart failure. This was an illustrative instance of the importance of systematically considering other etiologies in accounting for "venous" symptoms.

There have been cases as well where these factors act in concert. Thus, a global evaluation is all the more important. A patient with a BMI of 35 for 20 years had a history of chronic heart failure, infections (cellulitis), and a lack of physical activity. The combination of his heart failure and obesity could be the key to understanding his venous progression, beyond venous pathologies alone.

Conclusion

The effective management of chronic venous disease requires seeing the patient as an entity and not a disease. Whereas reflux and obstruction may remain the most common contributors to chronic venous disease, they are by far not the only ones. Other systemic factors from vascular lymphatic functioning to obesity, and physical activity, musculoskeletal pumps, pedal morphology, and heart failure, all may play critical roles in accounting for the clinical presentation. They may coexist with obstruction and reflux and simply accentuate conditions or be the driving factors for the progression of chronic venous disease. Careful consideration of these factors in a synergistic fashion for each patient will allow for the best treatment. Further work is needed in exploring how these factors act in combination with one another, and better metrics are needed to track their management. Finally, the impact of emphasizing well-being from diet to exercise and setting appropriate expectations should not be discounted in patient healing and recovery.
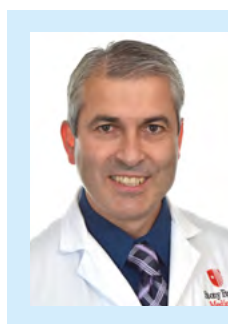
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Is it essential to treat the AASV during thermal ablation of the GSV?

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Abstract

Recent decades have experienced the substantial development of endovenous techniques to treat varicose veins. Such techniques are guided by ultrasound through use of increasingly efficient equipment, and operators have become better trained. This, in parallel with the study of cadaver dissections, has led to a marked improvement in the knowledge of vein anatomy in the lower limbs. The treatment of varicose veins has always been known for its risk of recurrence, which can have several origins. The most widely accepted cause right now is recurrence attributed to the anterior accessory saphenous vein. But the anatomy of this vein, when it's present, varies greatly from one patient to another, even from one limb to another. Apart from open surgery, phlebologists and vascular surgeons use different treatments for varicose veins. These mainly include endovenous thermal ablation (EVTA, by laser or radiofrequency), sclerotherapy (liquid or foam), and cyanoacrylate closure. All those procedures are ultrasound guided. The goal of this article is to discuss the pertinence of a preventive treatment for an accessory anterior vein when that vein is competent and when it's practically feasible.

Introduction

The role of the anterior accessory saphenous vein (AASV) in recurrence of varicose veins after treatment of the great saphenous vein (GSV) seems to persist, even if recurrence is decreasing with mostly using minimally invasive endovenous ablation techniques—endovenous laser ablation (EVLA) or radiofrequency ablation—instead of surgical treatment (recurrence rates reported vary, eg, 43%[1] to 8%-35%[2-4]).

Formerly, surgical ligations of the saphenofemoral junction (SFJ) were often used to treat the AASV even when it was competent. Nowadays, preoperative duplex scanning allows better visualization of the SFJ, and the minimally invasive endovenous ablation techniques are precise and done under ultrasonographic control. Phlebologists and vascular surgeons are often keen to protect the functional portions of the SFJ when possible.

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In 2019, Marianne De Maeseneer, in an article in *Phlebolymphology* entitled "What a phlebologist should know about the anterior accessory saphenous vein,"[5] concluded that the AASV is "the eternal culprit" in varicose veins after surgery and endovenous ablation.

The cause of those recurrences might be the persisting incompetence of the SFJ after EVTA.[5]

In 2020, Baccellieri and colleagues, in *International Angiology*,[6] reported on the variable AASV anatomy at the SFJ as a possible risk factor for recurrent varicose veins after GSV radiofrequency thermal ablation. Their results showed that direct confluence of the AASV at the SFJ was a negative predictor of a recurrent varicose vein after 1 year and suggested that SFJ morphology could influence their formation; in particular, the authors suggested that concomitant incompetence of the AASV or direct confluence of the AASV at the SFJ could be an indication for simultaneous treatment by nonsurgical techniques (FTA or laser), while avoiding surgical ligation.

According to Garcia-Gimeno and colleagues,[7] the SFJ of the GSV is involved in 65% of all varicose vein disease and the isolated AASV is responsible for 10.9%.

Whiteley and colleagues, in 2008,[8] described in a retrospective review of a 2-year period including 1686 local anesthesia procedures that 29% of those undergoing thermoablation of the GSV also required treatment of the AASV, suspected to be due to an incompetence of the AASV (incompetence defined as a reflux greater than 0.5 seconds on an erect patient after manual calf compression, with the AASV inducing a "sump effect" [siphon effect] when enlarged with no reflux found).

In December 2021, an article published in *Phlebology* entitled "A systematic review and meta-analysis of treatment modalities for [AASV]" reported on an analysis of 860 articles. The authors concluded that it is "safe and effective" to treat AASV incompetence and suggested use of thermal ablation or cyanoacrylate, and maybe phlebectomy when the SJF is competent.[9]

Everyone seems to agree that treatment of the AASV is pertinent when incompetent. It causes similar disease severity and morbidity to that caused by the incompetence of the GSV.[10]

Following a promising case series published in 2021 entitled "Feasibility and potential significance of prophylactic ablation of the major ascending tributaries in EVLA of the great saphenous vein: a case series,"[11] there is a multicentered, prospective, controlled German study[12] including 1150 patients currently comparing the benefit on varicose recurrency afforded by preventive ablation of a competent AASV at the same time as the ablation of the incompetent GSV. For a 5-year follow-up, 2 groups—with and without AASV preventive ablation—will be compared with regard to rate of varicose recurrence and main complications.

However, the AASV is present in only 41% of people and responsible for varicose vein disease in less than 11%.[7] Is this culpability in varicose vein recurrence a good enough reason to treat every AASV, even when competent?

Anatomy of the saphenofemoral junction

The anatomical nomenclature published by Caggiati and colleagues in the *Journal of Vascular Surgery* in 2005 stated that the AASV "at the upper thigh courses deeply (superficial to the muscular fascia, like the GSV) to a hyperechoic fascia that resembles the GSV covering. However, the [AASV] can be easily identified, because it courses more anteriorly with respect to the GSV, with a path corresponding to that of the underlying femoral artery and veins."[13]

There are a lot of different possibilities for connection of the AASV to the femoral vein, passing by the SJF or not, which can explain the recurrence after endovenous ablation procedure (*Figures 1 and 2*).[14]

Below the femoral triangle, the "AASV is not only a tributary of the [SFJ], but it is one of the saphenous trunks, situated in its own saphenous compartment in the thigh, lateral to the [GSV]" says Marianne De Maeseneer,[5] at least the uppermost centimeters of the thigh. Under that, when incompetent, there is often a subcutaneous segment, visible to the naked eye, corresponding to varicose vein.

Mühlberger [15] carried out a study on the cadaver dissection of the last 25 cm of the GSV in 217 legs. It considers as major tributaries flowing into the last centimeters of the GSV the following (*Figure 3*[15]): i) the lateral pudendal vein, present in 90% of cases; ii) the superficial circumflex iliac vein, found in 83% of cases; iii) the superficial epigastric vein, present in 78% of cases; and iv) anterior and posterior accessory saphenous vein of the GSV (less frequently observed) in 51% and 68% of cases, respectively.[16]
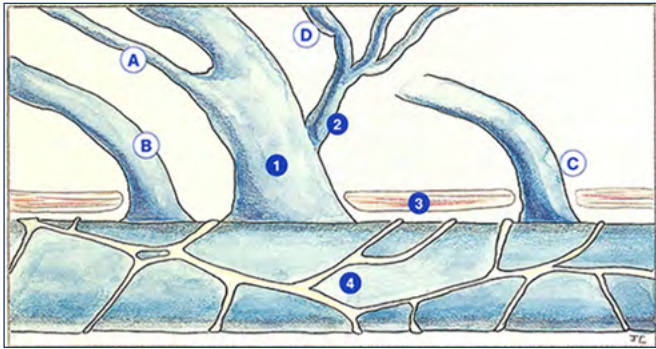
Figure 1. Schematic representation of connections for accessory saphenous vein.

1, saphenofemoral junction; 2, first tributary; 3, aponeurosis; 4, common femoral vein; A, anterior accessory saphenous vein draining in the saphenofemoral junction; B, anterior accessory saphenous vein draining directly into the common femoral vein below the saphenofemoral junction; C, anterior accessory saphenous vein draining directly into the common femoral vein above the saphenofemoral junction; D, anterior accessory saphenous vein draining into a tributary of the saphenofemoral junction.

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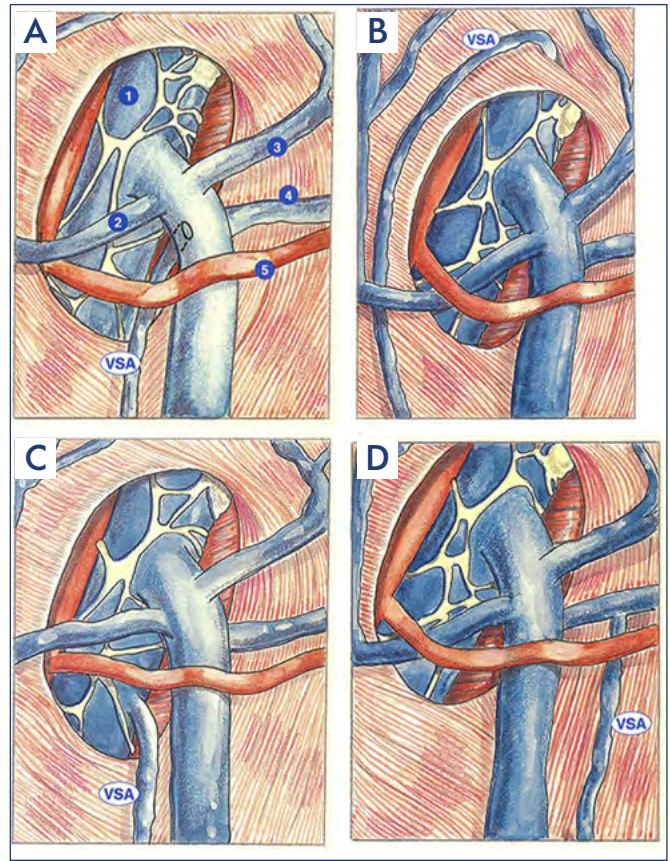
Figure 2. Schematic representation of different types of accessory saphenous vein junctions.

A) Abutment in the internal saphenous arch. 1, common femoral vein; 2, PEV, superficial external pudendal vein; 3, EpiV, superficial epigastric vein; 4, circumflex iliac vein; 5, inferior pudendal artery. B) Abutment in the common femoral vein below the saphenous arch. C) Abutment in the common femoral vein at a distance from the saphenous arch. D) Confluence in a collateral vein of the internal saphenous arch.

Abbreviation: VSA, anterior accessory saphenous vein.

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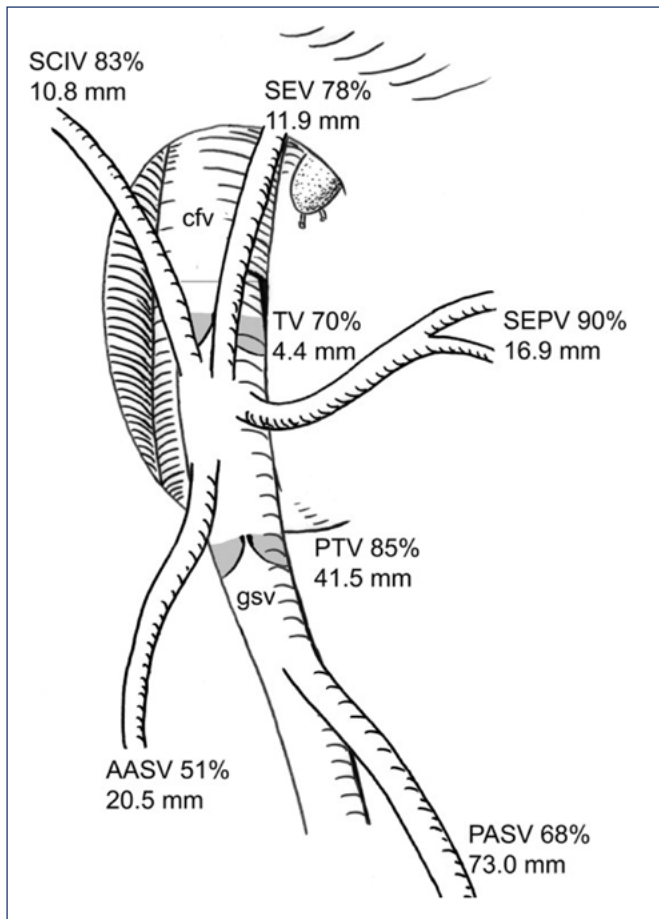
Figure 3. Saphenofemoral junction.

Abbreviations: AASV, anterior accessory saphenous vein; cfv, common femoral vein; PASV, posterior accessory saphenous vein; PTV, preterminal valve of the great saphenous vein; SCIV, superficial circumflex iliac vein; SEPV, superficial external pudendal vein; SEV, superficial epigastric vein; TV, terminal valve.

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Those examinations revealed that the terminal valve (TV) was "present between SFJ and first tributary in 70% of cases."[17]

Anwar and colleagues describe that reflux at the SFJ would be transmitted "into GSV and its major tributaries causing them to be incompetent in 23% of cases and develop into varicosities. Furthermore, major tributaries enter into GSV within the first few millimeters and may not be treated during endovenous ablation and can cause recurrent varicose veins in the future."[17]

There is another important anatomical variability: the femoral valve, which is located in the common femoral vein, above the SFJ. For Capelli,[18] when this femoral valve is not present (20% to 24% of cases) or is incompetent, with terminal and preterminal valves also incompetent, the indication for a surgical ligation is obvious. But this assertion is not confirmed in practice: there is no more recurrence after chemical or thermal ablation, no matter the status of these 3 valves.

We note that the anatomy of the veins in the lymph node at the groin has been described by Uhl et al,[19] with no history of surgery. Those veins are described as connecting to the femoral vein via direct perforators and joining the GSV and/or AASV.[19]

Thermal ablation procedure

Improvement in knowledge of the venous anatomy was made possible by the substantial development of EVTA over the 20 last years.

Indeed, these treatments make it possible to occlude a single incompetent vein, often a single saphenous axis (mainly great or small saphenous vein). One of the advantages of ultrasound-guided thermal occlusion is its precision: the tip of the fiber is perfectly visualized, and we know how to perform a treatment over a precise length, with no overflow. It is therefore possible to treat the entire junction (thermal ligation of the SFJ) or part of it, leaving the competent tributaries free.

The tip of the fiber should be positioned precisely between the termination of the GSV into the femoral vein, including the termination of the AASV when present. This is feasible without technical difficulty via ultrasound-guided endothermal procedures, as the tip is quite echogenic (*Figure 4*). The occlusion takes place precisely where the tip of the fiber has been positioned (*Figure 5*).
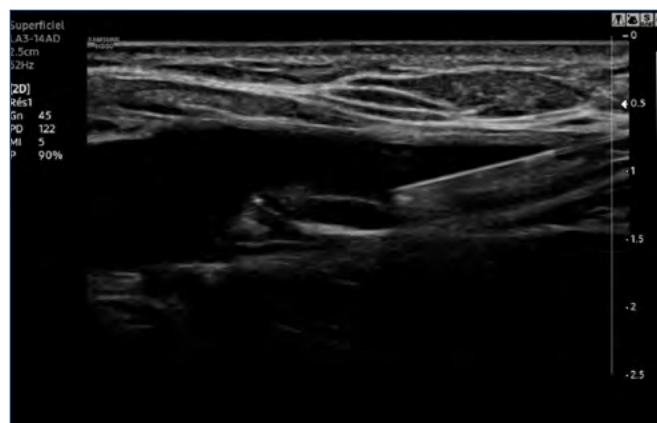
Figure 4. Ultrasound-guided endothermal procedure. The tip of the fiber (shown by arrow) is echogenic.
Image provided courtesy of Anne-Sophie Lensel.
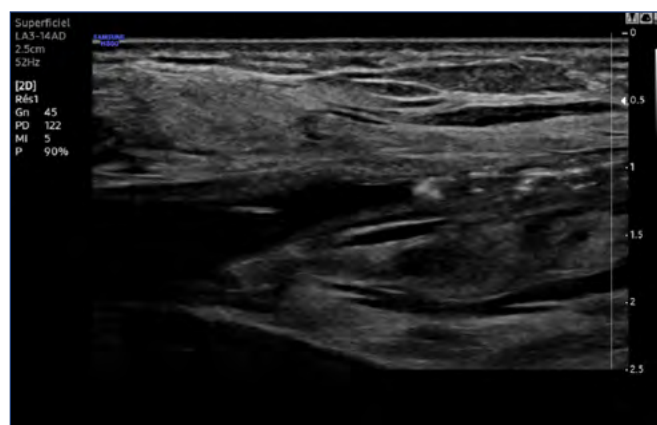
Figure 5. Ultrasound-guided endothermal procedure. Occlusion occurs where the fiber tip is positioned (see also Figure 4).
Image provided courtesy of Anne-Sophie Lensel.

What kind of treatment can we perform on a competent (and small) vein?

Endovenous thermal ablation?
Whereas an introduction by Seldinger technique[20] is easy to perform in an incompetent and large vein, it seems much more difficult to carry out in a thin, tiny one, especially when that vein is sinuous, with its intrafascial and straight portion not very long: the positioning of a tourniquet at the groin can be difficult, as would be the puncture.

A direct puncture with a 16-gauge Venflon cannula could then be proposed; the success of such step is to be studied. Some companies propose 400-μm laser fibers that can enter by a smaller Venflon cannula. The puncture of a small and competent vein in the superior third of the thigh can still be a practical issue.

For veins smaller than 4 mm, "thermal ablation by a seasoned operator, using suitable equipment, is tricky but technically feasible."[21]

Despite that misgiving, a case report[22] reviewing treatment of primary varicosis via EVLA of the GSV, including 278 procedures in 213 patients between May and December 2019, showed a 92.8% technical success rate early on. Occlusion of the GSV was achieved in 99.6%, and of the highest ascending SFJ tributary, if present, in 92.4%. The authors concluded that "a co-treatment of the tributaries is feasible and could improve the technical success of EVLA if a prophylactic closure of these veins is desired, especially if their distance to the SFJ is short." Its effect on the recurrence rate needs further research.

