

Management of Chronic Venous Insufficiency (CVI)

Literature Review

Maged Naser¹, Mohamed M. Naser², Lamia H. Shehata³

¹Mazahmiya Hospital, Ministry of Health, Kingdom of Saudi Arabia,
Department of Ob/Gyn,

² King Fahd Hospital, Ministry of Health, Kingdom of Saudi Arabia,
Department of Surgery, Consultant Endoscopic Surgery,

³ Care National Hospital, KSA,
Department of Radiology.



Abstract – Chronic venous insufficiency (CVI) of the lower extremities manifests itself in a variety of clinical spectrums, ranging from cosmetic issues that are asymptomatic to severe symptoms like venous ulcer. Due to a lack of understanding of the various presenting manifestations of primary and secondary venous disorders and an underestimation of the problem's magnitude and impact, CVI is a relatively common medical condition that is frequently overlooked by healthcare providers. Due to the possibility of underdiagnosis of CVI, an increase in obesity, and an aging population, it is anticipated that the prevalence of CVI will rise. Duplex ultrasound, radiofrequency ablation, and iliac vein stenting play an important role in the diagnosis, treatment, and prevention of CVI of the lower extremities.

Keywords – Venous insufficiency, diagnosis, and treatment.

I. INTRODUCTION

Chronic venous insufficiency (CVI) of the lower extremities is associated with a wide range of clinical symptoms, ranging from cosmetic issues to severe symptoms [1-4]. Varicose veins, reticular veins, telangiectasis (also known as spider veins), edema, pigmentation and/or eczema, lipodermatosclerosis, atrophie blanche, and venous ulceration are all examples of this. Due to a lack of understanding of the various presenting manifestations of primary and secondary venous disorders and an underestimation of its magnitude and impact, CVI is a relatively common medical condition that is frequently overlooked by healthcare providers [2]. Although the estimated prevalence of CVI varies depending on the population studies [5-7], abnormal venous flows of the lower extremities are seen in up to 50% of people.

CVI is thought to be caused by lower extremity trauma, previous venous thrombosis, the presence of an arteriovenous shunt, high estrogen levels, and pregnancy [5,8-13]. Other risk factors include increasing age, prolonged standing, obesity, smoking, sedentary lifestyle, and family history [5,8-13]. Albeit the pervasiveness of CVI in the Asian populace is essentially lower contrasted with non-Hispanic whites concurring with a multi-ethnic cross-sectional review [14], the predominance of CVI in South Korea is supposed to build because of the conceivable underdiagnosis of CVI, the expansion in stoutness, and a maturing populace. Duplex ultrasound (DUS), radiofrequency ablation (RFA), and iliac vein stenting are highlighted as tools for diagnosing and treating CVI of the lower extremities in this article.

1. Pathophysiology

Ambulatory venous hypertension, which is caused by venous valve reflux, venous flow obstruction, or both, is the primary pathophysiological cause of the clinical manifestation of CVI of the lower extremities [2]. In a standing position with no skeletal muscle contraction, the foot vein's venous pressure can reach as high as 80 to 90 mmHg. During ambulation, this pressure drops below 30 mmHg in a subject with functioning venous valves [15]. Nonetheless, in a patient with CVI, the decline in venous tension with leg developments is lessened. The high pressures caused by calf muscle contraction in the deep veins can be transferred to the superficial system and skin microcirculation if the perforator vein valves are not functioning properly. Ambulatory venous hypertension refers to this condition. After deep vein thrombosis (DVT), postthrombotic syndrome also results in venous hypertension and valvular reflux as a result of damaged valves [16].

2. Venous anatomy and its variations

To comprehend the pathophysiology of CVI or varicose veins and their treatment options, such as endovenous ablations, one must be familiar with the anatomy of the veins and their variations. An International Interdisciplinary Committee established the consensus on the nomenclature of anatomic terminology in 2001 and 2005 [17,18]. The venous framework can be isolated into three significant parts: the superficial, deep, and perforating veins of the venous system.

2.1 Superficial venous framework

The superficial venous framework empties the blood stream out of the skin and the subcutaneous tissues. By and large, any veins situated over the profound strong sash, which are not profound veins, are viewed as shallow veins. The superficial venous system can be divided into thin-walled superficial or epifascial tributaries, which are located between the skin and the saphenous fascia, and thick-walled truncal veins like the great saphenous vein (GSV) and small saphenous vein (SSV), which are located between the muscular fascia and the saphenous sheath [19,20]. On ultrasound, this relationship between veins and sheath or fascia resembles an Egyptian eye. It serves as a crucial identifier for the saphenous veins. However, the saphenous trunk, which extends from the ankle to the groin in only half of patients, is present [19,21].

The GSV is the body's longest vein. It drains into the common femoral vein (CFV) along the medial side of the calf and thigh after beginning on the medial side of the foot and ascending anterior to the medial malleolus [18,22]. The GSV is joined by two tributaries in the tibial portion: the great saphenous vein's posterior accessory (PASV, Posterior accessory saphenous vein; previously known as Leonardo's vein) and the anterior accessory of the great saphenous vein (AASV). Because the posterior tibial perforators, formerly known as Cockett, connect the PASV and the posterior tibial veins but not the distal GSV, the PASV is crucial clinically in patients with venous ulceration.

Understanding flow patterns, treatment options, and the recurrence of varicosities all depend on the saphenofemoral junction (SFJ, saphenous arch, or saphenous junction). The "Mickey mouse" sign is a landmark that includes the CFV, GSV, and common femoral artery. Between the CFV's terminal and preterminal valves, as well as three major tributaries draining into the GSV, is included in the SFJ: the external circumflex iliac, inferior epigastric, and pudendal veins. Endovenous heat-induced thrombus (EHIT) extension into the femoral vein is thought to be less likely if the superficial inferior epigastric vein is left intact during endovenous ablation. The SFJ exhibits significant anatomic variation [3]. The AASV is a significant SFJ tributary at its distal end. The AASV is present in approximately half of patients. The AASV is important for diagnosis and treatment because it can cause recurrent varicose veins [23].

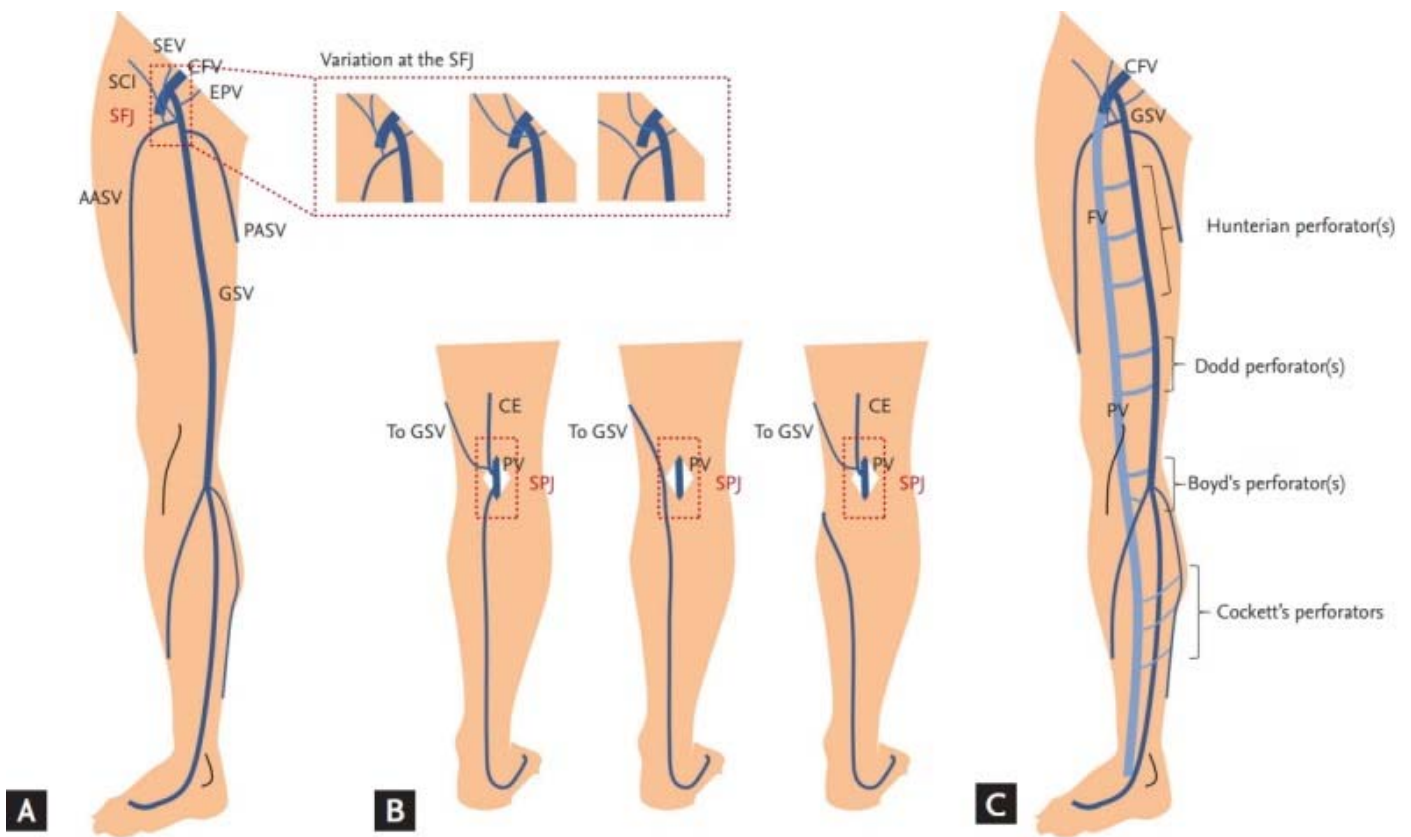
The SSV drains into the popliteal vein along the posterolateral aspect of the calf, ascends posterior to the lateral malleolus, and originates on the dorsolateral side of the foot. Variability can be seen at the sapheno-popliteal junction (SPJ), where the popliteal vein and SSV meet. The continuation of the SSV is the cranial extension (CE) of the SSV, which is present in 95% of limbs. However, the SSV does not connect to the deep vein in approximately 25% of limbs and instead continues as the CE up the posterior thigh. The area of the SPJ is situated over the popliteal wrinkle, however, is far over the popliteal wrinkle in 25% of limbs [20,24].

