INTRODUCTION

Chronic venous disease (CVD) refers to a wide spectrum of morphologic and/or functional abnormalities of the venous system of long duration. It varies in presentations, initially, it is asymptomatic. The most common presentations of CVD are telangiectases, reticular veins, and varicose veins (1).

Chronic venous insufficiency (CVI) describes a condition that affects the venous system of the lower extremities (1). It generally refers to an advanced form of chronic venous disease (2), by definition, is associated with clinical symptoms, so class C3 and above (according to CEAP classification) are designated as CVI (3).

CVI is one of the most common conditions affecting humankind (4,5). It is associated with a variety of symptoms and also the complications such as venous leg ulcer. This has substantial socioeconomic effects and significantly impacts patients’ quality of life (3).
VENOUS ANATOMY

- Vein
  - Venous anatomy is much more complex than arterial anatomy.
  - An official anatomic nomenclature of venous system was update in 2001. The changes were showed in table 1.
  - The extremity venous systems compose of three components; superficial, deep and perforator veins (Figure 1 and Figure 2).

1. Superficial veins
   - Superficial veins consist of great saphenous vein, small saphenous vein, accessory saphenous tributaries (anterior and posterior), the communicating veins, reticular venous plexus and subpapillary venous plexus.
   - They are located in the compartment above muscle fascia called 'superficial compartment'. In the leg, there is a saphenous fascia (previously called superficial fascia, the Colles or Scarpa fascia, or the subcutaneous pseudofascia) lies above muscle fascia contributes to subcompartment called 'saphenous compartment' which contains the main saphenous trunk. The remaining superficial veins are located in the superficial compartment above saphenous compartment.

2. Deep veins
   - Deep veins are located in the fascial muscle compartments.
   - Deep veins of lower extremity consist of axial vein, which follow the course of major arteries, and intramuscular veins, including venous sinusoids and plexi.
   - Most of them have the same names as arteries.

3. Perforator veins
   - They transverses the muscular fascia, connecting between the deep and superficial veins.
   - They direct flow from the superficial to deep systems to return deoxygenated blood to the heart.
   - They are located at 6-cm interval from the base of the heel to the upper part of the thigh.

Table 1: Changes in Nomenclature for the Superficial and Deep Veins of the Leg Based on the 2001 Conference

<table>
<thead>
<tr>
<th>Old term</th>
<th>New term</th>
</tr>
</thead>
<tbody>
<tr>
<td>Greater/long saphenous</td>
<td>Great saphenous vein</td>
</tr>
<tr>
<td>Lesser/short saphenous</td>
<td>Small saphenous vein</td>
</tr>
<tr>
<td>Saphenofemoral junction</td>
<td>Confluence of the</td>
</tr>
<tr>
<td></td>
<td>superficial inguinal veins</td>
</tr>
<tr>
<td>Giacomini’s vein</td>
<td>Intersaphenous vein</td>
</tr>
<tr>
<td>Posterior arch/Leonardo’s</td>
<td>Posterior accessory great</td>
</tr>
<tr>
<td></td>
<td>saphenous vein</td>
</tr>
</tbody>
</table>

Deep

<table>
<thead>
<tr>
<th>Superficial femoral vein</th>
<th>Femoral vein</th>
</tr>
</thead>
<tbody>
<tr>
<td>SFV (Superficial femoral)</td>
<td>FV (Femoral)</td>
</tr>
<tr>
<td>Perforators</td>
<td></td>
</tr>
<tr>
<td>Cockett perforators (I, II, III)</td>
<td>Posterior tibial perforators (lower, middle, upper)</td>
</tr>
<tr>
<td>Boyd’s perforator</td>
<td>Paratibial perforator (proximal)</td>
</tr>
<tr>
<td>Sherman’s perforator</td>
<td>Paratibial perforator</td>
</tr>
<tr>
<td>24 cm perforator</td>
<td>Paratibial perforator</td>
</tr>
<tr>
<td>Hunter’s and Dodd’s</td>
<td>Perforators of the femoral canal</td>
</tr>
<tr>
<td>May’s or Kuster’s</td>
<td>Ankle perforators</td>
</tr>
</tbody>
</table>