A current German study is underway aiming to evaluate prevention of varicose vein recurrence via synchronous EVLA treatment of sufficient AASV in patients undergoing EVLA of an insufficient GSV.[12]

Cyanoacrylate closure?
Cyanoacrylate glue ablation is a nontumescent, nonthermal ablation technique for treatment of varicose veins and is safe and effective,[23] at least in the short term; long-term studies are lacking as it was first used in 2013.[24]

Side effects have been described; for example, in 2020, Langridge and colleagues reported that rarely, cyanoacrylate glue embolization leads to extravasation and a chronic foreign body reaction requiring surgery. They concluded that "the relative novelty of cyanoacrylate glue embolization in the treatment of varicose veins requires clinicians to monitor for rare complications during its use in clinical practice. Patients should be aware of the rare risk of glue extravasation and foreign body reaction for fully informed consent prior to treatment."[25]

Furthermore, endovenous glue-induced thrombosis (EGIT) is not that rare, and a diameter of <5 mm for saphenous veins is a risk factor for its development.[26]

Studies with that technique were also based on incompetent veins that are mostly big (diameter of 7 mm [range 5.6–8 mm]).[23] The feasibility on thinner veins is also to be determined.

Sclerotherapy?
The direct puncture of the vein, which is the most common technique in Europe, is feasible, with no difficulty, whatever the size of the vein. A phlebologist usually performs injections with ultrasound guidance in veins smaller than 2 or 3 mm, using 22- or 23-gauge needles. This can be done just after EVTA of the GSV for varicose veins in the tributaries (that are incompetent). The technical feasibility is good, being careful about vein-spasm risk.

Side effects of liquid or foam sclerotherapy are acceptable for the treatment of varicose veins, but they should raise questions if for the treatment of a competent vein.

Conclusion
In a 2019 review article entitled the "Fate of the tributaries of saphenofemoral junction following EVTA of incompetent axial vein," Anwar and colleagues[17] noted that a systematic review and meta-analysis by O'Donnell et al[27] found that causes of recurrence are different after EVTA (mostly recanalization [32%] and development of incompetent AASV [19%]) than after surgical ligation (18% of neovascularization).

The European Society for Vascular Surgery reminds us in 2022 that "recurrent [varicose veins] often display recanalization of a saphenous trunk, previously treated by endovenous ablation, neovascularization at the location of previous surgery (in particular at the SFJ), or reflux in other veins such as the AASV, the SSV, or [perforating vein], which may have been healthy previously. The aim of investigation is to identify the nature and source of the recurrence."[28,29]

Anwar and colleagues in their review[17] found 3 main causes for AASV reflux (or any para-axial reflux) after EVTA of an incompetent GSV. These are as follows: i) true development of para-neoreflux (developing from incompetent SFJ into the AASV); ii) an AASV reflux missed in the initial scan; and iii) occult AASV reflux caused by "steal" effect of gross reflux in the untreated GSV in the initial scan. They note that "the true incidence of neoreflux into para-axial veins causing clinical significant recurrence is not known."

With this knowledge, should it be mandatory to do preventive treatment of competent AASV of the thigh (when it is present and drains directly into the SFJ)?

The feasibility and benefits do not seem to justify the risks, even if they are often reversible. The cost is also an important issue, especially for cyanoacrylate closure (in France for example, a dose costs €1000 with no possibility of reimbursement through insurance).

It is not always easy for the patient to accept side effects like deep venous thrombosis or skin pigmentation, even after well-informed consent. It would be much more difficult to explain that those troubles are caused by treatment of a competent vein, solely as a preventive measure against risk of recurrence, which is in a range between 8% and 35%.

The aim in prevention of recurrent varicose veins today seems mainly to improve success of EVTA. "Neoreflux into tributaries of GSV including AASV is the most common (8–31%) pattern of recurrence following endovenous ablation of GSV. Successful GSV ablation depends on many factors including the mode and amount of thermal energy delivered, laser wavelength and pullback rate, use of perivenous tumescent infiltration, manual compression over the vein during the procedure and a fiber tip position below the SFJ."[17,30] However, the main factors determining successful abolition of reflux from GSV tributaries depend on how far the successful GSV ablation extends toward the SFJ and the distance of tributaries from the SFJ. It is reasonable to assume that any technique that ablates incompetent GSV far from the SFJ is unlikely to control the reflux into its tributaries. This may explain such variation in recurrence results (8%–31%).[17]

Therefore, today, I would not (yet) propose that my patients undergo concomitant treatment of a competent AASV during the procedure of thermoablation of the GSV, whether by sclerotherapy, cyanoacrylate closure, or thermoablation.

However, when more results from the German study[12] become available in 5 years, they may change our practice relative to contemporary thought. We'll need to wait and see!

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Update on treatment methods for telangiectasia

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Abstract

Telangiectasias make up a heterogeneous group of diseases that can affect various parts of the body in humans. Although generally limited to the face, telangiectasia can cover different parts of the body in various collagen tissue diseases. The appropriate treatment options for telangiectasias are sclerotherapy, laser therapy, thermocoagulation, and microphlebectomy. The purpose of sclerotherapy is to cause endothelial damage by injecting a sclerosing agent into the vascular bed. Agents such as polidocanol, sodium tetradecyl sulfate, hypertonic saline, and glycerin are used for this treatment. Intense pulsed light is a noncoherent light source and is an important laser in the treatment of telangiectasia with wavelengths in the 500-nm to 1200-nm range. With thermocoagulation, also known as the radiofrequency energy method, high-frequency waves (4 MHz) are transmitted from the skin to the venous structures via a thin needle, and thermal ablation is provided. In microphlebectomy, venous networks are destroyed by needle puncture through a tiny skin incision. Scarring rarely occurs because the skin incisions are made very small. The efficacy of each of these treatment options seems similar. Choosing the treatment method most suitable for each patient will increase the success rates.

Introduction

Telangiectasias make up a heterogeneous group of diseases that can affect various parts of the body in humans. Although generally limited to the face, they can cover different parts of the body in various collagen tissue diseases. The telangiectasias we have studied usually occur as the result of chronic venous diseases of the lower extremities. These structures occur due to intradermal dilatation of the subpapillary venous plexus, where the vein wall thickens asymmetrically and contains collagen and muscular structures. More rarely, they may contain elastic fibers.[1] The prevalence of telangiectasias in the general population varies between 60% and 86%, and varicose veins are also present in some individuals.[2] Although the prominent complaints in these patients are related to cosmetic concerns, complaints such as pain and burning are also reported.[3] The appropriate treatment options for these patients are sclerotherapy, laser therapy, thermocoagulation, and microphlebectomy. Here, we present the clinical results of various treatments for telangiectasias.

Sclerotherapy

The purpose of this application is to cause endothelial damage by injecting a sclerosing agent into the vascular bed. Agents such as polidocanol (POL), sodium

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tetradecyl sulfate (STS), hypertonic saline, and glycerin are used for this treatment. Among these, POL is widely used today in different ratios and applied as foam or directly as a liquid. These foam and liquid treatments of POL were compared in a meta-analysis by Bi et al, which includes 8 randomized controlled trials and analyzes the efficacy and complications of these 2 methods. In this meta-analysis, the primary outcome was treatment efficiency, whereas secondary outcomes were postprocedural complications. The efficacy rate was analyzed in 7 studies involving 771 patients, and foam sclerotherapy was found to be more effective (odds ratio [OR], 5.64; $P<0.0001$; 95% confidence interval [CI], 3.93−8.10). Postprocedural pain was evaluated in an analysis of 1001 patients in 7 studies, and the pain was significantly more common in patients who received foam (OR, 1.52; $P=0.030$; 95% CI, 1.04−2.21). In an analysis that included 959 patients in a total of 7 studies, no significant difference was found in terms of postprocedural local inflammation rates ($P=0.896$; 95% CI, -0.03 to 0.03). Postoperative thrombophlebitis evaluation in 709 patients in 5 studies in total showed no significant difference between groups ($P=0.900$; 95% CI, -0.02 to 0.02). Finally, a hyperpigmentation assessment was performed for 871 patients, which included 6 studies, and no significant difference was found between groups ($P=0.336$; 95% CI, -0.05 to 0.14). In this current meta-analysis, the authors emphasized that although foam sclerotherapy causes complications more frequently, its effectiveness was quite high.[4]

Studies comparing the efficacy of different sclerosing agents are found in the literature. In a prospective randomized study by Bukina et al, hypertonic glucose (HG) and STS were compared (81 patients in the STS group, 78 patients in the HG group). Efficacy evaluation was performed with vessel-clearing scoring on day 14, 28, 42, and 56 after the procedure. In the evaluation, HG treatment was found to be superior to STS at all time points ($P<0.01$, for all time points). Also, at the end of follow-up, more pigmentation was observed in the STS group than in the HG group (38.3% vs 2.6%, $P<0.001$). The authors concluded that a 0.2% STS solution was aggressive for the treatment of telangiectasia. They also found that pigmentation occurred more frequently in patients with large telangiectasia (0.8-1 mm) (52.9% vs 27.7%; $P=0.021$). The authors emphasized that both agents were safe, and no major adverse events were observed in any patient, but HG treatment was more effective.[5]

Notably, studies conducted in the early 1970s showed that hypertonic solutions did not cause the desired level of endothelial damage to the vessel wall[6]; however, other studies reported in the literature do show HG solution to be a sclerosing agent.[7]

Another recent study by Bertanha et al compared treatment with POL plus glucose (0.2% POL and 70% HG, 51 patients) versus glucose alone (70% HG, 47 patients). Post-application evaluations were carried out immediately after the procedure, 7 days after the procedure, and in the second month after the procedure. Combined therapy was found to be more effective in the target area (82.2% vs 63.9%; $P<0.001$). No major adverse events were reported in either group. When all patients were evaluated, pigmentation was the most common side effect, but larger pigmentation areas have occurred in patients using combined agents (median 0 cm vs 0.5 cm, respectively; $P=0.033$).[8]

In a study by Hoss et al, POL treatment was analyzed as sclerotherapy with 1:2 POL to air ratio versus 1:4. At the end of this prospective, randomized controlled study in which 30 patients were included, both methods were found to be effective and similar in terms of complications.[9] In another study, STS 0.25% and POL 0.75% were compared in the treatment of lower-extremity telangiectasia. In this study, which included 21 patients, both agents showed similar clinical improvement. When evaluated in terms of complications, it was determined that STS treatment was more painful during the procedure and caused more skin necrosis. However, more pigmentation was observed at the injection sites in POL treatment.[10]

Laser therapy

The first laser used in the photothermolysis of vascular lesions is the flashlamp-pumped pulsed dye laser (PDL). The wave duration of this laser is 450 μs and small and medium vessels are targeted. It was first used with a wavelength of 577 nm, and the vascular specificity of the laser was increased by making the wavelength 585 nm.[11,12] The energy density of the PDL varies between 3 and 10 J/cm^2 and the spot size varies between 2 and 10 mm, and these values can be adjusted according to the age of the patient and the lesion area. Purpura is the most common side effect of PDL treatment, and it occurs between 2 and 14 days after treatment. Hyperpigmentation, atrophic scar, hypopigmentation, and hypertrophic scar are complications that may occur in the late period. Because PDL energy can be absorbed by melanin, people with dark skin have less of an effect and a higher risk of complications. Therefore, laser treatment should be planned according to the skin characteristics of the patients (*Table I*[13]and *Figure 1*[14]).

Phototype	Sunburn and tanning history	Immediate pigment darkening	Delayed tanning	Constitutive color	UV-A MED (mJ/cm^2)	UV-B MED (mJ/cm^2)
I	Burns easily, never tans	None (-)	None (-)	Ivory white	20–35	15–30
II	Burns easily, tans minimally with difficulty	Weak (- to +)	Minimal to weak (- to +)	White	30–45	25–40
III	Burns moderately, tans moderately and uniformly	Definite +	Low +	White	40–55	30–50
IV	Burns minimally, tans moderately and easily	Moderate ++	Moderate ++	Beige-olive, lightly tanned	50–80	40–60
V	Rarely burns, tans profusely	Intense (brown) +++	Strong, intense brown +++	Moderate brown or tanned	70–100	60–90
VI	Never burns, tans profusely	Intense (dark brown) +++	Strong, intense brown +++	Dark brown or black	100	90–150

Table I. Fitzpatrick skin phototypes.

Based on reference 13: Pathak MA. J Invest Dermatol. 2004;122:20-21. doi:10.1046/j.1523-1747.2003.22248.x.

Figure 1. Fitzpatrick skin phototype images.

After reference 14: Hindustan Times. Google is searching for a new method to classify skin tones to curb bias in products. Updated August 21, 2022. https://tech.hindustantimes.com/tech/news/google-is-searching-for-a-new-method-to-classify-skin-tones-to-curb-bias-in-products-71624068839041.html © 2022, Tech Hindustan Times.

The effectiveness of treatment with PDL-585 in a 29-year-old White woman (Fitzpatrick skin type I) has been reported, evaluating treatment success via optic consonance tomography (OCT) imaging. In this case, treatment was applied at 5.5 J/cm^2 with a spot size of 10 mm and 0.5 ms pulse duration. After the treatment, OCT vindicated dropped vascular inflow.[15] A clinical report published by Bernstein et al, describes the use of a laser platform that incorporates a new 524-nm laser, pumped by a marketable hair junking laser treatment, in the treatment of spider veins and facial greenishness. In this report, a new 524-nm vascular laser was designed using a 755-nm hair removal laser as a pumping source. It was used to treat facial rosiness and leg telangiectasias in 24 subjects.

This laser could be set up safely and effectively for treating vascularity on the face and legs.[16] Thus, laser treatments can be applied clinically in various combinations; this area is open to development.

Intense pulsed light (IPL) is a noncoherent light source and is an important laser in the treatment of telangiectasia with wavelengths in the 500- to 1200-nm range. In this device, each pulse is between 2 and 25 ms, and the delay between pulses varies between 10 and 500 ms. The device gives single, double, or triple light pulses. This condition is also known as "additive healing" and provides an advantage in the treatment of deep vascular lesions.[17]

The neodymium-doped yttrium aluminum garnet (Nd:YAG) laser is a laser device with a wavelength of 1064 nm and a pulse duration of up to 200 ms, which can be used in the treatment of veins up to 3 mm in diameter in the lower extremities.[18] Compared with the PDL-595, this laser is more effective in the treatment of veins between 1 and 3 mm, but it is more painful. A device was also developed by combining PDL-595 and Nd:YAG 1064 from these laser devices (Cynergy with Multiplex, Cynosure, Westford, MA). In this application, the PDL laser is used as a "preheat" device to warm the blood to 70 °C. This event converts oxyhemoglobin to methemoglobin. Thus, the absorption of the Nd:YAG laser also increases 4 to 7 times.[19]

In a recent study, the early effectiveness and safety of an innovative combination of 532-nm and 808-nm transdermal diode laser cure in the treatment of 0.1- to 1-mm telangiectasia were investigated. In this study, which included 94 female cases, these were treated by 3 cycles with a 532-nm laser combined with a contemporaneous 808-nm beat. In these processes, the out-time between the cycles was 10 ms. The esthetic outgrowth was scored by the running physician in a range from 0 (no change) to 10 (100 exposure), and the pain was scored from 0 (no pain) to 10 (most painful experience ever). In inpatient follow-ups, depigmentation was observed in 3 out of 94 cases (3.2), hyperpigmentation in 14 (4.2), flash erythema in 14 (14.9), flash edema in 11 (11.7), and matting in 1 (1.1). The mean esthetic outgrowth was scored as 7.9 by the physician, and cases reported a mean periprocedural pain of 3.4. At the end of the study, the authors stated that contemporaneous operation of 532-nm and 808-nm laser emigration is safe and effective in 0.1- to 1-mm telangiectasia treatment.[20]

Thermocoagulation

In this treatment method, also known as the radiofrequency energy method, high-frequency waves (4 MHz) are transmitted from the skin to the venous structures via a thin needle, and thermal ablation is provided. This device is the TS-3000, and it includes a needle suitable for the classic surgical electrocautery tip, thus treatment can be performed in this way. It was developed as a special device specifically for the application of this treatment.[21,22]

The efficacy and side effects of the treatment were investigated in 145 patients (223 extremities), using the TS-3000 device.[21] In this study, thermocoagulation was applied to 0.3- to 0.6-mm diameter venous structures. Clinical outcomes were evaluated at 3, 6, and 12 months. At the end of the 1-year follow-up, treatment efficacy was 75.7%, pigmentation was 14.9%, and residual telangiectasia was approximately 15%. In addition to these findings, the absence of skin necrosis during follow-up was considered a positive effect.

In another study, thermal ablation was applied to 30 patients by replacing the cautery tip with a "Given Needle" (US Patent No. US 7,125,406; US 7,628,790) (Figure 2), using standard surgical electrocautery. Here, the device is set to cutting mode, and the wattage is set to 2 MHz (wattage will vary depending on the calibration of the generator). Afterward, ablation was performed by passing the needle through the skin and contacting the subcutaneous venous tissue. Clearance rates of 75% to 100% were observed in 14
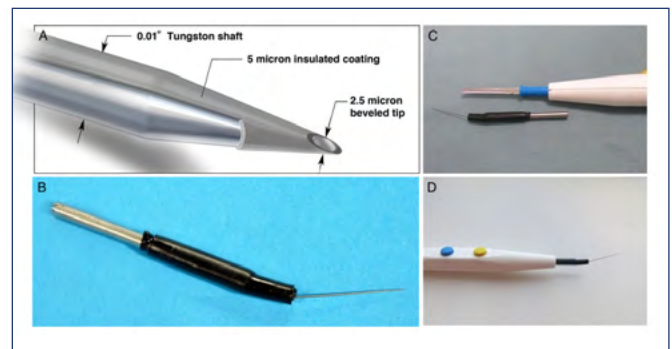
Figure 2. (A) Structures of Given Needle. (B) Given Needle (C) Comparison of the Given Needle and a standard handle type. (D) The Given Needle inserted into a standard handle.