The deep venous system is a low-pressure, high-volume system that is responsible for about 90 percent of the venous blood flow in the lower limbs. The wall of deep veins is typically thinner than that of superficial veins. However, the muscle and/or fascia provide support for them. This creates a rigid compartment and causes a vein to pump the ascending venous blood while walking. Except for the soleus and gastrocnemius, which are on the distal side of the intramuscular veins, all deep veins generally follow

corresponding arteries. In the infrapopliteal region are the gastrocnemius vein, peroneal vein, soleal vein, and anterior and posterior tibial veins. The deep venous system's primary function is to provide a venous return to the right heart. There are three primary vessels in the pelvic veins: the common iliac vein, the internal iliac vein, and the iliac vein on the outside. Block in the iliac vein assumes a huge part in CVI. Only 20% to 30% of DVTs are fully recanalized, and severe CVI is linked to residual obstruction [25,26].

A thrombotic occlusion is the term for this kind of occlusion. A stent can be used to treat this, but its patency is lower than that of non-thrombotic occlusion [27]. CVI, on the other hand, can also be caused by non-thrombotic iliac vein lesions like stenosis. A clinical condition known as Iliac vein compression syndrome (also known as May-Thurner syndrome) is caused by the compression of the left iliac vein between the right iliac artery and the fifth lumbar vertebra [28,29]. Clinical sequelae, such as DVT or CVI, are only observed in approximately 3% to 5% of patients, despite the fact that such lesions can be found in half of the asymptomatic population [30,31].

Endovascular embolization has emerged as the treatment of choice for pelvic congestion syndrome, a common cause of disabling chronic pelvic pain in women of childbearing age, which is caused by pelvic CVI, which is defined as retrograde flow in the gonadal and internal iliac veins [32]. Perforators are channels that connect the superficial and deep venous systems. Due to valves that prevent reflux from the deep venous system to the superficial venous system, these veins obliquely perforate the deep fascia and are essential for equilibrating blood flow during calf muscle contraction. Puncturing veins are various and profoundly factor in plan, association, and size. There are four groups of perforators with clinical significance: upper thigh (Hunterian), lower thigh (Dodd), knee-level (Boyd), and calf (Cockett) regions. In spite of the fact that perforator valve incompetence is constantly connected with CVI [33], the reason for perforator deficiency isn't known, and the routine treatment of puncturing veins in C2 patients isn't supported [3]. **(Figure1)**



Venous system of the lower limb. (A) Great saphenous vein and its tributaries. (B) Small saphenous vein and its variations. (C) Perforating veins. SEV, superficial epigastric vein; SCI, superficial circumflex iliac vein; CFV, common femoral vein; EPV, external pudendal vein; SFJ, saphenofemoral junction; AASV, anterior accessory of the great saphenous vein; PASV, posterior

accessory of the great saphenous vein; GSV, great saphenous vein; CE, cranial extension of the small saphenous vein; PV, popliteal vein; SPJ, saphenopopliteal junction; FV, femoral vein.(Figure1)

2.2 Vein valves

Blood returning to the circulation in the standing position must overcome gravity and intra-abdominal pressure in the lower venous system. As a result, the venous system's valves are crucial to ensuring that blood flows in the right direction. Bicuspid and unidirectional are typical features of normal venous valves. These valves can be found in a vein that is ordinarily somewhat widened. They keep the blood flowing from the peripheral to the central area, eventually reaching the right heart. Patients with CVI can experience venous reflux, also known as retrograde flow, when these valves fail to function properly. To prevent gravitational effects from increasing pressure in the distal veins, the number of venous valves increases from the proximal to the distal [2]. Additionally, perforating veins have valves that stop reflux from the deep to the superficial venous systems. However, there are no valves in the foot veins or the iliac veins. The SSV has 7 to 10 valves, while the GSV has at least six. There are up to two valves per 2 cm in tibial veins [34,35].

For venous competence, the calf muscle pump is also important. The calf muscle is the pumping muscle in the calf. The veins are squeezed by the calf muscle contracting, and the blood is pumped upward in accordance with the one-way valves [36]. The calf muscle pump drains the venous system during ambulation, lowering the pressure in the veins. The deep venous system can then receive blood thanks to relaxation of the muscle pump. CVI is caused by malfunctioning valves in the superficial, deep, perforating, or venous tributaries. These valves allow blood to flow backwards, which is called "venous reflux." 90% of patients who present with CVI have superficial vein reflux [37].

3. Clinical presentation

Discomfort, swelling, varicose veins, and skin changes or ulceration are clinical signs of CVI. After prolonged standing, venous leg discomfort is typically referred to as a dull ache, throbbing or heaviness, or a sensation of pressure. It can be alleviated by elevating the leg, wearing compression stockings, or walking. Notwithstanding, leg distress is missing in an expected 20% of patients with other clinical highlights of CVI, while it is the main clinical component in around 10% of patients [1]. Tenderness may indicate venous distension in patients with varicose veins. Vein claudication is a condition that can occur in patients who have a blocked deep vein.

A frequent sign of CVI is edema of the legs. It is typically pitting, but it varies significantly depending on orthostasis and the time of day [38]. It ascends the leg from the perimalleolar region. Congestive heart failure, hypoalbuminemia as a result of nephrotic syndrome or severe hepatic disease, myxedema as a result of hypothyroidism, and medications like dihydropyridine calcium channel blockers and thiazolidinediones can all result in bilateral leg edema. Lipedema, caused by fat deposition, should also be taken into consideration for non-pitting leg edema. Lipedema does not involve the feet. Clinically, it can be difficult to distinguish it from lymphedema (phleboedema). One of the clinical characteristics of lymphedema is the Stemmer's sign (*inability to lift and pinch the skin of the base of the second toe*). Additionally, secondary lymphedema (phlebolymphedema) may subside if the underlying CVI is treated in up to one third of CVI cases.

Varicose veins are superficial, dilated, bulging veins that measure at least 3 millimeters in diameter and gradually become more tortuous and enlarged. Varicose vein patients frequently don't show any symptoms, but they still worry about how their legs look. If superficial thrombophlebitis occurs, they can cause prolonged bleeding and cause pain. Skin hyperpigmentation, stasis dermatitis, and ulceration are examples of cutaneous changes. Hemosiderin deposition is the cause of hyperpigmentation. Hyperpigmentation in non-venous conditions like hemosiderosis or acanthosis nigricans is more dispersed or spreads to other parts of the body. Psoriasis, periarteritis nodosa, and allergic dermatitis should be distinguished from stasis dermatitis. A type of inflammation of the subcutaneous fat is lipodermatosclerosis. An ischemic ulcer and a venous ulcer can be distinguished; Ischemic ulcers typically have gangrenous edges or a gangrenous base and are deeper than venous ulcers.

4. Classification

The clinical, etiologic, anatomic, and pathophysiological (CEAP) system uses a variety of chronic venous disorders' symptoms and signs to determine their severity (Table 1).

4.1 CEAP classification of chronic venous disorders (Table 1)

CEAP classification of chronic venous disorders

Clinical classification (C) ^a	
C ₀	No visible sign of venous disease
C ₁	Telangiectasis or reticular veins
C ₂	Varicose veins
C ₃	Edema
C ₄	Changes in skin and subcutaneous tissue ^b
	(A) Pigmentation or eczema
	(B) Lipodermatosclerosis or atrophie blanche
C ₅	Healed ulcer
C ₆	Active ulcer
Etiologic classification (E)	
E _c	Congenital (e.g., Klippel-Trenaunay syndrome)
E _p	Primary
E _s	Secondary (e.g., post thrombotic syndrome, trauma)
E _n	No venous cause identified
Anatomic classification (A)	
A _s	Superficial
A _d	Deep
A _p	Perforator
A _n	No venous location identified
Pathophysiologic classification (P)	
P _r	Reflux
P _o	Obstruction, thrombosis
P _{r,o}	Reflux and obstruction
P _n	No venous pathophysiology identified

CEAP, clinical, etiologic, anatomic, pathophysiological.