Figure 1. Relationship between the fascia and veins of the lower extremity. The fascia covers the muscle and separates the deep compartment from the superficial compartment. Superficial veins (a) drain the subpapillary and reticular venous plexuses and they are connected to deep veins through perforating veins (b). The saphenous fascia invests the saphenous vein. The saphenous compartment is a subcompartment of the superficial compartment. (From Pounds Lori L., Killen L., Venous Physiology. In: Cronenwett, Jack L., Johnston K. Wayne, editors. Rutherford’s Vascular Surgery. 8th ed. Philadelphia: Elsevier; 2014)
Venous valves

- Venous valves can be found throughout the body, but highest concentration in lower extremities. They can be found in both deep and superficial veins and in all size of veins down to the level of venules (6).
- The valves are 1-way bicuspid, functioning to prevent the retrograde flow of the blood from proximal to distal direction (6).
- The frequency of the valves increases from proximal to distal leg to prevent an increase pressure within the distal veins because of gravitational effects (1).
- Venous valve distribution (6)
  - IVC: no valve was found
  - Iliofemoral system: a mean of 1.2 valves on the Right and 0.97 valves on the left
  - Femoral vein: 1-4 valves, 90% of population have at least 2 valves
  - Popliteal vein: 2 valves
  - Great saphenous vein: range between 2-9 valves (7), 2.26 valves on the left side and 2.07 valves on the right side (8).
- Venous valves are consistently located in specific sites in the common femoral, femoral and popliteal veins of the leg. Valves in the CFV, near the inguinal ligament, in the FV just distal to the DFV tributary and in the PV near the adductor hiatus were the most consistently reported sites (Figure 3) (9).

Venous wall

Vein wall are composed of 3 layers.

1. Intima
   - Intima is a single cell layer resting on connective tissue.
   - The valve is a layer of intima. Venous valves are lined on both sides of the vein.

2. Media
   - The media composes of smooth muscle and connective tissue such as collagen.
   - In the large vein, it has thick media which has a great capacity of muscle contraction and in preventing dilatation and varicosity formation. In contrast, the tributaries of the great saphenous vein have little media and are prone to form varicosity.

3. Adventitia
   - This layer contains loose connective tissue, vasa vasorum and adrenergic nerve fibers.

Figure 2. anatomy of deep and superficial venin of lower extremities.

Figure 3. The most constant locations of valves within the femoral and popliteal veins. (From Moore HM, Gohel M, Davies AH. Number and location of venous valves within the popliteal and femoral veins – a review of the literature. J Anat. 2011 Oct;219(4):439–43.)
VENOUS PHYSIOLOGY

- **Functions:** The venous system has two important functions.
  1. Returns the blood from peripheral back to the heart.
  2. Maintains the cardiovascular hemostasis by changing in capacities.

- **Hemodynamics**
  Normally, in supine position, blood pressure at capillary bed is about 12-18 mmHg which is higher than the pressure in right atrium which is about 4-7 mmHg, so the blood from the capillary bed can flow back to the heart along this gradient in normal condition. In upright position, venous flow in the lower extremities is dominated by the effects of hydrostatic pressure, which is derived from the weight of the column of blood below the right atrium. This hydrostatic pressure needed to be overcome and the calf muscle pump plays an important role in generating high pressure, working together with venous valves to return the blood back to the right atrium.

- **Muscle pump**
  Muscle pump facilitates the return of venous blood to the heart. It takes place in the thigh, in the calf and in the conjunction with the venous plexus on the plantar aspect of the foot. The calf muscle pump, which includes the soleal and gastrocnemius muscles (figure 4), their intramuscular venous sinusoids, and the superficial and deep veins, appears to be more important than the thigh pump. It generates pressure up to 200 mmHg during muscle contraction and expels 40-60% of the venous blood of the calf (100-150 mL) (6).

  Muscle contraction produces higher pressure in the deep venous system than in the superficial venous system. However, the reflux of the blood from the deep to the superficial venous system is prevented by the one-way valve in the perforating veins which direct the flow from the superficial veins to the deep veins. When the muscles relax, the intramuscular venous sinusoids are refilled from the distal deep veins to proximal deep veins, and from the superficial venous system to the deep venous system.

- **Venous compliance and Capacitance**
  The veins also play an important role in maintaining cardiovascular hemostasis by storing large volumes of blood, about 60-80% of systemic blood volume at a time. They have an ability to maintain the pressure, even there is a massive change in blood volume, by changing in their shapes which is regulated by reflex change in vasomotor tone, together with passive distention or recoil of veins (6,10).