After reference 22: Mujadzic et al. Aesthet Surg J. 2015;35(7):NP221-NP2219. © 2015 The American Society for Aesthetic Plastic Surgery, Inc.

cases, 50% in 7 cases, 25% to 50% in 5 cases, and 0% to 25% in 4 cases. Complications included, most commonly, skin erythema (15 cases) and bruising (13 cases), both of which resolved in 2 to 3 weeks with no permanent sequelae, and needle-stick pain (14 cases), which resolved within 3 days. No serious complications such as major vessel thrombosis, serious antipathetic responses, pigmentation problems, ulceration, scar formation, or prolonged pain at the treatment point were observed.[22]

Microphlebectomy

Phlebectomy was first described by Aulus Cornelius Celsus. In this method, venous networks are destroyed by needle puncture through a tiny skin incision. Scarring rarely occurs because the skin incisions are made very small. Long-term results are excellent when done in the right indication. Complication development is very rare.[23]

Comparative literature review of different telangiectasia treatment modalities

Various studies have investigated the effectiveness of different techniques used in the treatment of telangiectasia. The efficacy of long-pulsed 1064-nm (LP1064) and 755-nm (LP755) laser treatments in the treatment of telangiectasia was investigated by Nguyen et al, in which 22 patients with skin type IV were included, and the treatment areas were determined as 2x2-cm areas. In this study, after a 1-month follow-up, the clearance rates for the 2 types of spotlights were not significantly different (71.87 and 71.69, respectively; P=0.99). At the 3-month follow-up, the effectualness was constant, and no recurrence

happened. Pain reported with both styles was moderate and significantly lower for LP755. The authors concluded that LP1064 and LP755 laser treatments were comparatively effective and safe for telangiectasia and reticular modes of Fitzpatrick skin type IV cases.[24]

Munia et al compared sclerotherapy and laser treatments in their prospective study. In this study, 75% glucose solution was used as a sclerosing agent, and Nd:YAG 1064-nm laser was used as a laser device. In this report, in which 30 female patients were included, the treated legs were randomly assigned to the laser and sclerotherapy groups. Pre- and postprocedure photos of all patients were also taken, and these photos were evaluated independently by 2 investigators. In the procedural evaluation of pain, the treatment in the laser group was found to be significantly painful ($P<0.001$). Effectiveness in terms of appearance was similar in both groups. The authors concluded that both treatments were effective but emphasized that sclerotherapy is a less painful and inexpensive treatment method compared with laser treatment.[25]

Tepavcevic et al studied the effectiveness of 3 different treatment styles in the treatment of lower-extremity telangiectasia. In the study, which included 30 female cases, persons with skin characteristics ranging from Fitzpatrick I to IV were included. In this study, sclerotherapy (1 mL of 0.5 Aethoxysklerol, 30-gauge needle), laser (Nd:YAG 1064-nm laser wavelength, fluence 110–150 J/cm², pulse duration 20–40 ms, 3–6-mm spot size; the gel was used for skin contact and after treatment; ice was packed on the skin), and radiosurge coagulation (Ellman Surgitron, blood vessel electrode, coagulation impulse 2 units) treatments were compared. At the end of the 3-month follow-up, sclerotherapy was found to be significantly better than other styles in terms of treatment success ($P<0.01$) and pain complaints were also significantly lower for sclerotherapy treatment ($P<0.01$). At the conclusion of this study, the authors emphasized that sclerotherapy is the most comfortable treatment system.[26]

Parlar et al compared sclerotherapy (POL 0.5%) and Nd:YAG laser (1064-nm long-beat) treatments for lower-extremity telangiectasia in their prospective randomized study. The treated leg was determined randomly, and treatments were applied in 2 sessions at 6-week intervals. Treatment success was evaluated at 6 weeks and 6 months, with 2 independent investigators basing scoring in the range of 0 (no effect) to 6 (100 cleared) on evaluations of pictures. This study found that sclerotherapy brought more rapid improvement, although at the last follow-up visit, blinded assessment showed no difference in clearance between the 2 groups ($P=0.84$). Still, pain complaints were less common in the sclerotherapy group. The authors concluded that the 1064-nm long-pulsed Nd:YAG laser was associated with more pain, suggesting suitability of this treatment for those with needle phobia, allergy to sclerosants, and in the presence of small veins with telangiectatic matting.[27]

Since then, the efficacity of laser (Nd:YAG laser with a wavelength of 1064 nm, StarLux 500; Palomar Technologies, Carlsbad, CA, USA) and sclerotherapy in the treatment of lower-extremity telangiectasia has been further studied by Ianosi et al. In this study, sclerotherapy cases were divided into hypertonic saline (20% saline and 2% lignocaine) and POL (0.5%) groups, and treatment efficacity was assessed for 244 (488 legs) female cases over a 6-month period. There were 169 legs in the POL group, 154 in the hypertonic saline group, and 165 in the laser group. Photos of all cases were made before and after the procedure. This evaluation assigned scores between 0 (no change) and 6 (100 cleared) points. From this study, the authors concluded that for telangiectasias under 1 mm, periphery laser was more effective (risk ratio [RR], 9.72; $P<0.0001$) than hypertonic saline, as was POL (RR, 2.70; $P=0.003$); for telangiectasias over 1 mm, periphery laser and POL were more effective (RR, 2.70; $P=0.003$ and RR, 1.44; $P=0.00756$; respectively); for telangiectasias under 1 mm, laser treatment was superior to POL treatment; for telangiectasias over 1 mm, the hazard regression model showed a hazard ratio of 3.97 ($P=0.047$) for laser and 4.96 ($P=0.486$) for POL vs hypertonic saline treatment. The authors concluded that laser treatment is effective in lower telangiectasias and that sclerotherapy with POL becomes more effective as the periphery increases.[28]

In another recent study, laser (Nd:YAG laser, LAS- StarLux 500), POL-1 (1% polidocanol) and POL-0.5 (0.5% polidocanol) were investigated, including 132 cases (264 branches) with treatments performed by the same physician. The authors concluded that laser treatment was effective in telangiectasias below 1 mm, and both POL treatments were more effective in larger vascular structures.[29]

Conclusion

Telangiectasias can be treated with various methods. The efficacy of treatment seems to be similar across the different options. Choosing a treatment according to suitability for the individual patient will increase the success rates.
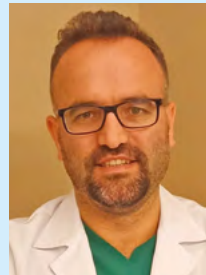
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May-Thurner diagnosis and management

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Abstract

May-Thurner syndrome, known for decades as a unique pathology, has been included recently with other pelvic compression maladies in the S-V-P CEAP (symptoms-varices-pathophysiology, clinical-etiology-anatomy-pathophysiology) classification sponsored by the American Venous and Lymphatic Society as part of several anatomic lesions in the abdominopelvic region that have variable clinical presentations. This classification will fully characterize and accurately describe a particular lesion; also, it will facilitate clinical interaction and precise treatment and in the long term the development of patient-reported outcome measures and clinical trials. In the interim, epidemiologic data reported so far have been questioned recently because of the lack of adequate clinical trials. The pathophysiology originally described is still currently accepted, and the clinical presentation is better known. The noninvasive vascular armamentarium (ultrasound, computed tomography, and magnetic resonance imaging) is very reliable, and the invasive methods (venography, intravascular ultrasound) allow us to assure the diagnosis and evaluate treatment. Endovascular treatment is the preferred approach to dissolve a thrombus should one be present, with then treatment of the underlying compression via stent placement. The stent most used globally is probably the Wallstent because of its results, and the dedicated nitinol venous stents are tending to show good results in long-term follow-up. There is no consensus on optimal anticoagulants given post stenting; however, the newer oral anticoagulants are used in patients with a history of thrombosis. So far, May-Thurner syndrome is underdiagnosed, but probably overtreated. That is why reviews like this are useful to avoid it. Finally, I believe that the term May-Thurner syndrome will continue to be used, alongside the new classification.

Introduction

May-Thurner syndrome (MTS) is an anatomopathologic entity described in 1957, also known as iliac vein compression syndrome or Cockett syndrome. May and Thurner named the syndrome after their findings, based on the work of Rudolph Virchow (1851)[1] and his proposal of an increased incidence of left leg venous thrombosis due to compression of the left common iliac vein (LCIV) by the right common iliac artery

(RCIA), and on later work of others. In the first half of the 1900s, Mc Murrich studied 107 cadavers with the same pattern of deep venous thrombosis (DVT), finding higher prevalence in the left leg (29.9%) than in the right (2.8%); this study included both neonates and adults, suggesting a possible congenital origin.[2] In 1943, Ehrich reported 412 autopsies with special attention to iliac vein dissection and suggested an acquired etiology for left iliac vein obstruction (IVO).[3]

May and Thurner knew about the previous studies and in an effort to disclose a cause for DVT they dissected 430 cadavers; their findings indicated an important focal intimal venous thickening and septa formation in 22% of the subjects; these they named "spurs." They hypothesized that "the repetitive trauma caused by the RCIA pulsation over the LCIV against the lumbar spine produces endothelial injury, collagen and elastin accumulating in the vein intimal layer originating webs and spurs"[4] (*Figure 1*).[5]

Cockett et al in 1965 correlated the DVT incidence, postthrombotic syndrome (PTS), and iliac vein compression clinically and pathologically and they called it "iliac vein compression syndrome." After those reports, some authors used the terms "May-Thurner-Cockett syndrome" and "iliac vein compression syndrome."[6,7]
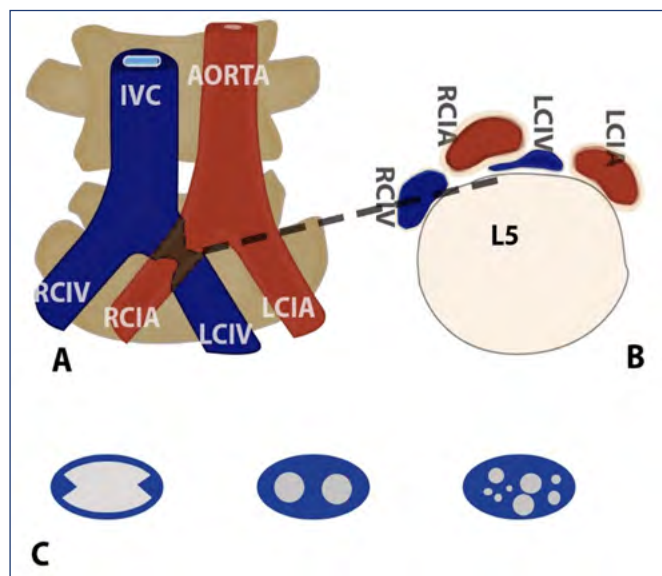

Figure 1. Anatomy of May-Thurner syndrome and types of spurs. A) Compression of LCIV between RCTA and vertebrae. B) Detail of compression. C) Types of Spurs – described in text.

Abbreviations: IVC, inferior vena cava; LCIA, left common iliac artery; LCIV, left common iliac vein; RCIA, right common iliac artery; RCIV, right common iliac vein.

After reference 5: Armenta-Flores et al. Phlebology. 2022;37(1):5-13. Digital illustration by Architect Gustavo Perez. © The Author(s) 2021. Sagepub.com/Journals.

Pathophysiology

Since the original description of the "spur theory" made by May and Thurner, little progress has been made to elucidate the pathogenesis of the LCIV obstruction, no animal model of MTS exists, and the molecular basis of venous spur development remains unknown.[8]

Recently, some authors have readdressed this issue with a diversity of hypotheses. Harbin et al wrote that the female pelvis has an accentuation of the lumbar lordosis that pushes lower lumbar vertebrae anteriorly, thereby compressing the LCIV against the RCIA.[8-10] Urbas and Brenner dissected 100 cadavers looking at the iliocaval junction and the left iliac vein. They described 5 forms of venous spurs—central, adhesion, bridges, valves, and bands—and their conclusion was that central venous spur occur only in the venous confluence and could be remnants of ostial valves, and that the adhesions may originate from embryological development (different wall thickness). They found considerable differences in caliber and circumference in the left iliac vein due to different embryological origin of the different quarters of the cardinal vein or venous anastomotic network; all these spurs mean an obstruction to flow and may be a predisposing factor for DVT. They concluded that these 5 structures do not have a causal relationship for obstruction with compression by the RCIA.[11] Despite the aforementioned theories, the most accepted is the one enunciated by May and Thurner in their original paper.[4]

Epidemiology

To date, no population-based studies have been made to document the prevalence or incidence of MTS.[8] So far, data published shows that the exact incidence and prevalence of MTS are unknown but are likely underestimated given that most individuals with MTS anatomy are asymptomatic and require no treatment.[12,13] Brazeau and others stated the difference between May-Thurner anatomy and MTS: May-Thurner anatomy is the compression of the LCIV by the overlying RCIA with no hemodynamic significance, and MTS refers to the extrinsic compression of the LCIV by the RCIA against the lumbar vertebrae alongside the presence of venous spurs, compromised venous flow, and venous collaterals with or without DVT.[12-14] These differences suggested that LCIV is necessary but not sufficient to cause MTS. Studies targeting the LCIV investigating asymptomatic subjects have found significant compression and diameter reduction in up to 80% of their cohort.

Therefore, compression of the LCIV is present in one-third of the population and both genders are equally affected.[12,13,15] MTS could cause 2% to 5% of all DVT. Many cadaveric and radiographic studies estimated the prevalence to be much higher. Several autopsy studies on unselected patients showed MTS prevalence to be between 14% and 32%[8,13,14] and in radiological studies with DVT patients, could be 22% to 76%.[8,12-16]

For all the aforementioned, the American Vein and Lymphatic Society International Group on Pelvic Venous Disorders recently published the "symptoms-varices-pathophysiology classification of pelvic venous disorders" to encompass most of the venous maladies of the pelvic-inferior extremities axis and to standardize classification and develop disease-specific outcome instruments and clinical trials. In the meantime, notation for a patient with MTS with left lower-extremity edema is written like this: $S_oV_oP_{lciv.o.nt:}$Left $C_{3s}E_{se}A_dP_{o(civ).}$ [17]

Clinical presentation

MTS is more common in young healthy women between ages of 20 and 50 years old, though it is not confined to this group. It is the most significant factor for left-sided DVT, being 3 to 8 times more common than right-sided DVT.[12,13,18] The most frequent presentation is chronic venous insufficiency and it is present in 20% to 50% of cases of left lower-limb DVT.[18,19] Patients complain of acute intermittent and progressive (activity-related) heaviness and swelling of left lower limb or venous claudication that is relieved with rest and leg elevation; they may also report tighter shoes in the affected leg at the end of the day with fatigue and swelling. The progression of the chronic venous insufficiency—manifested as pain, venous claudication, varices, skin hyperpigmentation, and ulceration—reduces quality of life (QOL). Rare symptoms include phlebitis and phlegmasia cerulea dolens. Other less common presentation is acute, spontaneous, and painful left-leg swelling (DVT) with no precipitating cause, or the disease may first present during or after pregnancy and a history of recent use of oral contraceptive pills. Many times, patients are studied for iliac vein compression after standard ablative treatment for varicose veins and poor medium- or long-term results. Actually, many patients live with progressive left-sided venous hypertension and do not recognize it. They have increased tightness or discomfort with activity but are better in the morning, so they delay medical consultation.[12,13,18,20-22] Besides the ancillary presentation in May-Thurner description, other variants exist, eg, right-sided MTS and compression of the inferior vena cava (IVC) by the RCIA. Moreover, rare MTS are described, including rupture of the iliac vein, secondary

to an iliac artery stent, prostate hypertrophy in patients with foramen ovale and cryptogenic stroke, and in pelvic congestion syndrome.[5,23-35]

A thorough history and physical exam are important to identify the clinical presence of LCIV obstruction in symptomatic patients with lower-extremity discomfort, edema, and/or discoloration. Kim et al described the 3 stages of iliac vein compression: stage I, asymptomatic iliac vein compression without any narrowing; stage II, development of venous spurs without thrombosis; and stage III, presence of left iliac vein DVT.[36] Diagnosis of MTS requires demonstration of the venous stenotic lesion in an appropriate anatomic location.[37] In patients with proximal DVT, history of DVT, or venous insufficiency with lower-extremity swelling, the initial investigation is via duplex ultrasound (DUS); in the absence of thrombus, computed tomography (CT) venography and/or magnetic resonance (MR) venography are indicated.[5.]