^a the descriptor A (asymptomatic) or S (symptomatic) is placed after the C clinical class.

^bC4 is subdivided into A and B, with B indicating higher severity of disease and having a higher risk for ulcer development.

Additionally, it broadly classifies the etiology as primary, congenital, or secondary; identifies the superficial, deep, or perforating nature of the affected veins; and classifies the pathophysiology as either reflux or obstruction, or neither. However, this system is ineffective for venous severity scoring due to the fact that some of its parts are relatively static and others use extensive alphabetical designations. A standardized clinical evaluation, assessment of clinical severity, and evaluation of the response to treatment are all made possible by an adjunctive scoring system (Table 2) [39-41]

4.2 Venous Clinical Severity Score

Attribute	Absent = 0	Mild = 1	Moderate = 2	Severe = 3
Pain	None	not confining day to day action Everyday	Daily, interfering but not preventing daily activity	Daily, limits most daily activity
Varicose veins	None	Few, isolated branch varices, or clusters, includes ankle flare	Restricted to calf or thigh	Involves calf and thigh
Venous edema	None	Limited to foot and ankle	Extends above the ankle but below knee	Extends to knee and above
Skin pigmentation	None or focal	Limited to peri malleolar	Diffuse, over lower third of calf	Wider distribution above lower third of calf
Inflammation	None	Mild cellulitis, ulcer margin limited to peri malleolar	Diffuse over lower third of calf	Wider distribution above lower third of calf
Diffuse	None	Limited to peri malleolar	Diffuse over lower third of calf	Wider distribution above lower third of calf
Ulcer number	0	1	2	≥ 3
Ulcer duration	NA	< 3 mon	> 3 mon but < 1 yr.	Not healed > 1 yr.
Ulcer size	NA	Diameter less than 2 cm	Diameter 2–6 cm	Diameter greater than 6 cm
Compressive therapy	Not used	Intermittent	Most days	Full compliance

An aggregate score for the limb is calculated by adding the individual component scores. The range of the total score is between 0 to 30. NA, not applicable.

5. Diagnosis

A thorough history and physical examination are necessary to make a correct diagnosis of CVI. In order to allow the veins to distend to their fullest extent during physical examination, it is best to perform it while standing. Painless and intrusive demonstrative testing should help the conclusion. The CVI assessment methods are outlined below, with an emphasis on DUS and brief reviews of the others. Detailed overviews have previously been published [42].

5.1 The Brodie-Trendelenburg test

The test can be used to tell the difference between deep and superficial reflux. In order to empty the veins, the patient lies down while the leg is raised. After the patient is asked to stand, a tourniquet or manual compression is applied to the superficial veins, and the veins are examined. If the varicose veins fill up for more than 20 seconds, superficial venous insufficiency is to blame. In contrast, when deep (or combined) venous insufficiency is present, the varicose veins will quickly dilate [2].

5.2 Plethysmography

Plethysmography is a non-invasive venous test that measures reflux, obstruction, and muscle pump dysfunction as potential components of the pathophysiologic mechanisms of CVI. It is possible to ascertain the venous volume, refilling times, maximum venous outflow, segmental venous capacitance, and ejection fraction [43,44]. Plethysmography can be broken down into four basic categories: photoplethysmography, air plethysmography, strain gauge plethysmography, and impedance plethysmography. When DUS does not provide definitive information on the pathophysiology of CVI, its application is restricted to academic or hospital settings due to its complexity.

5.3 Computed tomography and magnetic resonance venography

Although advancements in computed tomography (CT) and magnetic resonance (MR) images have made it possible to perform a more accurate evaluation of venous disease [45-48], these procedures are rarely necessary in order to identify the cause of CVI and advise a treatment plan for it. To get the best images and avoid artifacts in a particular venous system, image acquisition must be performed at the right time based on venous filling time. Additionally, these methods do not provide any useful data. However, these methods are most useful for assessing for intrinsic or extrinsic obstruction and evaluating for focal or complex lesions located at proximal veins and their surrounding structures [41].

5.4 Venous duplex ultrasonography

The most prevalent and useful method for diagnosing CVI, venous duplex ultrasonography DUS provides etiological and anatomical information [41]. DUS detects venous reflux and venous obstruction in both superficial and deep veins by combining B-mode imaging and spectral Doppler. Venous flow patterns can be visualized with color-assisted DUS.

5.5 Diagnosis of venous obstruction

The absence of flow, blunted augmentation, the presence of an echogenic thrombus within the vein, or the failure of the vein to collapse using a compression maneuver can all be used to infer the diagnosis of venous obstruction. Enormous veins, for example, the inferior vena cava, iliac, femoral, and popliteal vessels show unconstrained blood stream very still. Changes in respiration can be seen in this flow. The increased intra-abdominal pressure during inspiration causes normal flow to stop and resume during expiration. Due to their size, small veins, like calf veins, rarely exhibit spontaneous flow. An obstruction proximal or distal to the area under examination may be the cause of the absence of spontaneous flow. Additionally, a proximal stenosis or occlusion is indicated by nearly constant high velocity flow without significant respiratory changes. Instead of standing, spontaneous flow should be evaluated in a supine or slight reverse Trendelenburg position. In normal veins, enhancement can be evaluated by applying a moderately firm squeeze to the calf to increase central flow. It is best to squeeze and hold for about 0.25 seconds before releasing during a compression. The vein segment's patency is checked with this maneuver. Occlusion is implied by augmentation blurring. However, the variability of the compression force is this maneuver's primary drawback. Compressibility is the most dependable approach to diagnosing an intraluminal clot and this strategy is acted in a short-axis view. The increased blood velocity from DUS at the iliac veins can indicate iliac vein non-thrombotic stenosis. The direction of flow can identify venous reflux.

5.6 Diagnosis of venous reflux

Venous reflux is characterized by any significant reverse flow in the direction of the foot. In the reverse Trendelenburg position, venous reflux is evaluated. Although reverse flow can be detected without the provocation maneuver, venous reflux can be confirmed with the Valsalva maneuver or augmentation by compressing the calf. The Valsalva maneuver raises pressure inside the stomach. The essential objective of this test is to assess the stream qualities and valve capabilities in the focal vessels. The dysfunctional valves carry downward pressure until it reaches the functioning valve. Delayed inversion stream after expansion recommends venous reflux. Using a cuff inflation-deflation technique with rapid cuff deflation while standing is, however, the preferred provocation maneuver [49].

When it comes to detecting reflux in both the superficial and deep veins of the leg, this method yields results that are more consistent and quantifiable. The reflux time is the time during which reflux occurs. Venous reflux that is brisk is considered normal. > 1.0 second in the popliteal or femoral veins, > 0.5 second in the saphenous system, and > 0.35 second in the perforators are currently accepted values for pathologic reflux [50]. The severity of the disease is reflected by the duration of reflux, but it does not correlate with clinical manifestations [51]. A DUS examination of patients with CVI ought to reveal both abnormalities in venous blood flow in the limbs and anatomical patterns of veins. It is necessary to establish the following data:

1) the incompetent saphenous junctions, their locations, and their diameters; 2) the extent and diameter of the saphenous vein reflux in the thighs and legs; incompetent perforating veins' number, location, diameter, and purpose; (3) any additional relevant veins that exhibit reflux; 4) the veins that, if not already mentioned, are the source of the filling of all superficial varices; 5) veins that are hypoplastic, atretic, or absent; and (6) the state of the deep venous system, which includes evidence of previous venous thrombosis and the competence of valves. [50]

5.7 Intravascular ultrasound

Intravascular ultrasound The morphologic diagnosis of iliac venous outflow obstruction can be made more accurately with venous intravascular ultrasound (IVUS) than with conventional venography IVUS is rapidly gaining acceptance in venous percutaneous intervention for the treatment of chronic venous iliofemoral disease and provides valuable assistance in the precise placement of venous stents.[52,53]

6. Strategies in the treatment of varicose veins and venous insufficiency

The severity of the venous insufficiency, the cost, the risk of postoperative complications, and the preferences of the patient all play a role in determining the treatment strategy for varicose veins. The board choices for varicose veins incorporate moderate treatment and careful mediation. Endovenous laser ablation (EVLA), radiofrequency ablation (RFA), high ligation and stripping (HL/S) of the incompetent great saphenous vein (GSV), Conservatrice et Hemodynamique de l'Insuffisance Veineuse en Ambulatoire (CHIVA), mechanochemical ablation (MOCA), cyanoacrylate embolization (CAE), and other surgical options are suggested for symptomatic patients (Table 1)[54-56].