  Venous compliance is the change in blood volume that occurs for each unit of change in transmural pressure in the segment of vein. (transmural pressure is the difference between intraluminal pressure acting to expand a vein and tissue pressure acting to collapse the vein: Transmural pressure = intraluminal pressure – tissue pressure) (6). When transmural pressure is above 30 mmHg, the venous compliance is decreased which means the higher pressure is required to stretch the venous wall (figure 5). At the arterial pressure, veins become as stiff as arteries.
VENOUS PATHOPHYSIOLOGY

Dysfunction or incompetence of the valves in the superficial venous system allows retrograde flow of blood, which is called “reflux” and serves to increase hydrostatic pressures (1). Saphenous veins valve reflux is associated with varices. Varices are caused by systemic weakness in the vein wall. Varicose changes may involve the great and small saphenous veins (“truncal varices”), their tributaries (“branch varicosities”), or both (11).

The causes of superficial vein valve failure can be divided into

1. Primary cause which cause by pre-existing weakness in the vessel wall or valve leaflets.
2. Secondary causes such as direct injury, superficial phlebitis, or excessive venous distention resulting from hormonal effects or high pressure.

Pathogenesis of chronic venous insufficiency (CVI) is complex and not yet well understood (3,10). Venous hypertension plays an important role in developing CVI. This may result from venous valvular incompetence, venous obstruction, or a combination of these mechanisms, which is common (1,3,11). These factors are exacerbated by muscle pump dysfunction, most notably of the calf muscles. Venous hypertension activates leukocytes (10) and other inflammatory cytokines (3,11) point to adaptive responses to injury and abnormal healing causing the vein wall fibrosis. The vein wall fibrosis contributes to valvular damage, which then worsens the hydrostatic pressure regulation and consequently promotes greater venous hypertension with the upright position (10).

The reflux between the superficial and deep system, either at the perforator veins or through the junctions of the deep and superficial systems, at the saphenofemoral and saphenopopliteal junctions, accounts for an increase in venous hydrostatic pressure transmitted to the superficial veins and tissues and leading to CVI. This process is worsened by venous obstruction (10). Dysfunction of the deep vein valves has been shown to increase the rate of progression of venous disease with a higher rate of venous ulceration formation (1).

Venous outflow obstruction plays a significant role in the pathogenesis of CVI (1), especially iliac vein obstruction (11). Such lesions are present in about 60% of the asymptomatic general population but are found in more than 90% of symptomatic patients (11). Obstruction of iliac vein can be caused by both post-thrombotic and non-thrombotic obstruction. Non-thrombotic obstructions occur in the iliac vein where it is crossed by the iliac or hypogastric artery, and they are thought to be caused by the trauma of arterial pulsations (11).

Deep veins obstruction causes an increase in venous pressure with muscle contraction, leads to secondary muscle pump dysfunction. Muscle pump dysfunction often occurs with severe reflux or obstruction. Dysfunction of the muscle pumps may lead to ineffective emptying of venous blood from the distal lower extremity and appears to be a significant mechanism for the development of complications such as venous ulcers (1).

Figure 5. A, Cross-section of a venous lumen at various transmural pressures. At lower pressures the vein is elliptical, whereas at high pressures it is circular. B, Relationship of venous volume to transmural pressure. At low pressures, veins are compliant and change shape easily to accommodate large increases in volume. At high pressures, they become stiff and cannot accommodate large changes in volume. (From Pounds Lori L., Killevich Lois A. Venous Physiology. In: Cronenwett, Jack L., Johnston K. Wayne, editors. Rutherford’s Vascular Surgery. 8th ed. Philadelphia: Elsevier; 2014)
EPIDEMIOLOGY AND RISK FACTORS

- **Prevalence**

Prevalence estimates vary widely by geographic location, with the highest reported rates in Western countries. Reports of prevalence of chronic venous insufficiency vary from <1% to 40% in females and from <1% to 17% in males. Prevalence estimates for varicose veins are higher, <1% to 73% in females and 2% to 56% in males (5). Its prevalence is very low in African and Asian or Australasian aborigine populations although immigrant subjects from these regions have the same risk as the population of their host country (12).

- **Risk factors**

There are multiple related risk factors of CVI, including pregnancy (1), advance age, obesity, prolonged standing (2), female gender (1,13), genetics, (1,2), and rarely, congential absence of valves, prior DVT or trauma.

Kanchanabat et al. studied the risk factors of CVI in Thai population and found statistically significant risk factors were BMI, physical evidence of varicose veins, history of ipsilateral leg trauma and proportion of upright posture during working hours (2).