Diagnosis

Color venous duplex ultrasound
After clinical suspicion of DVT, the initial noninvasive diagnostic test is color venous DUS (CVDU), its sensitivity is 91% and specificity is 99% using compression in proximal DVT. Whereas the first aim of CVDU is to rule out DVT, it also evaluates venous reflux time. Venous DUS findings of iliocaval DVT are as follows: absence of flow variation, narrowed iliac veins, and poststenotic turbulence (noisy signal).[38-40] To evaluate the common femoral vein, a linear 4 to 7 MHz array transducer with a <60° angle of insonation is used, whereas a 2 to 3 MHz transducer should be used for iliac and caval vessels. B-mode compares vein diameter reduction at the smallest lumen area against normal vein diameter. Peak vein velocity (PW) is measured in the pre- and poststenotic segment; a PW gradient >2.0 is significant.[12,41] However, the deep location of the proximal iliac vein plus other factors (obesity, overlying gas) interferes with ultrasound for an accurate diagnosis of MTS.[41,42]

A recent maneuver in asymptomatic patients showed the presence of illusory MTS: even a well-hydrated patient in supine position can show compression of the LCIV; moving the patient to a semi-sitting 45° position (Semi-Fowler) releases the gravitational overload and flow recovery occurs in the LCIV (Zamboni maneuver); this has been corroborated by plethysmography, either in the semi-settle or in supine position, with and without leg elevation. The real MTS is nonreversible and/or associated with intraluminal defects. This maneuver could become an initial screening to avoid more invasive or

expensive diagnostic steps.[43,44] Current ultrasound technology allows for a greater penetration depth with improved image resolution, and DUS planimetry has recently been proposed to diagnose an obstruction better than hemodynamic criteria. DUS permits a full examination of the abdominopelvic and lower-limb venous system in a single session. It shows obstruction and reflux, detects intraluminal vs extraluminal causes of stenosis, and allows ongoing assessments after intervention and treatment. Transabdominal ultrasound is comparable to IVUS for the detection of IVO, and DUS planimetry measures are more reliable than hemodynamic measures. Nowadays, the results for the utility of DUS as a noninvasive workup diagnostic tool for IVO and tracking tool for IVO treatment, show that it can be used to guide clinicians and help determine which patients should be offered IVUS and IVUS-guided treatment.[45-47]

Cross-sectional imaging: CT/MR venography

Both imaging methods have more than 95% sensitivity and specificity in MTS but require particular protocols in order to obtain better imaging. CT venography (*Figure 2*) using 3-mm to 5-mm cuts allows visualization of structural details (spurs, webs), rules out extrinsic compression, identifies location and stenosis degree in nonthrombosed veins, and shows DVT and collateral pathways.[48-55] If the contrast opacification is suboptimal with the standard (indirect) method, a direct technique could be used with good results.[49,50]

As with ultrasound, the patients can be put in different positions (supine or prone) or the Valsalva maneuver can be used to identify an illusory MTS.[43,56] CT venography advantages over CDUS or venography include lack of operator dependence, clearer pelvic vein images, and shorter exam time. However, because of the radiation dose, it should be avoided in pregnancy, and the use of contrast medium contraindicates its use in patients with renal failure.[49,50]

With recent advances in software and technology, eg, 3-dimensional CT venography, some researchers have compared it with IVUS and described noninferiority for the evaluation of the degree of stenosis, its length and luminal caliber of the left iliac vein, and for the prediction of stent sizing, rendering it a good tool for diagnosis and treatment of chronic iliofemoral venous obstruction.[57,58]

MR venography provides information similar to CT venography with better characterization of the pathology in pelvic and spinal structures, including lumbar vertebral degeneration, bulging or protruding intervertebral disks, osteophytes, or spondylolisthesis[59]; and further assessment of
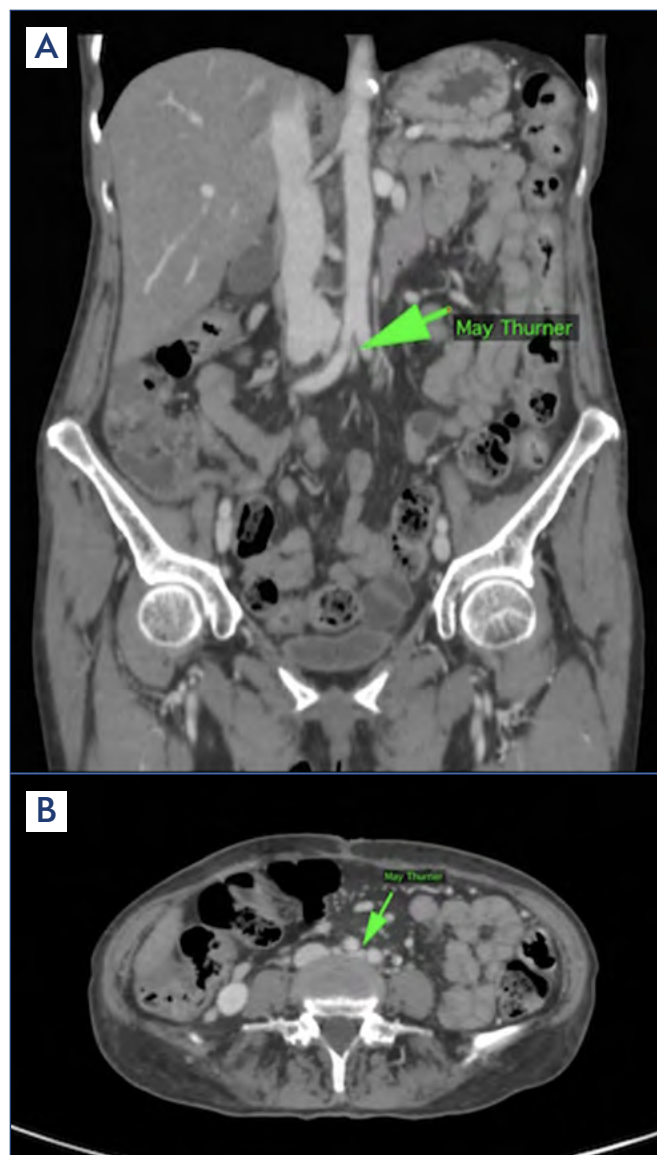
Figure 2. Contrast computed tomography in May-Thurner syndrome. A) Coronal view. B) Axial view.

Green arrow, left common iliac vein compressed.

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hemodynamic significance by demonstrating pelvic collaterals and flow reversal (on time-of-flight pulse sequence) within the ascending lumbar veins. With advances of techniques, high-resolution variable-flip-angle turbo-spin-echo (CUBE) MR imaging allows separation of the vessel wall and lumen and can demonstrate DVT. A few studies showed the use of noncontrast MR venography to diagnose MTS without using a control cohort, and they concluded that MR venography and CUBE have similar results in assessing the degree of luminal stenosis, the site, and number of compressions in MTS; however, they underestimate the narrowest diameter in comparison with CTV; hence, high clinical suspicion of an

occlusive left iliac vein stenosis with a suggestive color DUS could lead to performance of invasive venous imaging; but, if there is any anatomical concern, cross-sectional imaging—preferentially CT venography—is in order.[12,13,60,61]

Invasive venous imaging

Catheter venography

Catheter venography was the gold standard in diagnosing MTS until recently. It is nowadays reserved for cases in which cardiovascular intervention is planned or diagnosis by noninvasive modalities is equivocal.[21] It measures pressure gradients across the stenotic area; a gradient >2 mm Hg at rest and >3 mm Hg during exercise has hemodynamic significance.[12,18,21,55] It determines location and severity of the stenosis; to improve its accuracy, multiplanar views—anterior posterior and lateral projections—are obtained during injection to avoid "the pancaked vein effect" (externally compressed in the AP plane).[18,20,21,50.] So far, no study has validated a specific diameter threshold for a stenotic lesion in the venous system leading to symptoms; that is due to various factors, including compliance of veins, volume status, and position of the patient. However, a stenosis of more than 50% has been accepted empirically to stent for relieving symptoms.[37,39,40,50,62]

Confirmation of a stenotic lesion in MTS is made by pressure measurements. There are various methods, but the more accurate is the pullback method, which measures the pressure in the lower IVC, comparing it with the distal iliac vein, and a gradient pressure is obtained.[52,55] Venography helps to define collaterals or the presence of congenital venous anomalies; it shows blood flow patterns and the presence of thrombi (*Figure 3A*).

However, venography is invasive, time consuming with an increased bleeding risk, and does not contribute to extravascular information; also, patients are exposed to radiation and contrast dye.[12,13,18,21]

Intravascular ultrasound

Nowadays, the gold standard for MTS is venography plus intravascular ultrasound. IVUS is more sensitive than venography (>98%). It provides high-resolution images through high-frequency sound waves from the ultrasound transducer on the catheter. IVUS shows precisely the morphology of the spur and estimates the severity and distribution of pathology.[18,37,40,41,55,62,63] There are 2 types of IVUS available: mechanical and solid state (digital and rotational catheters). IVUS catheters use a 0.035-inch wire and are chosen on the basis of their maximal imaging diameter and transducer frequency, eg, Volcano 60 mm, 12 Mhz.[12,18,52,55]
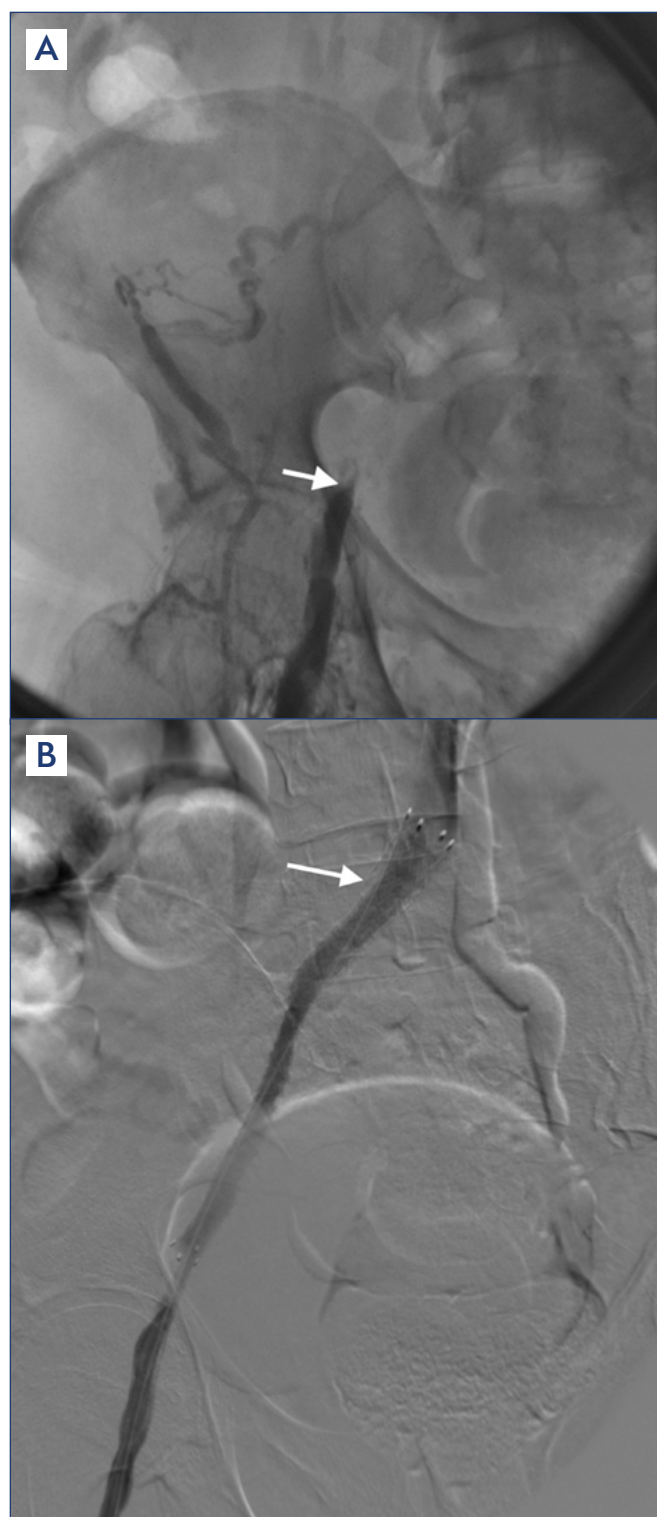
Figure 3. Catheter venography in May-Thurner syndrome. A) Deep venous thrombosis with collateral circulation. B) Left common iliac vein, stented.

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IVUS provides data on minimal luminal area at the compression site, reference lumen area, and signs of fibrosis within the vein. Since the inception of IVUS in the turn of this century, it has been considered an integral part of stent deployment. It has advantages in subtle iliac vein pathology and is useful before intervention—for proper vessel sizing—and after therapeutic interventional procedures. It measures cross-sectional area gain, stent placement, its expansion, and in-stent restenosis (*Figure 4*). Specific measurements of luminal areas and diameters can be obtained without the requirement of contrast and lateral projection imaging.

IVUS visualizes wall thickening caused by compression and adjacent structures, eg, iliac artery. It identifies subtle stenosis when the vein wall and lumen appear otherwise normal. IVUS does not utilize contrast or ionizing radiation.

IVUS is useful for measuring iliac luminal areas and diameters, which are important in selecting stent size and length for placement of the optimal stent for the patient, and thereby minimize the chance of stent migration. Finally, IVUS allows for more precise stent deployment by facilitating accurate identification of the iliac vein confluence. This assists in a right deployment by reducing the chance that a portion of the stent will unduly obstruct the RCIV. The limitations of IVUS are invasiveness of the procedure, limited extravascular information, and in some places, lack of availability.[12,18,20,37,41,52,55,62,64]

Management

Current treatment of MTS

Management depends upon the presence of symptoms, severity, and whether or not DVT is present.

1) In patients with nonthrombotic iliac vein lesions (NIVL) who are symptomless or with mild symptoms (CEAP 1–3), conservative treatment with compression stockings is enough.[12,13,18]

2) In patients with nonthrombotic MTS with moderate to severe symptoms (CEAP 4–6), angioplasty and stenting is indicated.[12,20,62]

3) For thrombotic MTS without contraindication to lytic therapy, initially, anticoagulation is indicated, then catheter-directed thrombolysis and/or pharmacomechanical thrombolysis, and finally, angioplasty and stenting; after this, the rate of PTS is less than 10%; without treatment it is 80% to 90%.[12,20,62]
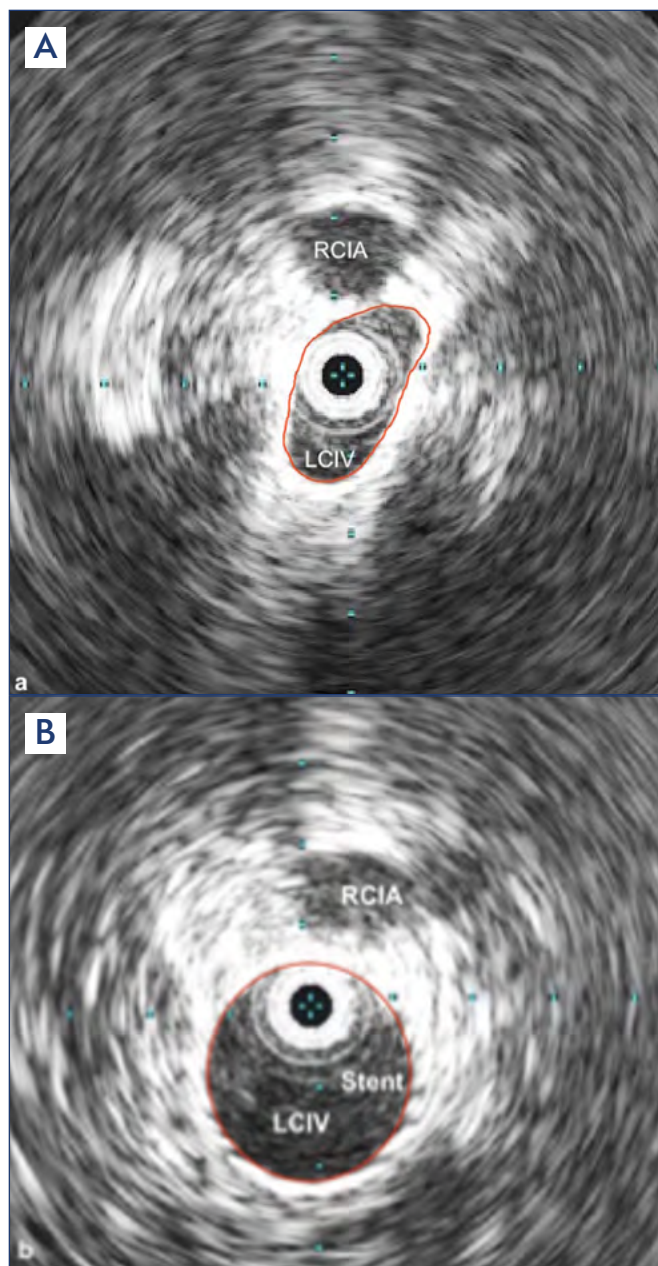
Figure 4. Intravascular ultrasound (IVUS). A) Stenotic left common iliac vein, compressed by right common iliac artery. B) Left common iliac vein, stented.

Abbreviations: LCIV, left common iliac vein; RCIA, right common iliac artery.

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4) In patients with thrombotic MTS with contraindications to lytic therapy, mechanical (suction) thrombectomy or open surgical thrombectomy are indicated, then angioplasty and stenting.[12,18,20,62,64] Application of IVC filter is not recommended unless an IVC thrombus is present.[5,12,13,18]

The endovascular approach begins as follows: 1) a presumptive MTS based on clinical suspicion; 2) CDVU with the Zamboni maneuver to avoid an illusory image[56]; then, either CT venography or MR venography; 3) venography and IVUS to demonstrate and confirm the degree of LCIV stenosis, the affected vein stenosis segment; and finally, 5) stenting (*Figure 3B*).[12,13,18,43,64]

DVT and PTS are 2 of the clinical maladies more visible in angiology practice; it is estimated that PTS develops in 20% to 50% of DVT cases.[65] However, the risk is greatest after thrombosis in the iliofemoral region. Alternatively, obstructive chronic deep venous disease can occur owing to NIVL, of which MTS is an example.

Imaging studies showed that NIVL can be present in 24% of asymptomatic patients and up to 60% of patients with chronic deep venous disease. The development of improved endovascular skill sets in various specialties treating venous diseases has led to the offering of endovascular treatment in outpatient clinics; also, the availability of dedicated venous stents is a factor in this enthusiasm for the treatment of venous outflow obstruction.