6.1 Compression therapy

Varicose veins with venous ulcers can be effectively treated with compression therapy, which is the foundation of conservative treatment [57]. Ankle edema can be controlled with compression bandaging. However, due to itching, pain, and difficulty putting on shoes, many patients can barely tolerate bandaging. Hence, clinical stockings are more invited than pressure bandaging [58]. While picking pressure stockings, patients are instructed to favor pressure stockings with graduated pressure to non-evaluated ones. Gradually graduated compression stockings that are thigh-length rather than knee-length should be worn by patients who have varicose veins that affect the main axial superficial veins above and below the knee. Patients with varicose veins (C2 to C3) should wear stockings with a moderate pressure (20-30 mmHg), those with skin changes or ulcers (C4 to C6) should wear stockings with a pressure between 30 and 40 mmHg, and those with recurrent ulcers should wear stockings with a pressure between 40 and 50 mmHg as an adjuvant treatment to prevent ulcer recurrence [58,59]. The use of compression stockings for at least one week following EVLA is recommended because, in terms of reducing postoperative pain at one week and returning to work, long-term (1-2 weeks) use is superior to short-term (24-48 hours) use [59]. However, since there is insufficient evidence to support compression stockings in the treatment of varicose veins C1-C4, a trial of compression therapy prior to endovenous thermal ablation is unnecessary [57]. The use of compression stockings is restricted by arterial insufficiency, the difficulty of application, and the preferences of patients.

6.2 Medical therapy

Patients with venous ulcers, ankle swelling, and varicose veins who are exhibiting symptoms are prescribed venostimulants to enhance venous tone and capillary permeability. Spooning, such as horse chestnut seed extract, the micronized purified flavonoid fraction (MPFF), and flavonoids are the most frequently used drugs [60, 61]. At the microcirculatory level, it is thought that pentoxifylline targets inflammatory cytokine release, leukocyte activation, and platelet aggregation. Compared to compression and placebo, the closure of venous ulcers may be better when pentoxifylline or MPFF is used in conjunction with compression therapy [62]. According to a Cochrane meta-analysis, vasoactive drugs may alleviate chronic venous insufficiency-related pain and swelling, but the precise mechanism is unknown. Phlebotomists' safety and efficiency need to be studied over time [60,63].

6.3 Surgical therapy

Historically, the best treatment for varicose veins has been surgery with high ligation of the saphenofemoral junction (SFJ) or saphenopopliteal junction with or without vein stripping (HL/S)[64].In particular, after general or lumbar anesthesia, an incision is made in the upper calf or groin, the GSV is located and incised, the proximal end is ligated below the SFJ, a stripping wire with a probe is inserted into the GSV and advanced distally, and the GSV's proximal part is tied to the wire and stripped. The 2013 National Institute for Health and Care Excellence clinical guidelines recommend surgery as a third-line therapeutic option after EVLA or RFA and sclerotherapy [56,65-67]. This is in light of the fact that a growing number of research data do not consistently favor surgery as the standard treatment option due to postoperative complications.

When the saphenous veins themselves dilate by more than one centimeter in diameter, the HL/S of the GSV and their respective junctions are visible. In a cohort study, Navarro et al. (68) looked at the relationship between the clinical severity of reflux and the GSV diameter measured in the thigh and calf in 112 legs of 85 consecutive patients with SFJ and truncal GSV incompetence. They found that a GSV diameter of 5.5 mm or less predicted having no abnormal reflux, with a sensitivity of 78 percent, a specificity of 87 percent, positive and negative predictive values of 78 percent. The surgical results of HL/S are generally positive; RFA and ultrasound-guided foam sclerotherapy (UGFS) have lower anatomic closure rates at 30 days and 5 years than HL/S [56,65].

At 5 years, HL/S and EVLA have similar rates of saphenous vein closure [56,65,67]. DVT, hematoma, ecchymosis, wound infection, nerve injury, pain, and a delayed return to normal activity are the postoperative complications. Underreported injuries to femoral arteries, such as ligation or stripping of the femoral artery, were caused by inexperienced operators. A high rate of varicose vein recurrence following ligation alone may necessitate a second procedure [69]. To reduce the risk of nerve damage, stripping the GSV below the knee or the SSV is rarely done.

6.4 Ambulatory phlebectomy

The ambulatory phlebectomy (AP), also known as hook phlebectomy, mini-phlebectomy, microphlebectomy, or stab phlebectomy, is a minimally invasive outpatient procedure that can remove the majority of varicose veins, with the exception of the proximal long saphenous vein [21]. It is also referred to as technical terms of long-term recurrence of GSV and SFJ reflux, AP performs technically better than UGFS. In particular, varicose veins are removed by making a small puncture or stab wound. Before making a stab, it may be easier to retrieve a longer section of unwanted veins by administering a certain volume of saline around the target veins. Most of the time, AP is done in conjunction with other procedures. However, if junctional reflux is not treated, recurrence rates can be high [70]. The junctional reflux ought to be overseen by HL/S or EVLT as opposed to basic AP [70]. After AP, patients can walk right away. When broad compression pads are placed over the wounds following AP, the proportion of postoperative complications, such as hemorrhage and localized thrombophlebitis, that are associated with AP is significantly lower than that of HL/S.

Based on venous hemodynamics, the ambulatory conservative hemodynamic management of varicose veins known as CHIVA preserves the saphenous vein and collaterals intentionally [71]. Under local anesthesia, CHIVA is an office-based treatment for varicose veins. Preservation of the saphenous vein, local anesthesia, low cost, low pain, and fewer bruising, nerve damage, and recurrence are the primary benefits of stripping saphenectomy [72]. In terms of long-term efficacy for treating varicose veins, it appeared that CHIVA had superior clinical benefits [73]. The CHIVA procedure is likely practical equivalent to AP. After CHIVA surgery, patients can leave the theater immediately and go home to observe for a while. However, the most recent Cochrane review [74] looked at six RCTs with 1160 patients and compared the effects of CHIVA to those of RFA, vein stripping,

and EVLT, respectively. In terms of repeat of varicose veins, there is practically no distinction among CHIVA and stripping, RFA, or on the other hand EVLT. CHIVA may result in more bleeding than RFA or EVLT, but it has no effect on the rate of limb infection, superficial vein thrombosis, nerve injury, or hematoma. Three RCTs comparing CHIVA to vein stripping revealed that while CHIVA may lessen nerve injury and hematoma in the legs, it has little or no effect on limb infection, superficial vein thrombosis, or bruising [74]. In a single RCT comparing CHIVA to compression dressings for patients with venous ulcers, the effectiveness of CHIVA in reducing recurrence is unclear. It is important to guide and find the departure point (EP) of the veins before CHIVA. The majority of EPs (82.3%) are found below the knee, and 65.8% are found between the knee and the midcalf. Near the EP, tributary veins (TVs) have a diameter about 90% larger than the GSV. The nerve may be damaged by thermal ablations of the varicose vein below the knee [75].

6.5 Transillumination powered phlebectomy

Transilluminated powered phlebectomy (TIPP) has been described as a minimally invasive treatment for varicose veins, typically under spinal or general anesthesia [76]. Aremu et al [27] contrasted customary wound separations with TIPP also, tracked down that repeat at 52 wk in the TIPP bunch is higher than that in the wound separation bunch (21.2% versus 6.2%) [77]. All varicose veins, particularly truncal ones, cannot be treated with TIPP. At the one-year follow-up [78], a more favorable outcome can be achieved when RFA is used in conjunction with it. To evaluate the effect of TIPP, Passman et al. [79] divided their patients into three groups: EVLT-TIPP, combined saphenous vein stripping-stab avulsion phlebectomy (STRIP-TIPP), and saphenous stripping-stab avulsion phlebectomy (STRIP-AP) are all procedures. Procedures involving TIPP had a higher rate of complications (STRIP-AP 5.6%, STRIP-TIPP 6.5%, and EVAB-TIPP 2.0%; $P = NS$), and procedures involving TIPP resulted in a greater number of hematomas (STRIP-AP 5.6%, STRIP-TIPP 16.3%, and EVAB-TIPP 6.9%; $P < 0.05$) [79].

6.6 Endovenous thermal ablation therapy

Endovenous thermal ablation (EVLA or RFA) is recommended as a first-line treatment for symptomatic varicose veins and has replaced surgery to heat destroy and occlude the veins [57,80,81]. At the International Union of Phlebology in 1999, Dr. Carlos Bone first reported using EVLA to treat varicose veins. After the laser fiber is inserted into the target vein, a heat generator releases laser energy. The thermal light from the fiber tip causes local thermal injury to the veins, resulting in blood thrombosis, venous fibrosis, and contraction of the veins. Patients with incompetent saphenous veins appeared to benefit from safe and effective treatment with or without HL/S [82]. Within six months of EVLA, occlusion rates of the GSV and small saphenous vein were all greater than 90%, according to a systematic evidence review [69]. The SFJ anatomical success closure rate detected by DUS five years after treatment was found to be comparable between HL/S Gao RD et al. and Wallace et al. [83]. Treatment of varicose veins (85%) and EVLA (93%). After five years, Kheirelseid et al.'s meta-analysis [84] revealed that there were no significant differences between HL/S and EVLA or RFA. Radial fibers and lasers with high wavelengths (1470–1940 nm) are introduced for homogeneous damage of the vein wall to improve the efficacy and reduce the side effects of procedures [85].