The use of self-expanding stents for the treatment of venous outflow obstruction was reported by Drs Neglen and Raju more than 20 years ago. Their described technique included the use of the venous Wallstent endoprosthesis stent (Boston Scientific Corporation), a braided, self-expanding stent composed of Elgiloy (a cobalt-chromium-nickel alloy).[66]

Although the venous Wallstent was not initially designed as a venous stent, its large diameters, compression (crush) resistance, radial force, and fracture resistance lent itself well to venous stenting.[67]

The Wallstent is the stent most used in the United States. It improves patency and symptoms compared with angioplasty alone. However, it has a high rate of recoil and significant foreshortening (83.75%) when deployed, making it difficult to position accurately at the compression site; for this, the proximal landing zone must be 3 to 5 cm in the IVC.[22,68-70] Clinical experience with the Wallstent in the iliofemoral venous region in the last 2 decades showed its efficacy as reported in one of the largest retrospective studies, including 982 lesions; the 5-year primary patency, assisted-primary patency, and secondary cumulative patency rates were 79%, 100%, and 100% in nonthrombotic disease and 57%, 80%, and 86% in thrombotic disease, respectively.[22,68,69] The last several years have witnessed the shift from use of the Wallstent alone to a combination of Wallstent and Z stent (Cook Medical)–a composite stent. This approach enables better handling of the iliocaval confluence, and the overall patency seems to be comparable with the use of Wallstents alone. Additionally, use of the composite stent configuration not only decreases the need for contralateral stenting from chronic obstruction, but also decreases the incidence of contralateral iliofemoral deep venous thrombosis; this result argues for the use of a composite stent configuration in patients undergoing iliofemoral venous stenting as opposed to Wallstents alone; it will allow for comparison of outcomes with the use of dedicated venous stents.[71]

Dedicated venous stents were developed to overcome the Wallstent problems. Nitinol stents do not foreshorten as much as the Wallstent; the implanted length should be near nominal of the intended when sized properly, so the foreshortening is not significant, providing a more accurate positioning of the stent.[22,70,72] Hence, nitinol stents are not put in the IVC. Several of these stents have good outward and compression radial force and crush resistance. There is no comparative data between the Wallstent and the new nitinol stents with relation to patency and target-lesion revascularization; the stent must be large enough to bypass the stenotic area, and the distal landing zone has to be wide enough to avoid blood flow perturbations.[68]

There is no comparative data between venous stents following angioplasty and stenting for MTS.[22]

The ideal venous stent would be adaptable to a variety of venous anatomic features, available in a wide range of diameters and lengths, strong and able to resist both recoil and compressive forces, flexible and able to negotiate the curves of the venous anatomy in the pelvis without kinking or distorting the vein, durable and able to withstand repetitive movement without loss of integrity, and able to offer accurate and precise deployment at both the stent ends. By the year 2021,[67,70] the US Federal Drug Administration (FDA) had approved 5 dedicated venous stents; but 2 withdrew voluntarily, allegedly due to issues with stent deployment and migration (Vici and Venovo). Hence, nowadays, there are 3 brands available: Wallstent (Boston Scientific), Zilver (Cook), and Abre (Medtronic).[67]

The Zilver Vena stent has a distinctive venous-specific design; it has flexibility, kink resistance, and balanced radial force, giving it conformability in venous anatomy. There is no stent foreshortening beyond 5 mm, and a stent length up to 14 cm is available, suitable for stenting the diseased venous

segments with 1 or 2 stents only from CIV to common femoral vein. There would be no need to extend through the IVC. Mohamed-Salem et al report a 5-year experience using the Zilver Vena stent in 58 patients.[73] In the follow-up, primary, assisted primary, and secondary patency of 60.3%, 65.5%, and 81% were observed, respectively; they concluded that the Zilver Vena stent is a good choice and is noninferior to the Wallstent with respect to 1-year and 5-year patency and provides good clinical improvement.[73]

The most recent dedicated venous stent approved by the FDA is the Abre (Medtronic), supported by a multicenter, prospective, nonrandomized, single-arm international study in patients with symptomatic iliofemoral venous outflow obstruction (IFVOO). The Abre venous self-expanding nitinol stent has an open-cell structure tailored to perform in the iliofemoral veins. The primary objective of the study was to evaluate the safety and effectiveness in patients with symptomatic IFVOO. The study included 200 patients from 24 international study centers between the years 2018/2019 and the follow-up at 12 months.

Venous obstruction was classified as acute DVT (16.5%, 33/200), PTS (47.5%, 95/200), or NIVL (36.0%, 72/200). Primary patency at 12 months was 88.0% (162/184). Twelve-month primary-assisted and secondary patency were 91.8% (169/184) and 92.9% (171/184) respectively. Mean target limb Villalta score decreased from 11.2±5.6 at baseline to 4.1±4.8 (88/200) at 12 months. The authors concluded that symptomatic IFVOO can be successfully treated with an Abre venous stent; the study showed a high patency rate with a good safety profile, and patients had a significant reduction in clinical symptoms and improvement in QOL through 12-month follow-up.[74]

The success or failure of a venous outflow intervention does not end with stent placement; there is no comparative data between venous stenting after angioplasty and stenting for MTS.[22] In PTS patients, oral anticoagulation for at least 6 to 12 months or indefinitely in patients with a history of DVT or thrombophilia is indicated.[12,22] For nonthrombotic MTS, compression, antiplatelets or anticoagulants or both are used. There is no randomized controlled trial (RCT) comparing these antithrombotic strategies.[12,22,75-77.] There is no comparative

data between direct oral anticoagulants and warfarin in postvenous stenting.[22,78]

Finally, after successful iliac stenting solving leg venous hypertension, compression stockings are no longer needed.[79.]

So far, most studies on follow-up QOL after endovascular treatment have relied on the Villalta score—useful but partial in describing some important factors—and the adoption of the VEINES-QOL classification (VEnous INsufficiency Epidemiological and economic Study on Quality of Life), which is the most validated venous disease–specific measurement scale nowadays. Several authors have reported their results and generally agree that QOL improved significantly after the endovascular treatment either in thrombotic or in NIVL, and this improvement is sustained for years.[80-84]

Conclusion

MTS is underdiagnosed; hence, when evaluating patients with left leg DVT, it should be considered. Early diagnosis and adequate treatment are paramount; so, clinical presentation and imaging findings can help. Venography and IVUS are now the gold standard for precise diagnosis and treatment. The minimal invasive endovascular treatment is now first choice: in thrombotic iliac vein occlusion, pharmacomechanic thrombectomy, angioplasty, and stenting will minimize morbidity of PTS; in NIVL, stenting has showed better patency rates on long-term follow-up. The venous stents in use now are near the ideal of what a prosthesis must be; and very-long-term results are in progress. Overall, MTS and its variants will be a subject of continuous research in coming years, so, we will see whether the MTS eponym is still used as time goes by.

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Endovenous laser ablation or radiofrequency ablation for varicose veins: a review

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Abstract

Varicose veins are a part of chronic venous insufficiency syndrome, presenting with dilated veins, skin changes, and even ulceration in the lower limbs. Untreated, it can result in many complications and has an impact upon one's quality of life. Management depends upon the stage and etiology of varicose veins. Conventional vein stripping surgery is now being replaced by minimally invasive modalities, among which endovenous laser ablation (EVLA) and radiofrequency ablation (RFA) are the mainstays of treatment. Each procedure has its own sets of procedural technique, variants, performance, outcomes, and complications. Here, we discuss the various aspects of EVLA and RFA on varicose vein treatment.

Introduction

Varicose veins are dilated tortuous veins that have significant impact on a person's quality of life (QOL).[1] For ease of communication, clinical-etiology-anatomy-pathophysiology (CEAP) classification is used to clinically classify varicose veins.[2] Treatment of varicose veins ranges from conservative management, pharmacotherapy, endovenous treatments, and surgery.

The size of the affected vessels determines the treatment modality—spider telangiectasias and reticular veins are best treated with foam sclerotherapy, thermocoagulation, and cutaneous lasers, whereas larger varicosities are preferably treated with surgery and microinvasive procedures, such as endovenous laser ablation (EVLA) and radiofrequency ablation (RFA).[3] Nonthermal ablation techniques include sclerotherapy, glue, mechanochemical ablation (MOCA), and steam. They provide an advantage to patients with below-the-knee disease, owing to less risk of nerve injury or skin burn. MOCA is a hybrid process of using mechanical trauma and simultaneous sclerotherapy to ablate and treat varicose veins.[4] Intradermal, subcutaneous, and perforator veins can be treated by chemical ablation of a varicose vein by intravenous injection of liquid or foam sclerosant via a method known as sclerotherapy.[5] Cyanoacrylate glue can be used to ablate vessels as it polymerizes on contact with blood, causing vessel inflammation and fibrosis and occlusion, whereas

the steam technique works via steam applied through the catheter canal, which releases thermal energy, causing vessel ablation and sclerosis.[6] These are emerging technologies that are being explored for their use in varicose veins.

Owing to complications, such as bruising, postoperative pain, anesthesia complications, hematoma, saphenous nerve injury, and wound infection, conventional surgical stripping is gradually being replaced by new minimally invasive techniques like EVLA and RFA.[7] Relevant contraindications of EVLA and RFA include an incompetent superficial vein diameter of less than 2 mm, history of extensive deep venous thrombosis (DVT) in the same leg, active superficial venous thrombosis in the vein to be treated, history of a prior surgical or endovenous treatment of the same leg, pregnancy, known malignancy and systemic conditions resulting in overall poor health, frailty, immobility, and known bleeding or clotting disorders.[8] Various scores are used for assessment of severity and impact of varicose veins such as the Aberdeen Varicose Vein Questionnaire (AVVQ), the Aberdeen Varicose Vein Severity Score (AVVSS), the Chronic Venous Insufficiency Questionnaire (CIVIQ-2), health-related QOL (HRQOL), the Venous Clinical Severity Score (VCSS), and the Visual Analog Scale (VAS) for pain. We have described some of the outcomes with these scores.

Although both EVLA and RFA follow the principle of thermal ablation of varicose veins, there are fundamental differences in mechanism of ablation, devices used, procedure, outcomes, and complications. Here we discuss the principles and differences between EVLA and RFA techniques for the treatment of varicose veins.

Endovenous laser ablation

EVLA is a minimal invasive procedure in which a percutaneous laser fiber is introduced within the incompetent varicose vein resulting in nonthrombotic occlusion and inflammation of the vein.[7] The major mechanism of EVLA is the conversion of absorbed light energy into heat either through direct absorption of the laser power emitted from the fiber into the blood and perivenous tissues or through direct contact between the fiber tip and the vein wall.[9]

EVLA is indicated in an ambulatory patient with great, small, or accessory saphenous vein reflux with surface varices, and/or symptoms or complications related to superficial venous insufficiency. It can be used in all stages of varicose veins.[10] Studies have shown better resolution of venous ulcers with EVLA. So, for stage C5 and C6 varicose veins, EVLA is generally

preferred over RFA.[7] EVLA can also be done in tributaries of sufficient length.[11]

Operative procedure

Although it is a common practice to have an institutional operative protocol for EVLA and RFA, it's mainly based on steps learned during training and on publications mentioning the procedures. The protocol is often tailored to the institution based on the experience with the procedures. Preoperative planning for these procedures along with access site determination is generally done by mapping the hemodynamic status of the veins via an ultrasound before and during the procedure.

EVLA is routinely performed using dilute local anesthesia, with or without supplemental oral anxiolytics, in an office setting. Buffered local tumescent anesthesia, especially cold tumescence, along with general anesthesia (GA) has shown improved immediate postoperative pain in EVLA compared with GA only.[12-14] Bupivacaine used in tumescent solution had a better outcome than the use of lidocaine and prilocaine.[15]

Generally taking 30-60 minutes to perform, procedure times are dependent on the length of segment treated, experience of the operator, and whether ancillary procedures, such as ambulatory phlebectomy, are done.[10] For better results, it is necessary to empty the veins by external compression and Trendelenburg positioning.[16,17] After positioning, the great saphenous vein (GSV) is cannulated by EVLA laser fiber. A study mentioning protocol on EVLA mentions 100 J/cm delivered empirically to the first 3 cm distal to the saphenofemoral junction (SFJ) and 40 J/cm in remaining segments.[18] Regardless of how underlying saphenous incompetence is treated, ancillary treatments, such as sclerotherapy and phlebectomy, along with compression, are typically needed to treat residual varices.[10]

The use of elastic compression stockings after EVLA has shown reduced severity of pain and edema postoperatively.[19,20] Use of compression stockings for longer than 2 days and eccentric compression applied by a new crossed-tape technique is suggested after the procedure.[21,22]

Endovenous laser ablation variants

Commonly used laser ablator devices are the Biolitec laser machine (Biolitec), VenaCure EVLT System (Angiodynamics), Diomed D15plus (Diomed, Inc., Andover, MA), etc.[7] A popular dedicated laser fiber for EVLA has a wavelength of 1470 nm, 980 nm, 940 nm, or 840 nm in power settings of 3-12

watts. Pullback speed is adjusted to 1-4 mm/s. Thus, the combination of higher power and lower pullback velocity leads to maximum burn of the veins. Maximum temperature ranges from 91 °C to 97 °C. EVLA using a shorter wavelength (usually 980 nm) has a higher temperature by about 10 °C.[9]

Different variants of treatment with EVLA have been explored through various randomized controlled trials (RCTs) and other studies (*Table I*).[13-15,19-42] When contrasting different

methods of EVLA, in relation to the fibers, lesser induration and lesser postoperative pain along with better VCSS score was seen with higher wavelength of EVLA than with lower wavelength EVLA.[28,29,41] However, a higher chance of superficial thrombophlebitis was seen more with EVLA 1470 nm than EVLA 940 nm.[40] Reduced chance of postoperative ecchymosis and pain was seen with the EVLA tulip fiber.[30] In a study of EVLA wavelengths, at 4 weeks, both laser wavelengths were successful in curing GSV insufficiency (810 nm and

Study No.	Author	Summary
1	Kabnick et al,[23] 2006	A single-center study on primary incompetence of the GSV (51 patients) showed both using an 810-nm and 980-nm diode EVLA laser, both bare fiber, and continuous withdrawal with tumescent anesthesia, to be effective in treating insufficiency with no major complications.
2	Disselhoff et al,[24] 2008 Disselhoff et al,[25] 2011	A multicenter study on bilateral GSV incompetence (43 patients; 86 limbs, C2 stage) did not show a difference between high ligation and without ligation of saphenofemoral junction in terms of groin recurrence and VCSS improvement at 2 and 5 years.
3	Theivacumar et al,[26] 2008	A monocenter RCT with primary GSV incompetence with SFJ incompetence (68 lower limbs, C2 to C6 stage) treated with EVLA (in local tumescent anesthesia) in above- and below-knee reflux showed improved AVVSS without saphenous nerve injury in below-knee EVLA.
4	Lugli et al,[22] 2009	A monocenter RCT on primary GSV insufficiency (200 patients, C2 to C6 stage) showed reduced postoperative pain in a group receiving eccentric compression by a crossed-tape technique after EVLA.
5	Hogue et al,[27] 2008	A multicenter study on primary GSV insufficiency (75 patients) showed venous dilatation easing targeted venous access for EVLA after pretreatment with topically applied nitroglycerin ointment (2%).
6	Doganci et al,[28] 2010	A monocenter RCT on primary GSV insufficiency (60 patients; 106 lower limbs, C2 to C4 stage) showed lesser postoperative pain and better VCSS scores with the use of an EVLA 1470-nm radial fiber than with a 980-nm bare tip fiber.
7	Pannier et al,[13] 2010	Multicenter study with GSV primary incompetence in 85 lower limbs. EVLA with cold tumescence anesthesia (5 °C) showed reduced postoperative pain and analgesic intake in comparison with warm tumescence anesthesia (37 °C). No difference in terms of occlusion was seen in 1-month follow-up.
8	Dumantepe et al,[14] 2015	Multicenter study with GSV primary incompetence in 101 patients. Cold tumescence anesthesia (8 °C) showed reduced postoperative pain intensity, analgesic intake, and significant reduction in side effects compared with warm tumescence anesthesia (24 °C). No difference in terms of occlusion was seen in 1 week of follow-up.
9	Vuylsteke et al,[29] 2011	A multicenter RCT on primary GSV insufficiency (180 lower limbs without SSV incompetence, C2 to C6 stage) showed lesser induration, analgesics, and better HRQOL in group undergoing EVLA with a 1500-nm compared with 980-nm bare tip fiber in local tumescent anesthesia. There was no difference in terms of occlusion.
10	Vuylsteke et al,[30] 2012	A multicenter RCT on primary GSV incompetence (174 patients without SSV incompetence, C2 to C6 stage) showed less postoperative ecchymosis, less pain, and better HRQOL with use of a tulip fiber with EVLA 1470-nm diode bare fiber than with bare fiber alone. However, there was no difference in obliteration rate.
11	Bakker et al,[21] 2013	A multicenter study on primary GSV incompetence (109 patients, C2 to C5 stage) showed better pain reduction with use of 7 days of postoperative compression therapy (stockings, 35 mm Hg at ankle) compared with 2 days of compression after EVLA.

Study No.	Author	Summary
12	Bogachev et al,[31] 2019	A monocenter study on primary GSV or SSV insufficiency (1519 patients, C2 stage) treated by endovascular thermal ablation showed reduced local adverse effects in group with perioperative administration of venoactive substance (micronized purified flavonoid).
13	Stoiko et al,[32] 2015	A monocenter study on primary GSV insufficiency (60 patients, C2 stage) treated by endovascular thermal ablation showed reduced pain and faster restoration of motor activity in a group with perioperative administration of a venoactive substance (micronized purified flavonoid).
14	Ayo et al,[33] 2017	A monocenter study on primary GSV varices (70 patients) treated with high compression (30-40-mm Hg) 24 hours after the procedure for 7 days showed no significant difference in patient-reported outcomes of postprocedural pain after endovenous ablation.
15	Nandrah et al,[34] 2018	A monocenter study on primary GSV insufficiency (97 patients, C2 to C6 stage) treated by endovascular thermal ablation showed lower pain score and analgesic use with use of buffered tumescent anesthesia.
16	Ye et al,[19] 2016	A monocenter study on primary incompetence of GSV (400 patients) treated with EVLA showed less postoperative pain and edema with use of high elastic compression for 2 weeks (23-32 mm Hg at ankle).
17	Elderman et al,[20] 2014	A multicenter study on primary incompetence of GSV (79 patients) with incompetence of the SFJ showed less postoperative pain and less analgesic requirement until day 14 with the use of high elastic compression.
18	El-Sheikha et al,[35] 2014	A monocenter RCT on primary incompetence of GSV (50 patients) treated with delayed and concomitant phlebotomy after EVLA revealed more need of a secondary procedure with delayed phlebotomy at 5 years.
19	Carradice et al,[36] 2009	A monocenter RCT on primary incompetence of GSV (50 patients) treated with delayed and concomitant phlebotomy after EVLA revealed reduced need for a secondary procedure with concomitant phlebotomy.
20	Samuel et al,[37] 2013	A monocenter RCT on primary GSV insufficiency (76 patients, C2 to C5 stage) showed better long-term venous occlusion and lowered recurrence rates without increasing postoperative morbidity using EVLA in 14 W continuous power settings compared with 12 W laser pulse setting.
21	Flessenkämper et al,[38] 2013 Flessenkämper et al,[39] 2016	A multicenter RCT on primary GSV incompetence (349 patients, C2 to C6 stage) showed lesser pain and lesser inguinal reflux in GSV with high ligation and stripping compared with EVLA and EVLA with high ligation at 2 months follow-up, but clinical recurrence of reflux was similar in all groups at 6 years follow-up.
22	Malskat et al,[40] 2016	A monocenter RCT on primary GSV insufficiency (142 patients) showed lesser pain with use of 1470-nm than with 940-nm tulip tip fiber EVLA. But more superficial thrombophlebitis was observed with use of a 1470-nm laser.
23	Hirokawa et al,[41] 2015	A multicenter RCT on primary GSV or SSV insufficiency (113 patients) showed lesser pain with use of 1470-nm radial 2 ring EVLA than with 940-nm bare type fiber EVLA.
24	Gunes et al,[15] 2015	A multicenter study on primary incompetence of GSV (90 patients) had a reduced intraoperative and 1-day postoperative pain with use of bupivacaine in tumescent solution compared with lidocaine and prilocaine.
25	Mendes-Pinto et al,[42] 2016	A multicenter study on primary GSV insufficiency (67 patients, 90 extremities) showed less ecchymosis, induration, and analgesic use with use of 1920-nm EVLA (5-W power) than with 1470-nm EVLA (10-W power). However, the closure rate was lower with 1920-nm EVLA at the end of 1 year.

Table I. Endovenous laser ablation (EVLA) outcomes.

AVVSS, Aberdeen Varicose Vein Severity Score; EVLA, endovenous laser ablation; GSV, great saphenous vein; HRQOL, health-related quality of life; RCT, randomized controlled trial; SFJ, saphenofemoral junction; SSV, short saphenous vein; VCSS, Venous Clinical Severity Score.

980 nm), and 1 study also showed that below-knee EVLA was not associated with saphenous nerve injury.[23,43] Also, EVLA done with nitroglycerin produced a statistically significant venous dilatation, easing targeted venous access.[27]

The limitation of EVLA is the need for uniform pullback or adjustable pullback for segments with perforators in varicose veins, which is difficult to standardize. This can result in incomplete burning or excessive burning.[9]

Radiofrequency ablation

RFA involves insertion of the RFA catheter inside the varicose vein that causes spasm of the vessel, ablation of endothelium of the vessel, and complete closure of the defective vein.[44] Radiofrequency waves are electromagnetic energy within a frequency range of 300 kHz to 1 MHz. The wave causes vibration and friction of atoms, resulting in thermal energy. The procedure was introduced in 1999; since then, the procedure has been gaining widespread acceptance and availability.[11]

RFA can be used in all stages of varicose veins; but in stage C5 and C6, RFA is found to be slightly inferior to EVLA.[7] Also, RFA can be combined with concomitant phlebectomy of tributaries.[45] Major advantages of this technology are cosmetically better procedures, less pain, early return to work, less scar, and less chance of infection.[46]

Operative procedure

Preoperative mapping is done as for EVLA, and access site is determined. RFA too can be done under general, regional, or tumescent local anesthesia (under ultrasound guidance), and the Trendelenburg position can be used to achieve maximum vein collapse. The distance between the RFA catheter tip and SFJ should be at least 2 cm, and tumescent anesthesia is injected between GSV and skin with ultrasound guidance. There is a "standard technique," where heating treatment is done at 85 °C, in which the first 5.0 cm of saphenous vein is ablated at 1.0 cm per minute followed by the remainder of the GSV being ablated at 1 cm per 30 seconds, or "modified technique," in which the first 5.0 cm of saphenous vein is heated and ablated at 1.0 cm per minute with the generator set at 90 °C after which the catheter is slowly and continuously pulled back at a rate of 1 cm per 20 seconds, which maintains a vein wall temperature of 90 °C. In both techniques, there is 0.5-cm overlap of each pair of segments, and the pullback is continuous until the desired vessel length is treated. When the final segment is treated, pulling off the heating element of the catheter into the sheath is avoided because it might melt

the sheath. Usually, double ablation is done in the segment 2 cm distal to the SFJ, and adjunct sclerotherapy is done for residual veins.[47]

There have also been studies on the use of venoactive drugs during the perioperative period to reduce pain and enhance recovery.[32] Use of micronized purified flavonoid fraction (MPFF)—a venoactive drug—in the perioperative period showed reduction in pain, ecchymosis, paresthesia, pigmentation and heat-induced thrombosis, and enhanced recovery after endovenous ablation.[31,32]

In recent trials, postoperative compression by superposition of stocking class I and class II after RFA under local tumescent anesthesia when done for 4 hours had lesser complications and greater reduction in leg volume then compression for 72 hours; there was no difference in venous occlusion, postoperative pain, and time to full recovery with and without postoperative compression in RFA.[33,48-50]

Radiofrequency ablation variants

Popular RFA generator devices are the ClosureFast RFA system (Medtronic) preceded by the ClosurePlus catheter, Olympus Celon RFITT (Olympus Medical Systems, Hamburg, Germany), and CelonLab POWER radiofrequency generator (Celon AG Medical Instruments, Teltow, Germany).[7,11,51] One popular RFA device is the VNUS ClosureFast device that uses RFA catheters of 60- and 100-cm lengths and which has a heating segment of 7 cm. The temperature attained during RFA is 120 °C with a duration of 20 seconds. Usual watt requirement is 10 to 20 watts. The second generation of RFA catheters, the ClosureFast was designed to improve on procedural deficiencies such as length of time and ease of the procedure. They use a segmental approach to ablation and involve activating the heating element for 20-second cycles. The heat is then automatically shut off, and the catheter is repositioned to the next treatment zone indicated by shaft markers on the catheter. The new catheter also no longer needs the saline drip and eliminates the high impedance issues caused by coagulum build up with the previous catheter. The segmental approach, sometimes referred to as segmental RFA ablation also speeds up the procedure and decreases the variability in dose delivered to the tissue. The new design also involved changes in the method of energy delivery in that the energy field was now shielded and an electrical field is not produced in the tissue, thereby reducing the potential concerns for interference with other indwelling devices, such as pacemakers, etc.[52] They are very accurate to attain 120 °C within 3 seconds by varying wattage from 15 to 40 watts. Any deviation from this watt

range and temperature will stop the radiofrequency cycle and will prompt a warning. This allows RFA to be more uniform and safer during the procedure.[11]

Various studies have compared different RFA devices and their outcomes (*Table II*).[45,48-50,53-55] When different RFA technologies—VeneFit, radiofrequency induced thermal therapy (RFITT), and endovenous radiofrequency (EVRF)—were compared, mean treatment time was faster in RFITT; pain score/discomfort at 2 weeks differed in that fewer in the EVRF group reported no problems. However, there was no difference in clinical outcome when compared at 6 and 12 months. Truncal ablation failure at 12 months was lesser with VeneFit.[55] Comparisons have also been made between direct RFA (dRFA; radiofrequency-induced thermotherapy) and

indirect RFA (iRFA; VNUS ClosureFast) in which primary GSV occlusion rates were better after iRFA and EVLA than with dRFA.[53] In another study, the F-care (EVRF, F Care Systems, Antwerp, Belgium) method was safe and fast, but the 1-year closure rate was significantly lower than with the conventional endovenous RFA ClosureFast method.[54]

The limiting factor for RFA is the need for a special setup including RFA generator and RFA catheter, which is costly relative to conventional open surgery. Also, it takes special training and familiarization with the setup and technique to properly perform surgery. There is a learning curve, with possibility of minor to major complications.[46] RFA can only be done in the main saphenous system, such as GSV and short saphenous vein, and not in the tributaries.[11] Veins that are too

Study No.	Authors	Summary
1	Lane et al,[45] 2015	Single-center study on both GSV and SSV varicose veins (111 patients) comparing delayed phlebectomy and simultaneous phlebectomy shows VCSS score improvement in simultaneous phlebectomy.
2	Hamann et al,[53] 2019	A single-centered study with 451 symptomatic primary GSV has divided the participants into 3 groups—EVLA, dRFA, and iRFA—and found similar treatment results in symptom improvement, but patients who underwent EVLA had a higher adverse event rate than the other two groups. AVVQ shows significantly better score for iRFA than dRFA.
3	Krasznai et al,[50] 2016	A multicenter study with 101 symptomatic patients reported 4 hours of postoperative compression by superposition of stocking class I and class II had lesser complications and greater reduction in leg volume than compression for 72 hours, but no difference in postoperative pain and time to full recovery.
4	Bitargil et al,[54] 2020	A monocenter study on symptomatic primary incompetent GSV (114 patients) showed higher occlusion rates with ClosureFast and Covidien than with endovenous radiofrequency, F-care systems, and continuous pullback.
5	Pihlaja et al,[49] 2020	In a multicenter RCT with 117 patients presenting with primary GSV and/or SSV varices treated with RFA ClosureFast with complementary UGFS of incompetent tributary, there was no difference in postoperative pain and full physical activity, with comparable AVQQ at 6 months in groups with and without the use of postoperative compression after RFA.
6	Nyamekye et al,[55] 2019	When different RFA technologies—VeneFit, RFITT, and EVRF—were compared for primary GSV incompetence (180 patients), the mean treatment time was faster in RFITT, pain score/discomfort differed in that fewer in the EVRF group reported no problems at 2 weeks, and truncal ablation failure at 12 months was lesser for VeneFit. However, there was no difference in clinical outcome and AVVQ.
7	Onwudike et al,[48] 2020	A multicenter RCT on primary GSV/SSV varices (100 patients, C2 to C6 stage) showed no difference in pain and vein occlusion with and without the use of compression stockings after RFA.

Table II. Radiofrequency (RFA) outcomes.

AVVQ, Aberdeen Varicose Vein Questionnaire; dRFA, direct radiofrequency ablation; EVLA, endovenous laser ablation; EVRF, endovenous radiofrequency; GSV, great saphenous vein; iRFA, indirect radiofrequency ablation; RCT, randomized controlled trial; RFA, radiofrequency ablation; RFITT, radiofrequency induced thermal therapy; SSV, short saphenous vein; UGFS, ultrasound-guided foam sclerotherapy; VCSS, Venous Clinical Severity Score.

small or tortuous for catheter access or too large to successfully ablate would not be appropriate for treatment via RFA.[52]

Discussion

Both EVLA and RFA are shown to be comparable to conventional vein stripping surgery and are advantageous in terms of being minimally invasive, with lesser postoperative complications. Many studies have been done comparing various aspects of EVLA and RFA, addressing pros and cons of both (*Table III*).[53,56-63] Although there were no sharp demarcations regarding use of EVLA and RFA preferencing one over the other, we have tried to explore their differences and variations in use (*Table IV*).[7,9,11,16,17,56,64]

Study No.	Authors	Summary
1	Almeida et al,[56] 2009	Comparison between RFA ClosureFast and EVLA Diode 980-nm bare fiber in 87 primary incompetent GSVs (69 patients), both in local tumescent anesthesia, showed lower scores related to pain, ecchymosis, and tenderness in RFA, low VCSS and HRQOL measures in EVLA, with more prevalent minor complications in EVLA. No difference was observed in postoperative vein occlusion and truncal reflux elimination.
2	Shepherd et al,[57] 2010	Comparison between RFA ClosureFast and EVLA Diode 980-nm bare fiber in 131 patients with primary incompetent GSV and some with SSV incompetence and/ or deep venous disease (CEAP C2-C6), both in general anesthesia, showed lesser postoperative pain with RFA with no difference in HRQOL.
3	Gale et al,[58] 2010	RCT: Comparison between RFA ClosurePlus and EVLA Diode 980-nm bare fiber in 141 primary incompetent GSV (118 patients), both under local tumescent anesthesia, showed less bruising and pain with RFA at 1 week but no difference at 1 month. VCSS score was higher in RFA with more frequent recanalization at 1 year.
4	Goode et al,[59] 2010	RCT: Comparison between unilateral (45 limbs) and bilateral (17 limbs) primary incompetent GSV using Celon RFITT RFA ClosurePlus (23+17 limbs) and EVLA Diode 980-nm bare fiber (22+17 limbs), both under general anesthesia, showed less postoperative pain and bruising with RFA in the bilateral disease goup but no difference in the unilateral disease group.
5	Nordon et al,[60] 2011	RCT: Comparision between RFA ClosureFast and EVLA Vari-Lase Bright tip 810-nm bare fiber in 159 primary incompetent GSV, both under general anesthesia, showed less bruising and pain with RFA at 1 week, but 2 GSV reopened in the RFA group and 2 in the EVLA group at 3 months.
6	Shepherd et al,[61] 2015	RCT: Comparision between RFA ClosurePlus and EVLA Diode 980-nm bare fiber in 110 patients with primary incompetent GSV, both under general anesthesia, showed significant gain in QOL and clinical improvements with both procedures. EVLA was more likely to be cost-effective than RFA but had very small absolute differences in costs and HRQOL.
7	Bozoglan et al,[62] 2016	A multicenter study comparing RFA and EVLA in 60 patients with bilateral primary incompetent GSV, both under local anesthesia, showed less pain, analgesic requirement, time to return to activity and work, with lesser minor complications with RFA though not statistically significant.
8	Sydnor et al,[63] 2017	RCT: A multicenter study comparing RFA and EVLA in 200 patients with bilateral primary symptomatic GSV insufficiency (CEAP C2-C6), both under local anesthesia, showed less pain and bruising with EVLA but no difference in VCSS scores. At 1 year, no superiority of one over the other was found in anatomic and clinical end points.
9	Hamann et al,[53] 2019	RCT: Comparison between EVLA Diode 980-nm bare fiber continuous pullback, dRFA, and iRFA showed more adverse events with EVLA. AVVQ scores were better with iRFA, but no difference between the procedures was observed for VCSS scores.

Table III. Comparison between endovenous laser ablation (EVLA) and radiofrequency (RFA) for varicose veins.

AVVQ, Aberdeen Varicose Vein Questionnaire; dRFA, direct radiofrequency ablation; EVLA, endovenous laser ablation; EVRF, endovenous radiofrequency; GSV, great saphenous vein; HRQOL, health-related quality of life; iRFA, indirect radiofrequency ablation; QOL, quality of life; RCT, randomized controlled trial; RFA, radiofrequency ablation; RFITT, radiofrequency induced thermal therapy; SSV, short saphenous vein; VCSS, Venous Clinical Severity Score.

Heading	EVLA	RFA
Technicalities	Laser fiber is used in EVLA. Pullback speed is adjusted to 1-4 mm/s. Thus, combination of higher power and lower pullback velocity leads to maximum burn. For better results, it is necessary to empty the veins by external compression and Trendelenburg positioning.[16,17]	RFA catheter is used, and the vein segments are burned one at a time. Pullback technique is not used.
Mechanism of action	Conversion of laser light energy into heat during absorption of the light.[9,64]	Electromagnetic waves cause a vibration and friction of atoms resulting in thermal energy.[11]
Preferred patient selection	Can be used in all stages of varicose veins. EVLA can also be performed in veins underneath venous ulcers.	Can be used in all stages of varicose veins, but in stage C5 and C6, RFA is found to be slightly inferior to EVLA.[7]
Major strengths	Better resolution of venous ulcers. So, for stage C5 and C6, EVLA is generally preferred over RFA.[7] EVLA can also be done in tributaries of sufficient length.[11] EVLA can also be done in selected tributaries.	RFA of varicose veins is more uniform and safer during the procedure because any deviation from set wattage and temperature will stop the RF cycle.[11] In large trials comparing RFA and EVLA, such as the RECOVERY trial, postoperative pain, ecchymosis, and swelling were lower in RFA.[11,56]
Weakness	Need uniform pullback or adjustable pullback for segments with perforators, which is difficult to standardize. This can result in incomplete burning or excessive burning.[9]	Ulcer resolution using RFA has been found to be inferior to EVLA.[7] Chances of deep venous thrombosis and pulmonary embolism are slightly higher with RFA than with EVLA.[7] RFA can only be done in the main saphenous system, such as in the great saphenous and short saphenous vein, and not in the tributaries.[11]

Table IV. Major details on endovenous laser ablation (EVLA) and radiofrequency (RFA).

EVLA, endovenous laser ablation; RECOVERY, Radiofrequency Endovenous ClosureFAST versus Laser Ablation for the Treatment of Great Saphenous Reflux trial; RF, radiofrequency; RFA, radiofrequency ablation.

Cost

RFA and EVLA have the extra upfront cost of the generator and cost per case for disposables. In some cases, these can be done outside the operation theater without anesthetist or surgical assistant fees.[52] RFA performed in the operating room was associated with net loss per case vs office-based interventions.[65] However, even though the initial setup cost was high, a cost analysis from hospitals in Michigan show that in the long run, treatment with vein stripping was associated with higher costs than RFA and EVLA. Another cost-effective analysis from the United Kingdom also showed that RFA had the highest median rank for net benefit, with MOCA second and EVLA third among varicose vein treatment options.[66] In low-resource settings, reusing the RFA catheter can also be one means for cost cutting. A study from India has shown promising results in terms of vein occlusion rates and cost cutting when the RFA catheter was reused.[67] Further studies on catheter-based interventions in an office setting and on reuse of catheters can significantly reduce the cost for treatment.

Technicalities

Although RFA and EVLA both cause thermal ablation, the mechanism of action and resulting technicality of thermal ablation is different between these 2 techniques. RFA causes a circular, homogeneous lesion, and there is no perforation of the venous wall. Whereas in laser ablation, the light energy is transmitted into heat energy, causing vascular wall disruption and venous wall perforation. The difference was studied in multiple experimental studies.[68,69] These could be the reasons for lesser postoperative pain in RFA patients. Also, RFA seems to be more dependent on adequate vein emptying, use of tumescent anesthesia, and compression techniques than EVLA techniques, which do not depend on vein wall contact.[52] But for even better results after EVLA, it was necessary to empty the

veins by external compression and Trendelenburg positioning in EVLA too.[16,17] Use of buffered tumescent anesthesia (to physiologic pH) has shown lower pain scores and analgesic use after endovascular procedures.[34]

In relation to ease of procedure and uniformity of the ablation, RFA is much more comfortable than EVLA as there is a segmental approach of ablation and the energy automatically stops after the standard duration in desired temperature.[52] This has made learning hands-on skills to do RFA and following the standard operating protocol much easier. In addition, the RFA catheter is much sturdier than the EVLA catheter, and there are lesser chances of physical damage to the RFA catheter during the procedure. Although not recommended, there is more possibility of reusing the RFA catheter than the EVLA catheter.[67]

Technical success and redo rates

A study compared EVLA and RFA in patients with bilateral varicose veins where one limb received RFA as treatment and another limb received EVLA. Here, rate of recanalization was 6.8% in the RFA group, whereas that was not present in the EVLA group. Time to return to normal activity was 0.9 days in the EVLA group and 1.3 days in the RFA group.[70] Similarly, higher technical success and low redo rates are found with use of EVLA as compared with RFA in a study from India.[7] When first-generation RFA catheters were used, studies showed lower technical success and higher redo rates.[71] Second-generation catheters using a segmental approach to ablation have improved technical ease, speed, and effectiveness of the RFA devices.