A variety of laser wavelengths can be used to achieve occlusion. A 1470-nm laser with a radial probe produces a temperature of 120–140 °C (20 °C) [36], and a 1470-nm wavelength fiber causes less pain in the first week than a 940-nm fiber. The recurrence rate of treated veins that were followed by ultrasound at 48 months was lower with the 1470-nm wavelength laser than with the 940-nm fibers (8.3 percent vs 15.9 percent, $P = 0.017$) [86]. According to the findings of another RCT, patients who received treatment using the 1470-nm catheter had a higher occlusion rate (94.7% vs. 87.5%; at the one-year follow-up ($P = 0.05$)). Patients treated with the 1920-nm EVLA catheter had less ecchymosis, induration, and pain-relieving use. However, a systematic review and meta-analysis demonstrate that commonly used EVLA parameters have no effect on efficacy, that no wavelength is superior to another, and that there are no statistically significant differences between wavelengths (short (810, 940, and 980 nm), long (1470, 1500, and 1920 nm), high or low administered energy (50 J/cm) or follow-up (1 year and >1 year). EVLA had a 92% success rate overall [87]. Malskat et al.'s [88] RCT concentrate demonstrated that treatment achievement and unfavorable occasion rates between a 1470-nm frequency fiber and a 940-nm fiber for the treatment of varicose veins was similar [88].

Bruising (24%-75%), thrombophlebitis (5%), superficial vein thrombosis (DVT), hematomas and ecchymoses, skin burn, pigmentation, nerve injury, recurrence, and retained catheter fragment are the most common complications of EVLA [89,90]. Perforator ablation has been linked to an artery-venous fistula. When endovenous treatment is administered to the lower leg, there is a greater chance of nerve lesions. The second ablation can be used to treat recurrence, and one year after the second ablation, the occlusion rate was 93.3 percent [91,92]. RFA is a minimally invasive treatment guided by ultrasonography that uses a

radiofrequency catheter to deliver thermal energy to the refluxing vein segment. RFA can be segmental methodology that incite intensity to 120 °C. An introducer sheath is advanced through the guidewire, which will be pulled away, before the RFA catheter is inserted into the sheath into the target position. Ultrasonography is used to guide the procedure. A tumescent anesthetic solution is injected around the GSV to prevent burns and nerve damage, provide good hemostasis, and reduce pain. The RF generator is then turned on after a tumescent solution has been injected, and the catheter is slowly pulled along the length of the vein. In order to lessen the likelihood of vein thrombosis, bruising, and tenderness following surgery, compression therapy is used. Following RFA, patients are encouraged to walk immediately [93]. The RFA devices differ from one another. F-Care, developed by F Care Systems in Antwerp, Belgium, is a brand-new RFA treatment for venous insufficiency. The F-Care and Closurefast groups had 30-day total occlusion rates of 96.2% and 98.1%, respectively (P = 0.5). The F-Care and Closurefast groups had 1-year full occlusion rates of 71.7% and 90.6%, respectively (P = 0.013) [94].

The first RCT to compare Venefit, radiofrequency induced thermal therapy (RFITT), and endovenous radiofrequency (EVRF) results is the 3-RF trial. At six months, complete GSV closure was significantly better with Venefit and RFITT treatment than with EVRF treatment (79%, P 0.001) (100% and 98%, respectively). However, at one year, there were no significant differences in clinical outcomes [95]. A high satisfaction rate and quality of life score are linked to RFA. Although RFA required significantly more time in the operating room than surgery, recovery was significantly quicker, with patients returning to their usual activities and jobs within a week and fewer major adverse events. At a median follow-up of 11 months, 98.2% of 135 patients (164 limbs) achieved complete GSV obliteration [96]. Two years after treatment, it was demonstrated that RFA was not superior in terms of CHIVA and HL/S recurrence. No distinctions in postoperative difficulties or agony were found among HL/S, RFA, and CHIVA [97].

7. Comparison of RFA and EVLA

In terms of clinical efficacy—occlusion rate, time to return to normal activity, and complications like thrombophlebitis, hematoma, and recanalization EVLA and RFA appear to be the same safe and effective modalities [80,98,99]. For 240 patients treated with a 1470-nm diode laser with radial fibers, a 10-year follow-up using duplex ultrasound revealed stable and useful long-term results [85]. In patients with GSV incompetence, EVLA is the most cost-effective therapeutic option, followed by RFA [56]. Most varicose veins, both above and below the knee, can be treated with EVLA; in contrast, RFA is utilized to remove the truncal varicose vein over the knee, and can't treat the varicose EVLA-manageable veins below the knee in order to achieve a better outcome, RFA is typically performed in conjunction with other procedures like HIPP [78].

In a 159-patient RCT, endovenous treatment for primary GSV with RFA or 810 nm EVLT was compared. Duplex ultrasound revealed complete occlusion in both groups at one week, with RFA achieving 97% and EVLT achieving 96% at three months. No critical unfavorable occasion was noticed. EVLA and RFA demonstrated comparable outcomes in terms of venous occlusion rates and return to normal activities, despite RFA showing less pain, ecchymosis, and hematomas [99,100]. In the first five years, both radiofrequency-powered segmental ablation and EVLA with bare-tip fibers have similar rates of GSV obliteration, are equally effective clinically, and both have minimal postoperative pain scores and short recovery times [101].

8. Sclerotherapy

Sclerotherapy is a less invasive method of injecting sclerosants into the target veins through the skin [101]. These veins will then close after being subjected to immediate pressure from the outside world. Sclerotherapy typically does not call for anesthesia. Pressure stockings or swathes ought to be applied followingsclerotherapy. Sclerotherapy complications can be reduced by encouraging patients to walk. Sclerotherapy is considered cosmetic for veins less than 2.5 mm in diameter and all other indications and is recommended to treat varicose tributaries or the incompetent saphenous vein [57].

Patients with reflux should be treated with EVLA or HL/S to reduce the risk of recurrence because sclerotherapy alone has not been shown to be effective for the treatment of SFJ or saphenopopliteal junction reflux. Detergents like polidocanol and sodium morrhuate, osmotic agents, and chemical agents are examples of sclerosants that are currently available. There is no reliable evidence to suggest that one type of sclerosant is superior to another. Foam sclerotherapy (FS) is performed by mixing sclerosant with air (usually 1:4), either with or without UGFS. It can be used by itself or alongside other treatments. At 12 months of follow-up, the vein closure rate with FS is higher (68%) than with liquid sclerotherapy (17.5%) [102]. or When compared to EVLA and surgical stripping, UGFS is associated with faster recovery and less postoperative pain. Hyperpigmentation, telangiectasia matting, and superficial venous thromboembolism are among the most common complications. Patients frequently

whine of nodular or straight hardness alone in the varicose veins with delicacy. After FS, DVT, tissue necrosis, or even arterial thrombosis have been observed, particularly when liquid sodium morrhuate is used. During the first year of follow-up, GSV recanalization was highest in the UGFS group (51%) [102]. Four treatments were compared in a prospective RCT involving more than 580 legs: GSV surgical stripping, EVLA, RFA, and UGFS at the 5-year follow-up, UGFS was associated with a higher rate of technical failure (16.3%) than other treatments (P 0.001). UGFS was used to treat 288 limbs in 233 patients, with a mean follow-up interval of 37.8 months. In just two UGFS sessions, 89.6% of the incompetent veins were occluded. At three months and twelve months, the treated veins' internal diameters decreased by 32.7%. It is qualified to realize that UGFS can't seal uncouth GSV sections totally and might be rehashed a few times in instances of recurrence [103].

The Clari Vein device was used in the 2010 MECHANOCHEMICAL ENDOVENOUS ABLATION MOCA study. A liquid sclerosant is simultaneously injected into the damaged venous wall below the catheter tip to seal the veins after a wire tip is inserted into the intended veins and mechanically rotated to remove the intimal layer of the venous wall (3500 rpm). The MOCA, a non-thermal, non-tumescent option (NTNT), seems to be as effective as stab avulsion without putting nerve damage at risk. MOCA was found to be significantly less painful than RFA for truncal vein reflux in a recent multi-center randomized study (P = 0.003). Occlusion rates, clinical severity scores, time to return to normal activities, and adverse effects like DVT and superficial thrombophlebitis were not significantly different between MOCA and RFA [104]. At the 6-month follow-up, the anatomical closure rate of MOCA is higher with 3% POL liquid than with 2% POL liquid. A multicenter RCA study found that the 2% group had a technical success rate of 69.8% at six months, while the 3% group had a success rate of 78.0% (P = 0.027). Compared to GSVs larger than 5.9 mm, the overall closure rate was higher in GSVs smaller than 5.9 mm (84.3% vs. 59.5%, P 0.001). The overall success rate of MOCA is lower than that of EVAL, RFA, or HL/S, regardless of the concentration of the sclerosant [104].

9. CAE

CAE is a novel endovascular NTNT ablation technique that uses n-butyl-2-cyanoacrylate (NBCA) glue to treat incompetent truncal veins [105-107]. Since its introduction in 2013, the effectiveness of CAE has been demonstrated by numerous studies. The VenaSeal™ Closure System and the VariCloseR vein sealing system are the two currently available methods [107]. In the former method, a catheter is pulled back segmentally, whereas in the latter, it is pulled back continuously. During endovenous treatment, NBCA glue is an adhesive that rapidly polymerizes to initiate vein fibrosis and rapid occlusion. 1981 patients received NBCA, 445 RF, and 484 EVLA in a review of 17 studies involving 2910 patients (3220 veins). The average duration of follow-up was 12.3 months (range: 1–36 months). NBCA, RFA, and EVLA had two-year occlusion rates of 93.7, 90.9, and 91.5 percent, respectively [107].

CAE had higher anatomic conclusion rates at 30 d than EVLA [16]. Postoperative ecchymosis was significantly lower in CAE-treated patients than in RFA-treated patients (P 0.01). Both groups felt the same amount of pain throughout the procedure. The lowest number of complications, including bruising, phlebitis, and pain, occurred in NBCA-treated patients. Even when used without compression stockings, NBCA is safe, effective, and simple to administer [58]. However, phlebitis, cellulitis, and DVT are CAE treatment complications. It is likely that the adhesive has not deteriorated and has remained in the vein for many years. Occasionally, cyanoacrylate glue embolization can spread and trigger persistent foreign body reactions that call for surgical intervention [106,107]. With the VenaSeal system, there has been a thread-like thrombus extension that has been reported. After six months of follow-up, it went away on its own without the need for any additional treatment. Recanalization in the peripheral region after CAE results in incomplete occlusion of the treated vein. In this case, USFS can be utilized to accomplish the total impediment of the veins. MOCA and CAE look promising, but they need to be proven effective [56].

II. CONCLUSION

CVI of the lower extremities is a medical condition that occurs fairly frequently but is frequently misdiagnosed. It is essential to approach patients with suspicion of the condition because it is associated with a wide range of clinical manifestations. To properly comprehend and diagnose the pathophysiology of CVI, a thorough understanding of normal venous anatomy and function is required. For patients with CVI, functional evaluation with DUS is essential, whereas anatomical evaluation with CT or MR may be sufficient to diagnose lower extremity arterial disease. Conservative management relies heavily on compression stockings, but low compliance is a major obstacle to this treatment. In patients who are experiencing symptoms, it may be possible to use venous ablation therapy earlier. The iliac vein stenting procedure has the potential to significantly alleviate symptoms in patients who suffer from severe symptoms and have iliac vein compression stenosis.

ABBREVIATIONS

- (CVI):** Chronic venous insufficiency
(DUS): Duplex ultrasound
(RFA): Radiofrequency ablation
(GSV): Great saphenous vein
(SSV): small saphenous vein
(CFV): common femoral vein
(PASV): Posterior accessory saphenous vein
(AASV): anterior accessory of the great saphenous vein
(SFJ): saphenous junction
(EHIT): Endovenous heat-induced thrombus
(CE): cranial extension
(IVUS): venous intravascular ultrasound
(EVLA): Endovenous laser ablation
(RFA): Radiofrequency ablation
(HL/S): High ligation and stripping
(CHIVA): Conservatrice et Hemodynamique de l'Insuffisance Veineuse en Ambulatoire
(MOCA): Mechanochemical ablation
(CAE): Cyanoacrylate embolization
(MPFF): Micronized purified flavonoid fraction
(UGFS): Ultrasound-guided foam sclerotherapy
(AP): ambulatory phlebectomy
(TIPP): Trans-illuminated powered phlebectomy
(RFITT): Radiofrequency induced thermal therapy
(EVRF): Endovenous radiofrequency
(FS): Foam sclerotherapy
(MOCA): Mechanochemical endovenous ablation
(NTNT): non-thermal, non-tumescent option

CONFLICT OF INTEREST

All authors declare no conflicts of interest.

AUTHORS CONTRIBUTION

Authors have equally participated and shared every item of the work.

REFERENCES

- [1] Raju, Seshadri, and Peter Neglén. "Chronic venous insufficiency and varicose veins." *New England Journal of Medicine* 360.22 (2009): 2319-2327.

- [2] Eberhardt, Robert T., and Joseph D. Raffetto. "Chronic venous insufficiency." *Circulation* 130.4 (2014): 333-346.
- [3] Baliyan, Vinit, et al. "Lower extremity venous reflux." *Cardiovascular diagnosis and therapy* 6.6 (2016): 533.
- [4] Santler, Bettina, and Tobias Goerge. "Chronic venous insufficiency—a review of pathophysiology, diagnosis, and treatment." *JDDG: Journal der Deutschen Dermatologischen Gesellschaft* 15.5 (2017): 538-556.
- [5] Callam, M. J. "Epidemiology of varicose veins." *Journal of British Surgery* 81.2 (1994): 167-173.
- [6] Evans, C. J., et al. "Prevalence of varicose veins and chronic venous population: Edinburgh Vein Study insufficiency in men and women in the general population: Edinburgh Vein Study." *J. Epidemiol. Community Health* 53.3 (1999): 149-153.
- [7] Kurz, X., et al. "Chronic venous disorders of the leg: Epidemiology, outcomes, diagnosis and management: Summary of an evidence-based report on the VEINES task force." *International Angiology* 18.2 (1999): 83.
- [8] Brand, Frederick N., et al. "The epidemiology of varicose veins: the Framingham Study." *American journal of preventive medicine* 4.2 (1988): 96-101.
- [9] Scott, Thayer E., et al. "Risk factors for chronic venous insufficiency: a dual case-control study." *Journal of vascular surgery* 22.5 (1995): 622-628.
- [10] Fowkes, F. G. R., et al. "Lifestyle risk factors for lower limb venous reflux in the general population: Edinburgh Vein Study." *International journal of epidemiology* 30.4 (2001): 846-852.
- [11] Sadick, Neil S. "Predisposing factors of varicose and telangiectatic leg veins." *The Journal of dermatologic surgery and oncology* 18.10 (1992): 883-886.
- [12] Park, Tae Yun, et al. "Epidemiological trend of pulmonary thromboembolism at a tertiary hospital in Korea." *The Korean Journal of Internal Medicine* 32.6 (2017): 1037.
- [13] Morrone, Doralisa, and Vincenzo Morrone. "Acute pulmonary embolism: focus on the clinical picture." *Korean circulation journal* 48.5 (2018): 365-381.
- [14] Criqui, Michael H., et al. "Chronic venous disease in an ethnically diverse population: The San Diego Population Study." *American journal of epidemiology* 158.5 (2003): 448-456.
- [15] Bergan, John J., et al. "Chronic venous disease." *New England Journal of Medicine* 355.5 (2006): 488-498.
- [16] Kahn, Susan R., et al. "The post thrombotic syndrome: evidence-based prevention, diagnosis, and treatment strategies: a scientific statement from the American Heart Association." *Circulation* 130.18 (2014): 1636-1661.
- [17] Caggiati, Alberto, et al. "Nomenclature of the veins of the lower limb: extensions, refinements, and clinical application." *Journal of vascular surgery* 41.4 (2005): 719-724.
- [18] Caggiati, Alberto, et al. "Nomenclature of the veins of the lower limbs: an international interdisciplinary consensus statement." *Journal of vascular surgery* 36.2 (2002): 416-422.
- [19] Caggiati, Alberto. "Fascial relationships of the long saphenous vein." *Circulation* 100.25 (1999): 2547-2549.
- [20] Caggiati, Alberto. "Fascial relationships of the short saphenous vein." *Journal of vascular surgery* 34.2 (2001): 241-246.
- [21] Cavezzi, A., et al. "Duplex ultrasound investigation of the veins in chronic venous disease of the lower limbs—UIP Consensus Document. Part II: Anatomy." *Phlebology* 21.4 (2006): 168-179.
- [22] Wendell-Smith, C. P. "Fascia: an illustrative problem in international terminology." *Surgical and Radiologic Anatomy* 19 (1998): 273-277.
- [23] Theivacumar, N. S., R. J. Darwood, and M. J. Gough. "Endovenous laser ablation (EVLA) of the anterior accessory great saphenous vein (AAGSV): abolition of sapheno-femoral reflux with preservation of the great saphenous vein." *European Journal of Vascular and Endovascular Surgery* 37.4 (2009): 477-481.