Outcomes and complications

Many comparative studies have shown similar outcomes between EVLA and RFA in terms of safety and efficacy, including vein ablated length, GSV occlusion, pain scores, QOL, and complications after the procedures–thrombophlebitis, hematoma, edema, ecchymosis, paresthesia, and recanalization.[72-74]

There are trials and studies that find EVLA superior in terms of ulcer resolution, lesser skin complications, faster return to work, patient satisfaction, and less recanalization.[7,74] EVLA has shorter procedure times and lower per treatment cost. Reported occlusion rates of EVLA generally are slightly higher than those obtained with RFA.[10] However, return to work has also been found to be significantly sooner with RFA than with surgery, but not for EVLA, in a meta-analysis.[75] This might result from different ablative mechanisms that can cause vein wall

perforation with EVLA (810 and 980 nm with bare tip) but not RFA. This has led to evolution of a new 1470-nm EVLA procedure with a radial fiber that is claimed to cause less pain with similar short-term efficacy.[28]

A study has shown that chances of DVT and pulmonary embolism are slightly higher for RFA than EVLA.[7] Large trials comparing RFA and EVLA, such as the RECOVERY trial (Radiofrequency Endovenous ClosureFAST versus Laser Ablation for the Treatment of Great Saphenous Reflux), also show that postoperative pain, ecchymosis, and swelling was lower in RFA.[11,56] EVLA may include more bruising and discomfort in the early postoperative period, although this may be technique dependent.[10] RFA has less periprocedural pain, analgesic requirement, and bruising. RFA has also been shown to have less technical failure and early recovery with less postoperative pain.[59,76,77]

Several meta-analyses have been done over time evaluating EVLA and RFA, but sufficient trials have not been done to give a more robust and significant answer for choosing between EVLA and RFA for varicose veins. Earlier analysis had shown both EVLA and RFA to be safe and comparable to surgical stripping with lesser procedural pain.[72,78,79] EVLA had better short-term outcomes with more occlusion and less recanalizations.[80] However, analysis of long-term follow-up of 5 years did not show a difference in outcomes between conventional surgery, EVLA, and RFA.[81] A Cochrane review was done focusing on the methods of treatment of short saphenous veins only, which showed that EVLA had lower recanalization and recurrence of reflux than conventional surgery.[82]

Guidelines provided by various societies and forums are not very specific in their recommendations. The Society for Vascular Surgery and the American Venous Forum, in a guideline issued in 2011, mentioned the role of endovenous thermal ablation for treatment of incompetent saphenous vein, but a separate recommendation for EVLA or RFA was not mentioned.[83] A recent guideline by the American Venous Forum in 2020 mentions the appropriateness of endovenous thermal ablation for stage C2 to C6 and does not recommended it for an earlier stage.[36] It is considered appropriate is for GSV, SSV, and accessory veins. The recent report also does not separate recommendation for EVLA and RFA.

Conclusion

Although both RFA and EVLA are near equally good in a large proportion of varicose vein cases, there are some instances where one method is better than the other. The RFA device

has a more robust mechanism for safety, making it easier for hands-on learning experience. EVLA has been used for all stages of varicose veins, including ulcers. Technical success and outcomes are similar for both the procedures, with lesser skin complications with RFA use. Larger clinical trials and more robust guidelines are required for all aspects of EVLA and RFA use.

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Investigations for identifying and treating iliac venous stenosis

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Keywords:

iliac vein compression, iliac vein CTV, iliac vein duplex, iliac vein MRV, iliac vein stenosis, IVUS, May-Thurner syndrome

Abstract

Iliac vein stenosis is a commonly present lesion in the general population that remains silent in the majority of individuals. It is, however, a *permissive* lesion that becomes symptomatic if homeostasis is upset by secondary insults such as trauma, infection, thrombosis, or onset of additional pathology. Duplex ultrasound is useful to rule out acute deep venous thrombosis (DVT), identify associated reflux, and exclude other relatively rare nonstenotic venous pathology such as tumor compression, arteriovenous (A-V) fistula, etc. Iliac vein stenosis is best graded on absolute residual area rather than relative stenosis compared with an adjacent reference segment. Intravascular ultrasound (IVUS) is the current reference standard in iliac vein caliber metrics. Duplex ultrasound is severely handicapped by an unacceptably high false positive rate for identifying stenosis. Duplex ultrasound assessment of common iliac vein caliber is a quarter smaller than measured by IVUS and a third smaller in case of external iliac vein. Assessments of caliber via magnetic resonance venography differs from IVUS assessment by nearly the same degree. Computed tomography (CT) imaging with contrast remains the most reliable diagnostic tool at present with only 2.5% mean variance from IVUS caliber measures for common iliac vein and 7.3% for the external iliac vein. The "two-segment" method of assessing the common iliac and external iliac vein calibers individually improves diagnostic accuracy. IVUS is also the favored procedural tool for iliac vein stent placement. There is no role for diagnostic investigations or prophylactic correction of silent iliac vein stenosis.

Introduction

Chronic iliac venous stenosis seldom poses a threat to life or limb. Most symptomatic lesions should be treated by conservative measures. Patients are often relieved to learn of the essentially benign nature of the lesion. Reassurance is an essential part of treatment. Interventional correction may be offered when conservative treatment fails to resolve symptoms within a reasonable time frame, when symptoms progress, or complications ensue. Initial investigation is influenced by the severity of clinical presentation. Duplex ultrasound is routinely used initially but has several limitations, including a very high false positive rate for identifying stenosis.

Silent lesions

Iliac vein stenosis is a common incidental finding during autopsy in the general population. The frequent presence of the lesion in silent form (around 30% of autopsies) was soon recognized after the lesion was initially described by pathologists in the last century.[1,2] Some degree of iliac vein stenosis may be found as an incidental finding in as many as 70% of imaging studies carried out for other purposes.[3] Yet severe iliac vein stenosis is the causative lesion in *some* patients presenting with specific severe symptoms.[4] This paradox is a feature of *permissive pathologies* that are a common cause of human disease.[5] A classic example is patent foramen ovale, which is present in about 20% of the general asymptomatic population. However, it is a source of embolic complications in a significant fraction of stroke victims. Innocent ureteral reflux is a common finding and requires no specific treatment. However, when urinary infection is superimposed, specific correction is indicated. Previously silent iliac vein stenoses often become symptomatic when homeostasis is perturbed by injury, infection, thrombosis, or onset of new reflux.[6] Iatrogenic trauma of joint surgery or onset of saphenous reflux with age are common examples in referral practice. Innumerable other examples of permissive lesions exist in virtually every organ/system disease: carotid stenosis and transient ischemic attack (TIA), obesity, and diabetes are other common examples. Symptoms may resolve if the secondary insult is reversible and corrected; when irreversible, correction of the permissive pathology itself is recommended to prevent recurrent or worsening symptoms. Silent iliac vein stenosis often coexists with other commonly occurring largely benign venous pathology, for example, varicose veins. There has been increasing concern that this may result in unethical and unwarranted iliac vein interventions. *There is no role for prophylactic correction of silent iliac vein stenosis regardless of its severity.* There are numerous reports in the literature of deep venous thrombosis (DVT) associated with iliac vein stenosis. But there are no epidemiological or longitudinal studies at present to support preventative treatment of silent iliac stenosis, including institution of anticoagulation, with significant morbidity of its own.

Routine investigation of patients for iliac vein stenosis in the absence of relevant symptoms is not recommended.

Absolute and relative stenosis

Relative stenosis is a feature of estimating the severity of arterial stenosis. For example, major regional arteries such as the renal or the femoral do not exhibit flow reduction until the stenosis exceeds a 60% to 70% threshold (*Figure 1*).[7] This is due to the presence of autoregulation in arterial inflow. As arterial stenosis progressively increases, there is compensatory distal vasodilatation, which results in an increased pressure gradient to augment flow in compensatory fashion. After a certain point, the mechanism tops out and is no longer able to maintain normal distal perfusion; further increase in the stenosis results in a rather abrupt drop in distal perfusion and pressure. The phenomenon underlies the papaverine test to estimate adequacy of "distal runoff." Correction of arterial stenosis is not usually considered until the stenosis exceeds the characteristic threshold (60%-70% for large regional arteries).
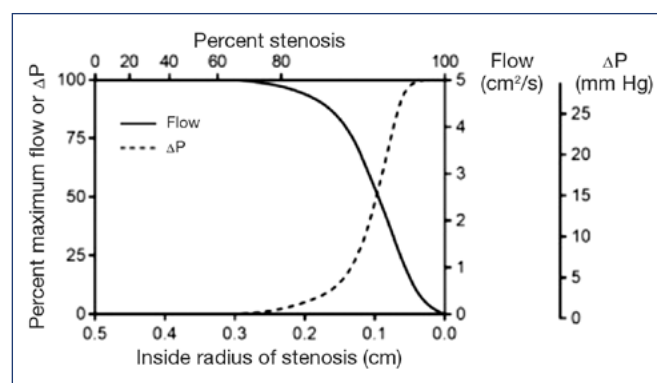

Figure 1. Relationship between flow and pressure drop and percentage stenosis. Flow and pressure remain fairly constant until stenosis reaches about 70%. Further increase in stenosis results in a precipitous drop in flow pressure.

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Such autoregulation is weak or absent in venous stenosis. A continuous rise in peripheral venous pressure with increasing stenosis devoid of any lag can be shown to occur in experimental simulations (*Figure 2*).[8] Nevertheless, many interventionalists apply a 50% stenosis threshold before correction of iliac vein stenosis. There is no published basis for the 50% threshold. It appears to be an ad hoc modification derived from arterial practice. In a recent analysis of 480 consecutive limbs, treated at our facility, the 50% stenosis threshold assessed by intravascular ultrasound (IVUS) had no correlation with severity of initial presentation, CEAP clinical class (clinical, etiology, anatomy, pathology classification system), peripheral venous pressure, or outcome.[9]

An absolute stenosis value in the iliac veins based on an optimal normal caliber area can be argued on the basis of the governing Poiseuille flow equation. Since the outflow in the iliac veins and the pressure gradient vary within a narrow range in the population, a caliber of 200 mm^2 and 150 mm^2
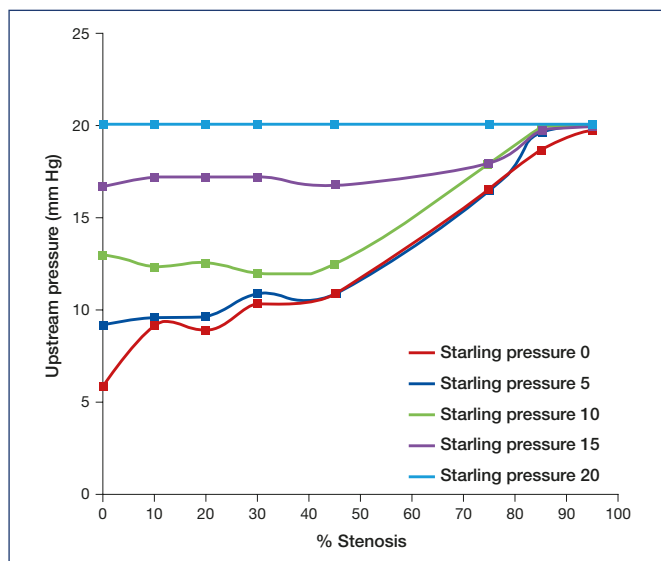
Figure 2. Relationship between outflow stenosis and upstream pressure for a variety of external (Starling) pressures surrounding a Penrose conduit. Note the initial sharp increase in upstream pressure without any lag as outflow stenosis increases from 0% to 10%. There is a further progressive increase in upstream pressure with increasing outflow stenosis. There is some flattening of the pressure curve as outflow pressure approaches external (Starling) pressures.

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respectively for the common and external iliac veins can be calculated from the equation to maintain "normal" peripheral venous pressures (<11 mm Hg).[10] The effect of any reduction in these caliber values on peripheral venous pressure and related parameters is likely to be nonlinear (tube law).[11] There is recent interest on the effect of aspect ratio changes on flow resistance.[12] Whereas an adverse flow effect is demonstrable in experimental simulations, few lesions in clinical practice evince a change in aspect ratio alone without a reduction in caliber area.[13,14]

Investigative tests to assess severity of iliac vein stenosis should preferably provide accurate caliber metrics. Relative stenosis percentage based on an adjacent "normal" segment used in evaluating arterial stenosis is unreliable in assessment of venous stenosis; the adjacent segment is often variably involved in a long diffuse stenosis ("Rokitanski" stenosis) that is common in iliac veins (Figure 3[15]).[16] If used as a reference, the net result will be an underestimation of the degree of stenosis.
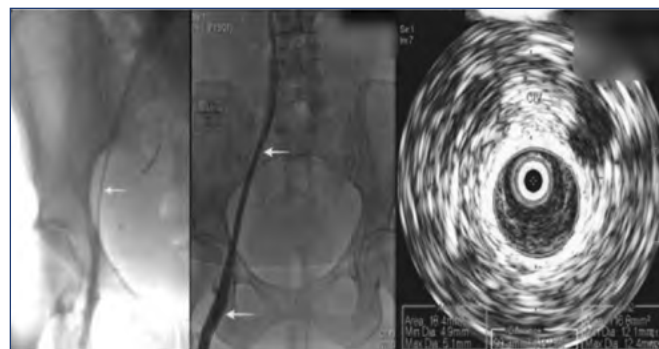

Figure 3. Extreme examples of Rokitansky stenosis are easily recognized (left). Milder examples are less obvious (middle). A subtle sign is the smaller caliber of the iliac vein compared with the common femoral vein (CFV; arrows). On intravascular ultrasound (IVUS) examination, the common iliac vein (CIV) measured 116 mm2, a 42% area of stenosis (right).

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Investigative tests

Duplex ultrasound assessment

Duplex ultrasound is widely used as the initial screening test for iliac vein stenosis in symptomatic patients. It is readily available and inexpensive. The major limitation of the test is the dimensional disparity present between Duplex ultrasound and IVUS (Figure 4).[17] Duplex calibers are a third to one-fourth less than corresponding IVUS measurements in the iliac veins, ie, duplex ultrasound tends to overestimate caliber stenosis. Because of this disparity, frequent false positives mixed in with true positives are inherent with this technique. It is mainly used to detect acute venous thrombosis, chronic occlusions, associated reflux, and other infrequent pathology that may present with similar leg symptoms. These include tumors, retroperitoneal fibrosis, pre- or poststenotic dilatations, retroperitoneal fibrosis, or arteriovenous (A-V) fistula. In some patients, the findings may be intermediate with indirect signs for a stenosis, such as thickened venous walls, collaterals, and high or low iliac venous velocities. A more invasive investigation for definitive diagnosis is usually required to confirm such duplex ultrasound findings.

The absence of an iliac stenosis on duplex ultrasound examination in the context of symptoms is an important finding and also requires another invasive test for confirmation; this may be a false- or true-negative duplex ultrasound finding
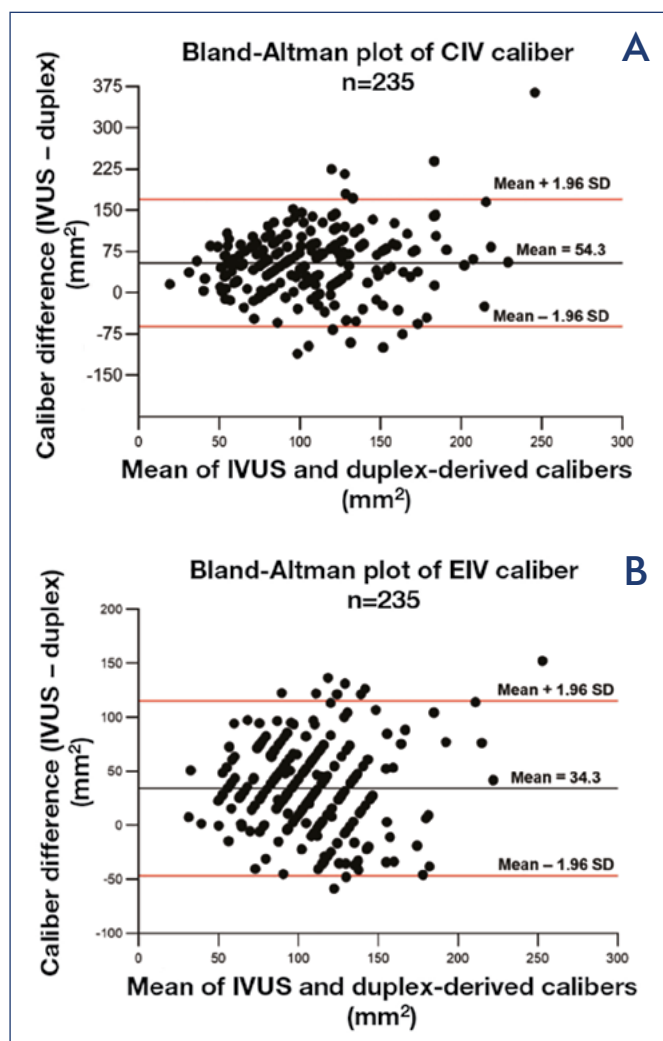
Figure 4. Bland-Altman plots of the difference in duplex-derived calibers compared with intravascular ultrasound (IVUS) measurements for A) common iliac vein (CIV); and B) external iliac vein (EIV). Duplex calibers were smaller by 54 mm² and 34 mm² respectively compared with IVUS.