- [24] Min, Robert J., Neil M. Khilnani, and Piyush Golia. "Duplex ultrasound evaluation of lower extremity venous insufficiency." *Journal of vascular and interventional radiology* 14.10 (2003): 1233-1241.
- [25] Johnson, Brian F., et al. "Relationship between changes in the deep venous system and the development of the post thrombotic syndrome after an acute episode of lower limb deep vein thrombosis: a one-to six-year follow-up." *Journal of Vascular Surgery* 21.2 (1995): 307-313.
- [26] Delis, Konstantinos T., Dimitris Bountouroglou, and Averil O. Mansfield. "Venous claudication in iliofemoral thrombosis: long-term effects on venous hemodynamics, clinical status, and quality of life." *Annals of surgery* 239.1 (2004): 118.
- [27] Razavi, Mahmood K., Michael R. Jaff, and Larry E. Miller. "Safety and effectiveness of stent placement for iliofemoral venous outflow obstruction: systematic review and meta-analysis." *Circulation: Cardiovascular Interventions* 8.10 (2015): e002772.
- [28] Kibbe, Melina R., et al. "Iliac vein compression in an asymptomatic patient population." *Journal of vascular surgery* 39.5 (2004): 937-943.
- [29] Kim, Jong Youn, et al. "Treatment of May-Thurner syndrome with catheter-guided local thrombolysis and stent insertion." *Korean Circulation Journal* 34.7 (2004): 655-659.
- [30] Lamont, Jeffrey P., et al. "Prospective evaluation of endoluminal venous stents in the treatment of the May-Thurner syndrome." *Annals of vascular surgery* 16.1 (2002): 61-64.
- [31] O'Sullivan, Gerard J., et al. "Endovascular management of iliac vein compression (May-Thurner) syndrome." *Journal of Vascular and Interventional Radiology* 11.7 (2000): 823-836.
- [32] Koo, Sonya, and Chieh-Min Fan. "Pelvic congestion syndrome and pelvic varicosities." *Techniques in vascular and interventional radiology* 17.2 (2014): 90-95.
- [33] Labropoulos, Nicos, et al. "Study of the venous reflux progression." *Journal of vascular surgery* 41.2 (2005): 291-295.
- [34] Czarniawska-Grzesinska, Malgorzata, and Malgorzata Bruska. "Development of valves in the small saphenous vein in human fetuses." *Folia Morphologica* 61.1 (2002): 37-42.
- [35] Tretbar, Lawrence L. "Deep veins." *Dermatologic surgery* 21.1 (1995): 47-51.
- [36] Arnoldi, C. C. "Venous pressure in the leg of healthy human subjects at rest and during muscular exercise in the nearly erect position." *Acta Chirurgica Scandinavica* 130.6 (1965): 570-583.
- [37] Labropoulos, Nicos, et al. "The role of venous outflow obstruction in patients with chronic venous dysfunction." *Archives of Surgery* 132.1 (1997): 46-51.
- [38] Katz, Mira L., et al. "Variability of venous hemodynamics with daily activity." *Journal of vascular surgery* 19.2 (1994): 361-365.
- [39] Rutherford, Robert B., et al. "Venous severity scoring: an adjunct to venous outcome assessment." *Journal of vascular surgery* 31.6 (2000): 1307-1312.
- [40] Scuderi, A., et al. "The incidence of venous disease in Brazil based on the CEAP classification: An epidemiological study." *International angiology* 21.4 (2002): 316.
- [41] Gloviczki, Peter, et al. "Report of the Society for Vascular Surgery and the American Venous Forum on the July 20, 2016 meeting of the Medicare Evidence Development and Coverage Advisory Committee panel on lower extremity chronic venous disease." *Journal of Vascular Surgery: Venous and Lymphatic Disorders* 5.3 (2017): 378-398.
- [42] Nicolaides, A. N., et al. "Management of chronic venous disorders of the lower limbs guidelines according to scientific evidence." *International angiology* 27.1 (2008): 1.
- [43] Christopoulos, D., A. N. Nicolaides, and G. Szendro. "Venous reflux: quantification and correlation with the clinical severity of chronic venous disease." *Journal of British Surgery* 75.4 (1988): 352-356.

- [44] Criado, Enrique, et al. "The role of air plethysmography in the diagnosis of chronic venous insufficiency." *Journal of vascular surgery* 27.4 (1998): 660-670.
- [45] Cai, Liang, and James E. Bear. "Peering deeply inside the branch." *The Journal of Cell Biology* 180.5 (2008): 853-855.
- [46] Cho, Eun-Suk, et al. "Computed tomographic venography for varicose veins of the lower extremities: prospective comparison of 80-kVp and conventional 120-kVp protocols." *Journal of computer assisted tomography* 36.5 (2012): 583-590.
- [47] Kim, S. Y., et al. "Preoperative determination of anatomic variations of the small saphenous vein for varicose vein surgery by three-dimensional computed tomography venography." *Phlebology* 27.5 (2012): 235-241.
- [48] Uhl, J. F. "Three-dimensional modelling of the venous system by direct multislice helical computed tomography venography: technique, indications and results." *Phlebology* 27.6 (2012): 270-288.
- [49] Markel, Arie, et al. "A comparison of the cuff deflation method with Valsalva's maneuver and limb compression in detecting venous valvular reflux." *Archives of Surgery* 129.7 (1994): 701-705.
- [50] Coleridge-Smith, P., et al. "Duplex ultrasound investigation of the veins in chronic venous disease of the lower limbs—UIP Consensus Document. Part I: Basic principles." *Phlebology* 21.4 (2006): 158-167.
- [51] Neglén, Peter, et al. "Hemodynamic and clinical impact of ultrasound-derived venous reflux parameters." *Journal of vascular surgery* 40.2 (2004): 303-310.
- [52] Neglén, Peter. "Chronic deep venous obstruction: definition, prevalence, diagnosis, management." *Phlebology* 23.4 (2008): 149-157.
- [53] Neglén, Peter, and Seshadri Raju. "Intravascular ultrasound scan evaluation of the obstructed vein." *Journal of vascular surgery* 35.4 (2002): 694-700.
- [54] Li, Xin, Shiyun Ren, and Xianlun Li. "Outcomes of foam sclerotherapy plus ligation versus foam sclerotherapy alone for venous ulcers in lower extremities." *Annals of Vascular Surgery* 45 (2017): 160-165.
- [55] Liu, Peng, et al. "Intravenous catheter-guided laser ablation: a novel alternative for branch varicose veins." *International surgery* 96.4 (2011): 331-336.
- [56] Epstein, David, et al. "Cost-effectiveness analysis of current varicose veins treatments." *Journal of Vascular Surgery: Venous and Lymphatic Disorders* 10.2 (2022): 504-513.
- [57] Gloviczki, Peter, et al. "The care of patients with varicose veins and associated chronic venous diseases: clinical practice guidelines of the Society for Vascular Surgery and the American Venous Forum." *Journal of vascular surgery* 53.5 (2011): 2S-48S.
- [58] Todd, Marie. "Compression therapy for chronic oedema and venous leg ulcers: AndoFlex TLC Calamine." *British Journal of Nursing* 28.12 (2019): S32-S37.
- [59] Chou, Jian-Hong, et al. "Optimal duration of compression stocking therapy following endovenous thermal ablation for great saphenous vein insufficiency: a meta-analysis." *International Journal of Surgery* 65 (2019): 113-119.
- [60] Gohel, Manjit S., and Alun H. Davies. "Pharmacological agents in the treatment of venous disease: an update of the available evidence." *Current vascular pharmacology* 7.3 (2009): 303-308.
- [61] Ulloa, Jorge H. "Micronized purified flavonoid fraction (MPFF) for patients suffering from chronic venous disease: a review of new evidence." *Advances in Therapy* 36 (2019): 20-25.
- [62] Akhmetzianov, Rustem V., and Roman A. Bredikhin. "Clinical efficacy of conservative treatment with micronized purified flavonoid fraction in female patients with pelvic congestion syndrome." *Pain and Therapy* 10 (2021): 1567-1578.

- [63] Krasinski, Zbigniew, et al. "Patients with chronic venous insufficiency in the times of COVID-19 and the risk of thrombus formation—suggestions on conservative treatment of such patients based on the principles of pathophysiology." *Polish Journal of Surgery* 93.2 (2021): 42-51.
- [64] Secretariat, Medical Advisory. "Endovascular radiofrequency ablation for varicose veins: an evidence-based analysis." *Ontario Health Technology Assessment Series* 11.1 (2011): 1.
- [65] Farah, Magdoleen H., et al. "A systematic review supporting the Society for Vascular Surgery, the American Venous Forum, and the American Vein and Lymphatic Society guidelines on the management of varicose veins." *Journal of vascular surgery: venous and lymphatic disorders* 10.5 (2022): 1155-1171.
- [66] Snyder, D., et al. "Key Messages." *Skin Substitutes for Treating Chronic Wounds [Internet]*. Agency for Healthcare Research and Quality (US), 2020.
- [67] Mazzei, Sergio, et al. "Dehydrated human amnion/chorion membrane treatment of venous leg ulcers." *Indian Journal of Dermatology, Venereology and Leprology* 86 (2020): 212.
- [68] Navarro, Tulio P., Konstantinos T. Delis, and Antonio P. Ribeiro. "Clinical and hemodynamic significance of the greater saphenous vein diameter in chronic venous insufficiency." *Archives of surgery* 137.11 (2002): 1233-1237.
- [69] Medical Services Advisory Committee. "Endovenous Laser Therapy (ELT) for Varicose Veins, MSAC Application 1113." *Canberra: MSAC* (2008).
- [70] Gao, Rong-Ding, et al. "Strategies and challenges in treatment of varicose veins and venous insufficiency." *World Journal of Clinical Cases* 10.18 (2022): 5946.
- [71] Faccini, Felipe Puricelli, et al. "CHIVA to spare the small and great saphenous veins after wrong-site surgery on a normal saphenous vein: a case report." *Jornal Vascular Brasileiro* 18 (2019).
- [72] Faccini, Felipe Puricelli, Stefano Ermini, and Claude Franceschi. "CHIVA to treat saphenous vein insufficiency in chronic venous disease: characteristics and results." *Jornal Vascular Brasileiro* 18 (2019).
- [73] Guo, Liqin, et al. "Long-term efficacy of different procedures for treatment of varicose veins: a network meta-analysis." *Medicine* 98.7 (2019).
- [74] Bellmunt-Montoya, A., et al. "CHIVA method for the treatment of chronic venous insufficiency." *Journal of Vascular Surgery: Venous and Lymphatic Disorders* 10.4 (2022): 976.
- [75] Yun, Sangchul. "Ultrasound-based topographic analysis of tributary vein connection with the saphenous vein during ambulatory conservative hemodynamic correction of chronic venous insufficiency." *Journal of Vascular Surgery: Venous and Lymphatic Disorders* 7.3 (2019): 356-363.
- [76] Aremu, M. A., et al. "Prospective randomized controlled trial: conventional versus powered phlebectomy." *Journal of vascular surgery* 39.1 (2004): 88-93.
- [77] De Zeeuw, R., et al. "Transilluminated powered phlebectomy accomplished by local tumescent anaesthesia in the treatment of tributary varicose veins: preliminary clinical results." *Phlebology* 22.2 (2007): 90-94.
- [78] Lawrence, Peter F. "Journal of Vascular Surgery: Venous and Lymphatic Disorders—January 2021 Audiovisual Summary." *Journal of Vascular Surgery: Venous and Lymphatic Disorders* 9.1 (2021): e14-e15.
- [79] Passman, Marc A., et al. "Combined endovenous ablation and transilluminated powered phlebectomy: is less invasive better?" *Vascular and endovascular surgery* 41.1 (2007): 41-47.
- [80] Kabnick, Lowell S., et al. "Classification and treatment of endothermal heat-induced thrombosis: Recommendations from the American Venous Forum and the Society for Vascular Surgery This Practice Guidelines document has been co-published in *Phlebology* [DOI: 10.1177/0268355520953759] and *Journal of Vascular Surgery: Venous and Lymphatic Disorders* [DOI: 10.1016/j.jvsv.2020.06.008]. The publications are identical except for minor stylistic and spelling differences in keeping with each journal's style. The contribution has been" *Phlebology* 36.1 (2021): 8-25.

- [81] Tofigh, Arash Mohammadi, Hamed Tahmasebi, and Javad Zebarjadi. "Comparing the Success Rate and Side Effects of Endovenous Laser Ablation and Radiofrequency Ablation to Treat Varicose Veins in the Lower Limbs: A Randomized Clinical Trial." *Journal of lasers in medical sciences* 11. Suppl 1 (2020): S43.
- [82] Hamann, Sterre AS, Simone K. van der Velden, and Marianne GR De Maeseneer. "Safety and effectiveness of endovenous thermal ablation for incompetent saphenous veins with an aneurysm close to the junction." *European Journal of Vascular and Endovascular Surgery* 58.2 (2019): 244-248.
- [83] Wallace, T., et al. "Long-term outcomes of endovenous laser ablation and conventional surgery for great saphenous varicose veins." *Journal of British Surgery* 105.13 (2018): 1759-1767.
- [84] Kheirleseid, Elrasheid AH, et al. "Systematic review and meta-analysis of randomized controlled trials evaluating long-term outcomes of endovenous management of lower extremity varicose veins." *Journal of Vascular Surgery: Venous and Lymphatic Disorders* 6.2 (2018): 256-270.
- [85] Pavei, Patrizia, et al. "Favorable long-term results of endovenous laser ablation of great and small saphenous vein incompetence with a 1470-nm laser and radial fiber." *Journal of Vascular Surgery: Venous and Lymphatic Disorders* 9.2 (2021): 352-360.
- [86] Arslan, Ümit, et al. "More successful results with less energy in endovenous laser ablation treatment: long-term comparison of bare-tip fiber 980 nm laser and radial-tip fiber 1470 nm laser application." *Annals of vascular surgery* 45 (2017): 166-172.
- [87] Malskat, Wendy SJ, et al. "Commonly used endovenous laser ablation (EVLA) parameters do not influence efficacy: results of a systematic review and meta-analysis." *European Journal of Vascular and Endovascular Surgery* 58.2 (2019): 230-242.
- [88] Malskat, W. S. J., et al. "Randomized clinical trial of 940-versus 1470-nm endovenous laser ablation for great saphenous vein incompetence." *Journal of British Surgery* 103.3 (2016): 192-198.
- [89] Nemoto, Hiroko, et al. "Venous thromboembolism complications after endovenous laser ablation for varicose veins and role of duplex ultrasound scan." *Journal of Vascular Surgery: Venous and Lymphatic Disorders* 7.6 (2019): 817-823.
- [90] Ren, Shiyang, et al. "Retained foreign body after laser ablation." *International surgery* 97.4 (2013): 293-295.
- [91] Santos, Fanny Rodriguez, et al. "Secondary Ablation of Recanalized Saphenous Vein after Endovenous Thermal Ablation." *Annals of Vascular Surgery* 68 (2020): 172-178.
- [92] Müller, Lars, and Jens Alm. "Feasibility and technique of endovenous laser ablation (EVLA) of recurrent varicose veins deriving from the sapheno-femoral junction—A case series of 35 consecutive procedures." *Plos one* 15.7 (2020): e0235656.
- [93] Somasundaram, Santosh K., et al. "Office based endovenous radiofrequency ablation of truncal veins: a case for moving varicose vein treatment out of operating theatres." *European Journal of Vascular and Endovascular Surgery* 58.3 (2019): 410-414.
- [94] Bitargil, Macit, and Helin E. Kılıç. "Ablation of the great saphenous vein with F-care versus Closurefast endovenous radiofrequency therapy: Double-blinded prospective study." *Phlebology* 35.8 (2020): 561-565.
- [95] Nyamekye, Isaac K., et al. "A randomised controlled trial comparing three different radiofrequency technologies: short-term results of the 3-RF trial." *European Journal of Vascular and Endovascular Surgery* 58.3 (2019): 401-408.
- [96] Borghese, O., A. Pisani, and I. Di Centa. "Endovenous radiofrequency for chronic superficial venous insufficiency: Clinical outcomes and impact in quality of life." *JMV-Journal de Médecine Vasculaire* 46.1 (2021): 3-8
- [97] Cañas, Elena González, et al. "A randomized controlled noninferiority trial comparing radiofrequency with stripping and conservative hemodynamic cure for venous insufficiency technique for insufficiency of the great saphenous vein." *Journal of Vascular Surgery: Venous and Lymphatic Disorders* 9.1 (2021): 101-112.
- [98] He, Guangzhi, et al. "Comparison of ultrasound-guided endovenous laser ablation and radiofrequency for the varicose veins treatment: An updated meta-analysis." *International journal of surgery* 39 (2017): 267-275.

- [99] Izzo, Luciano, et al. "High ligation of sapheno-femoral junction and thermal ablation for lower limb." *Ann. Ital. Chir* 91.1 (2020): 61-64.
- [100] Florio, G., et al. "Thermal ablation combined with high ligation of sapheno-femoral junction for lower limb primary varicosity." *Il Giornale di Chirurgia-Journal of the Italian Surgical Association* 40.5 (2019): 413-416.
- [101] Lawson, James A., et al. "Prospective comparative cohort study evaluating incompetent great saphenous vein closure using radiofrequency-powered segmental ablation or 1470-nm endovenous laser ablation with radial-tip fibers (Varico 2 study)." *Journal of Vascular Surgery: Venous and Lymphatic Disorders* 6.1 (2018): 31-40.
- [102] Epstein, David, et al. "Cost-effectiveness of current and emerging treatments of varicose veins." *Value in Health* 21.8 (2018): 911-920.
- [103] Chen, Chien-Hsun, Cheng-Sheng Chiu, and Chih-Hsun Yang. "Ultrasound-Guided Foam Sclerotherapy for Treating Incompetent Great Saphenous Veins—Results of 5 Years of Analysis and Morphologic Evolvement Study." *Dermatologic surgery* 38.6 (2012): 851-857.
- [104] Lam, Yee Lai, et al. "A multicenter, randomized, dose-finding study of mechanochemical ablation using ClariVein and liquid polidocanol for great saphenous vein incompetence." *Journal of Vascular Surgery: Venous and Lymphatic Disorders* 10.4 (2022): 856-864.
- [105] Chan, Sally SJ, et al. "Retrograde technique for great saphenous vein ablation using the VenaSeal™ closure system—Ideal approach for deep seated or small below the knee refluxing truncal veins." *Phlebology* 35.2 (2020): 102-109.
- [106] Langridge, Benjamin J., et al. "Cyanoacrylate glue embolisation for varicose veins—A novel complication." *Phlebology* 35.7 (2020): 520-523.
- [107] Dimech, Anthony Pio, and Kevin Cassar. "Efficacy of cyanoacrylate glue ablation of primary truncal varicose veins compared to existing endovenous techniques: A systematic review of the literature." *The Surgery Journal* 6.02 (2020): e77-e86.