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for stenosis. Duplex ultrasound may miss some significant stenotic lesions near the iliac-caval junction underneath the arterial crossover point (false negative). Nonstenotic pathology that may present with stenosis-like limb symptoms (true negatives) include a wide spectrum of diseases that are sourced in other organs and systems; nutritional, metabolic, or immune derangements; and drug interactions, etc. Though this is relatively infrequent compared with stenosis in clinical practice, such patients usually end up undergoing an IVUS examination because compression often fails in these patients. The negative IVUS finding results in an extensive multisystem workup to pinpoint the nonvenous source of leg symptoms. An increasing number of patients present with severe chronic venous disease caused by external compression of the iliac vein due to increased abdominal pressure related to obesity.[18] The compression does not result in luminal narrowing but manifests itself by increased femoral venous pressure (peripheral venous hypertension) and decreased velocity in the iliac segment.[19-21] Traditional iliac venous stenoses of primary or secondary etiology often coexist with external compression.[22,23]

Magnetic resonance venography

Magnetic resonance venography (MRV) caliber measurements of the iliac veins were significantly smaller than IVUS area measurements in a blinded comparison of the 2 techniques in 78 limbs at our institution.[24] MRV caliber measurements were derived from time of flight (TOF) measurements followed by gadolinium-enhanced images (*Table I*).[24] The differences from IVUS measurements were so large that MRV could not be reliably used for grading stenosis. Others have reported similar deficiency in MRV caliber metrics with and without contrast.[25] MRV has additional drawbacks: cost, contrast allergy, renal failure, and intolerance of the technique by patients due to metal implants or claustrophobia. These may preclude use of the technique in 20% to 30% of patients.

Venous segment	MRV area (mm²)	IVUS area (mm²)	P value
L CIV	57 ± 60	118 ± 89	0.0009
L EIV	87 ± 39	126 ± 47	0.0001
R CIV	81 ± 39	126 ± 27	0.001
R EIV	71 ± 40	113 ± 30	0.0005

Table I. Comparison of means of minimal areas for external iliac vein and common iliac vein noted on magnetic resonance venography and intravascular ultrasound.

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CIV, common iliac vein; EIV, external iliac vein; IVUS, intravascular ultrasound; MRV, magnetic resonance imaging. Bold face indicates significant P values.

Computed tomography (CT) venography

Computed tomography venography (CTV) is currently our preferred "go to" definitive technique before IVUS to confirm or rule out iliac venous stenosis. Contrast is administered peripherally through an arm vein. Imaging of abdomen and pelvis is commenced after a standard delay of 120 seconds. The stored images are later scanned in coronal, sagittal, and axial views to identify anatomic variations if any. All measurements in the area of interest are made with calipers from 5-mm interval axial sections.

A "two-segment" caliber metrics is used wherein the narrowest lumen diameter of the common iliac and external iliac veins are considered individually (*Table II*).[26] The narrowest diameter identified at each segment is converted to area for circle (πr^2). A stenosis is determined to be present if the caliber at the narrowest point is <200 mm^2 and <150 mm^2 for the common and external iliac veins respectively. Percentage stenosis is calculated based on these minimum normal thresholds. The increased accuracy of the method over considering only the common iliac vein caliber is based on the fact that the common iliac and external iliac vein are each stenotic in around 80% of limbs; an additional approximately 15% can be picked up by considering the other segment separately because one of the 2 segments is stenotic in individuals when the other is not; ie, common iliac and/or external iliac is found to be stenotic

Diagnostic CTV stenosis threshold	No.	Sensitivity, %	Specificity, %	Positive predictive value, %	Negative predictive value, %	Accuracy, %
CIV stenosis area <200 mm^2 (diameter <16 mm)	83	83	62	92	40	80
EIV stenosis area <150 mm^2 (diameter <14 mm)	91	79	70	90	48	77
CIV and/or EIV stenosis	79	97 P<0.01 vs CIV P<0.01 vs EIV	38 P<0.01 vs CIV P<0.001 vs EIV	93	60 P<0.05 vs CIV	91 P<0.05 vs CIV P<0.05 vs EIV

Table II. Diagnostic accuracy detail of computed tomography venography (CTV) assessment for iliac vein stenosis.

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CIV, common iliac vein; EIV, external iliac vein.

Two-segment diagnostic comparison was significantly superior to single-segment analysis.
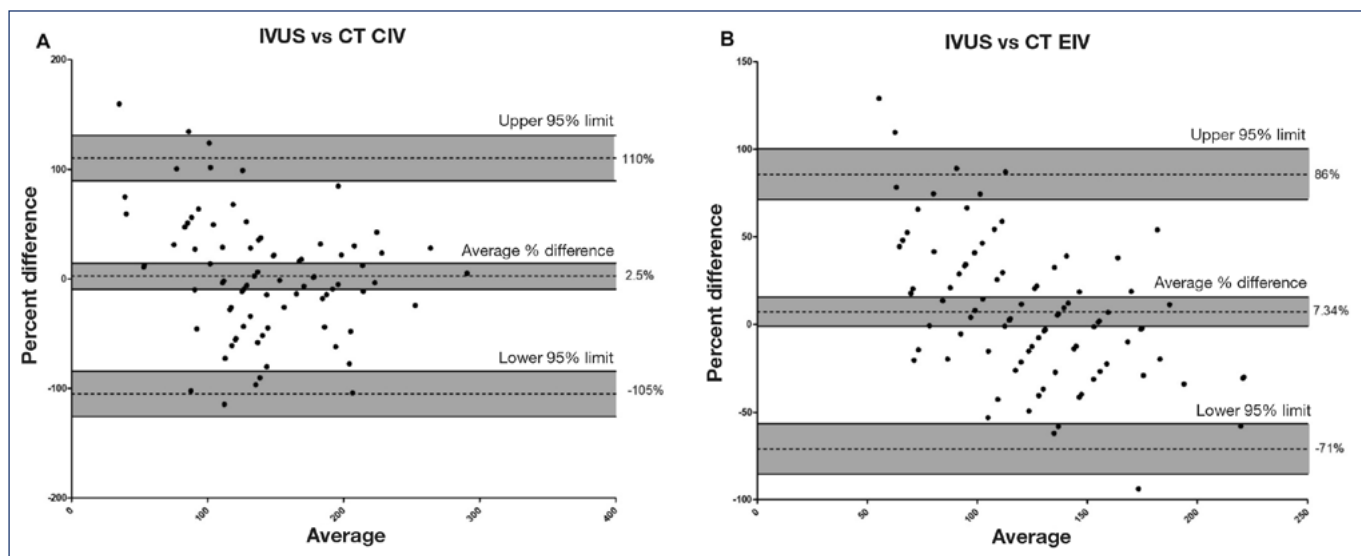

Figure 5. Bland-Altman plot of mean caliber difference between computed tomography (CTV) and intravascular ultrasound (IVUS). The difference was A) only 2.5% for common iliac vein (CIV); and B) 7.3% for external iliac vein (EIV).

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in around 95% of limbs. Bland-Altman plots show only 2.5% and 7.3% variance for common iliac and external iliac veins respectively between CTV and IVUS (*Figure 5*).[26]

Procedural tests to guide stent implantation

Transfemoral venography

The use of traditional contrast venography has sharply declined in recent years. Legacy equipment used for the technique lacked the vital internal scale integrated in modern imaging equipment. Nevertheless, the traditional technique provides a panoramic venous map useful in complex postthrombotic cases. Many interventionalists with a radiology background continue to use traditional venography as a procedural guide during stent placement.

Key minimum requirements of a procedural tool in venous stenting are as follows: identification and grading of the stenosis, and localizing optimal proximal and distal landing zones. In a blinded comparison of IVUS and venography in 155 stented limbs, venography was inferior in all respects[15]: venography failed to identify IVUS-positive lesions in 19%, and the median maximal area stenosis was significantly less (*P*<0.001). A typical example percentage stenosis estimation of the same lesion by contrast venography and IVUS are shown in *Figure 6*.[15] Venography missed the location of maximal
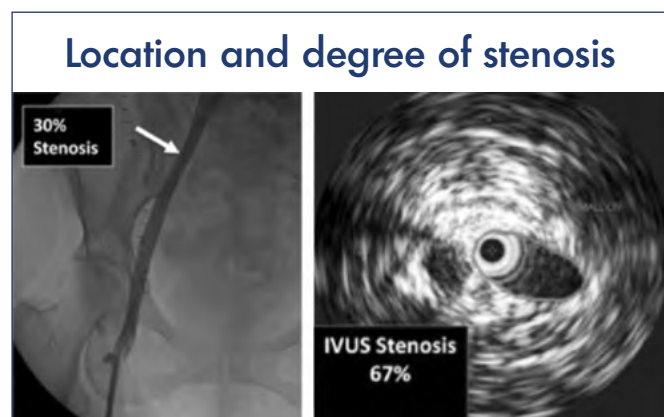
Location and degree of stenosis

Figure 6. Disparity between venography and intravascular ultrasound (IVUS) in estimating maximal stenosis. In the example shown, the common iliac vein (CIV) was identified as the site of maximal stenosis with an estimated 30% diameter stenosis (53% area stenosis) as shown (left). IVUS estimation of area stenosis at the same location was higher at 67% (right). See text.

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stenosis in over two-thirds of limbs. The iliac-caval confluence location was lower with venography than IVUS by as much as the height of 1 vertebral body. Agreement between venography and IVUS on location of distal landing zone free of disease was only 26%. Mislocating optimal proximal and distal landing zones is likely to result in recurrence of stenosis near these sites. The misestimation of confluence level is due to merging of contrast from the 2 sides resulting in obscuration of the boundary at the junction. The error is magnified when only the contrast-injected side opacifies and the estimation of confluence location is made on the basis of caliber or course change of contrast flow stream (*Figure 7*).[15]

Ideal distal landing zone chosen by venogram & IVUS. Landing zone 1-6 and related bony landmarks are shown (see text).

1: Common iliac vein
2: External iliac vein
3: Common femoral vein at lower border pubic ramus
4: Bottom of femoral head
5: Ischial crossing
6: Lesser trochanter

Figure 7. Where is the confluence? Lack of contralateral iliac opacification makes venographic localization difficult. Intravascular ultrasound (IVUS)-identified confluence was a vertebral body higher than estimated by venography (n=128). There were wide discrepancies between venogram and IVUS in choosing the distal landing site as well; see text.

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IVUS is frequently referred to as the "gold standard" for imaging iliac vein stenosis. Yet, it has deficiencies of its own that results in suboptimal imaging in as many as 15% to 20% of cases.[15] This arises because the IVUS catheter is not coaxial and exhibits a luminal bias toward one side or the

other in the complex 3-dimensional (3D) spiral of the iliac vein anatomy. This bias is particularly prominent at tributary junctions at the confluence of the internal/external iliac veins and the common iliac/inferior vena cava (IVC) junction. This results in incomplete visualization of the stenotic lesion where part of the circumference appears to be missing (*Figure 8*); incomplete caliber metrics is the result. It is generally possible to determine if the lesion is high or low grade by "balloon sizing" of the lesion and noting the degree of waisting at the site. A CTV if obtained before IVUS is able to provide caliber metrics in all such lesions.[26]
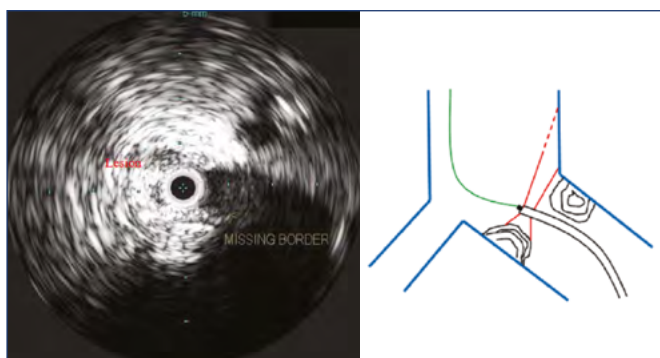

Figure 8. "Missing border" of a high-grade stenosis at the iliac confluence (left). This artefact results from tilting of the intravascular ultrasound (IVUS) catheter tip due to lack of a centering mechanism (right). Only part of the lesion is imaged with the sound beam missing the rest of the lesion. High-grade lesions will demonstrate waisting on "balloon sizing." More precise caliber measurement can be obtained from computed tomography venography (CTV) imaging if available. See text.

Notwithstanding this deficiency, IVUS is superior to venography as a procedural guide during stenting. It can be used as frequently as necessary without incurring undue radiation hazard or contrast-related problems. It can identify and measure lesions that may be missed by venography because too much or too little contrast was present for proper visualization. Similar comments apply to preference for IVUS to identify post-stent defects such as stent shelving, incomplete overlap, inadequate expansion, etc. The lack of internal scale is a distinct disadvantage in detecting late stent compression on contrast venography (*Figure 9*[16]).

Iliac vein stenting was carried out with IVUS and fluoroscopy alone in 31 limbs where contrast venography was prohibited due to renal failure or contrast allergy. The diagnostic yield of IVUS in highly symptomatic patients with features of chronic obstruction is very high. About 20% of procedures are currently carried out in our practice with IVUS guidance alone under fluoroscopy without use of contrast.
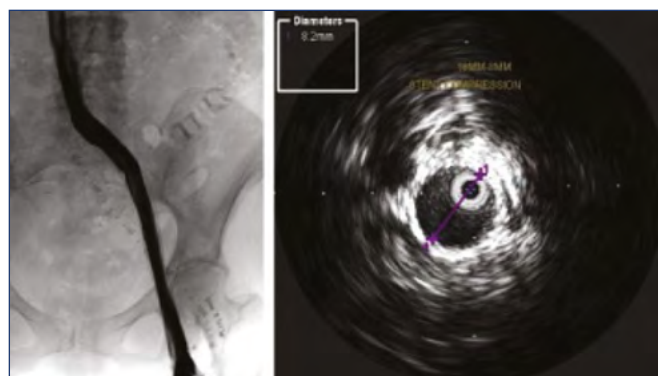

Figure 9. Post-stent venogram showed a smooth contrast profile without any apparent stenosis. Intravascular ultrasound (IVUS) showed severe stent stenosis due to compression. An 18-mm stent had been compressed to 8 mm with a caliber reduction of >75%.

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Multiplanar venography

Modern equipment has substantially improved the useability of contrast venography for iliac vein assessment. In the multicenter VIDIO trial (Venogram versus Intravascular ultrasound for Diagnosing and treating Iliofemoral vein Obstruction), multiplanar venography was compared with IVUS as procedural guide.[27] IVUS identified lesions in 26% of limbs missed by multiplanar venography. The treatment plan was significantly revised in 57% as a result of IVUS findings not evident on venography. Twenty-three percent required a longer stent stack than indicated by venography. Stenting was avoided in 3% because IVUS did not detect a lesion falsely identified on multiplanar venography. The authors used the 50% relative stenosis threshold in this study.

Saleem evaluated IVUS versus all contrast-enhanced multiplanar techniques (multiplanar venography, CTV, MRV) in a recent systematic review.[28] CTV appeared to have the highest sensitivity among the techniques using IVUS as the reference standard. However, all techniques had low sensitivities not useable for clinical decision-making in symptomatic patients.

Emerging techniques

Most radiologists use 5-mm slices from CTV images for identification and measurement of stenotic lesions. Even so, some lesions particularly near the iliac-IVC confluence can be missed. Even smaller slice cuts (0.6 mm) and higher image resolution are possible with newer equipment. 3D image

generation with automated measurement algorithms holds the promise of increased diagnostic accuracy (*Figure 10*).[29] 3D software specific for iliac venous stenosis is currently under development. Since iliac venous stenting in chronic disease is usually an elective procedure, the technique holds promise of broad adoption. Customized manufacture of stents to suit individual anatomy is a future possibility.
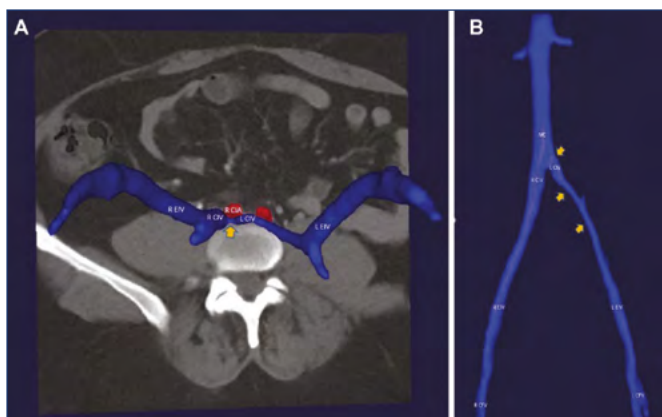

Figure 10. Three-dimensional (3D) computed tomography venogram (CTV) reconstructions in the A) axial and B) coronal views demonstrating severe left iliofemoral venous obstruction. Orange arrows point to areas of obstruction.

Abbreviations: CFV, common femoral vein; CIA common iliac artery; CIV, common iliac vein; EIV, external iliac vein; IVC, inferior vena cava; L, left; R, right.

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A clinical algorithm

The level of venous testing required in individual cases depends on the intensity of clinical presentation. Mild leg swelling and pain are common symptoms of diverse origin. Most of recent onset do not persist long term. It is appropriate to start compression therapy in such patients after ruling out acute DVT and other unexpected pathology by duplex ultrasound examination. Additional expensive or complex investigations looking for confirmation of stenosis is not necessary at this stage. If symptoms do not improve within a few weeks, additional testing may be desirable. If initial presentation is more severe (eg, CEAP class 3 or higher) a

CTV may be ordered. Many patients and referring physicians desire a confirmatory test for iliac venous stenosis short of IVUS. CTV fits this role. This may be unnecessary in geriatric or frail patients as contrast imaging is a potential source of renal or allergic complications. It is often possible to perform single-stage diagnostic IVUS and stenting at the same sitting with informed consent.

Conclusions

Chronic iliac vein stenosis is a commonly occurring lesion in the general population. Most remain silent lifelong. Investigation or treatment of asymptomatic patients is not warranted. There is a role for interventional correction of iliac vein stenosis in patients in whom compression fails or when symptoms progress to tissue damage or complications set in. An initial duplex ultrasound examination is useful to rule out acute thrombosis and other uncommon pathology that requires a different treatment approach. IVUS is the current reference standard for grading iliac stenosis severity. Relative stenosis grading is popular, but an absolute stenosis grading based on residual caliber is probably more appropriate for central veins. Several imaging techniques including duplex ultrasound, traditional venography, and MRV do not have dimensional parity with IVUS. Contrast-enhanced routine CT imaging of the iliac veins displays excellent dimensional parity (<10% variance) with IVUS for measuring iliac vein caliber. The common iliac and external iliac veins should be individually assessed for residual caliber. Considering both segments individually can increase sensitivity and reduce false positives. IVUS procedural guidance is superior to contrast venography including multiplanar venography for stent placement.

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