CLASSIFICATION

CVI is one of the most difficult pathologies to classify on account of the complexity of its expression. Several classifications have been proposed to better define CVI and assign degrees of severity (4). In 1994, an international group of experts, meeting at Maui, worked out a new classification that would be as precise and complete as possible (4). This classification is called "CEAP". The CEAP classification system was developed in an effort not only to incorporate use of Duplex scanning in diagnosis, but also to standardize evaluation for comparison of outcomes across clinical studies (5). The use of the CEAP classification in the evaluation of CVD has a strong recommendation in the CPG (1,15).

Each letter stands for a particular dimension (table 2) (1,4).

**C:** Clinical, divided into 7 categories (0-6) according to objective clinical signs of chronic venous disease. The presence of symptoms or their absence is identified by the letters S (symptomatic) or A (asymptomatic) positioned after the letter C.

**E:** Etiology, divided into Congenital (Ec), Primary (Ep), Secondary (Es) and no venous cause identified (En).

**A:** Anatomy, based on class is based on the venous systems; Superficial veins (As), Deep veins (Ad), Perforating veins (Ap) and no venous location identified (An).

**P:** Pathophysiology, divided into Reflux (r), Obstruction (o), Both (r,o) and no venous pathophysiology identified (Pn).
Most recently, the **Venous Severity Scoring (VSS) system** was introduced as a useful and reliable method for assessment of an individual patient’s response to treatment as well as to allow improved outcome assessment (15,16). The VSS system consists of three components as the followings (5,16):

1. **VCSS (venous clinical severity score)** which is a modification to replace CEAP clinical score.
2. **VSDS (venous segmental disease score)** which is a combination of the anatomic and pathophysiologic components of CEAP.
3. **VDS (venous disability score)** a modification of the original CEAP disability score.

From the study, Kakkos et al. found that VSS has correlation with severity of the CVI. VCSS, and VDS has a linear association with CEAP clinical class (16). However, Passman et al. suggested that VCSS has more global application in determining overall severity of venous disease, while at the same time highlighting the strengths of the other venous assessment tools (17). The revised venous clinical severity score provides clarification of the terms and better definition of the descriptors and has further clinical applicability (table 3)(1).

<table>
<thead>
<tr>
<th>Attribute</th>
<th>Absent = 0</th>
<th>Mild = 1</th>
<th>Moderate = 2</th>
<th>Severe = 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pain</td>
<td>None</td>
<td>Occasional, not restricting daily activity</td>
<td>Daily, interfering but not preventing daily activity</td>
<td>Daily, limits most daily activity</td>
</tr>
<tr>
<td>Varicose veins</td>
<td>None</td>
<td>Few, isolated branch varices, or clusters, includes ankle flare</td>
<td>Confined to calf or thigh</td>
<td>Involves calf and thigh</td>
</tr>
<tr>
<td>Venous edema</td>
<td>None</td>
<td>Limited to foot and ankle</td>
<td>Extends above the ankle but below knee</td>
<td>Extends to knee and above</td>
</tr>
<tr>
<td>Skin pigmentation</td>
<td>None or focal</td>
<td>Limited to perimalleolar</td>
<td>Diffuse, over lower third of calf</td>
<td>Wider distribution below lower third of calf</td>
</tr>
<tr>
<td>Inflammation</td>
<td>None</td>
<td>Mild cellulitis, ulcer margin limited to perimalleolar</td>
<td>Diffuse over lower third of calf</td>
<td>Wider distribution below lower third of calf</td>
</tr>
<tr>
<td>Induration</td>
<td>None</td>
<td>Limited to perimalleolar</td>
<td>Diffuse over lower third of calf</td>
<td>Wider distribution below lower third of calf</td>
</tr>
<tr>
<td>Ulcer number</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>≥3</td>
</tr>
<tr>
<td>Ulcer duration</td>
<td>NA</td>
<td>&lt;3 mo</td>
<td>&gt;3 mo but &lt;1 y</td>
<td>Not healed &gt;1 y</td>
</tr>
<tr>
<td>Ulcer size</td>
<td>NA</td>
<td>Diameter &lt;2 cm</td>
<td>Diameter 2–6 cm</td>
<td>Diameter &gt;6 cm</td>
</tr>
<tr>
<td>Compressive therapy</td>
<td>Not used</td>
<td>Intermittent</td>
<td>Most days</td>
<td>Full compliance</td>
</tr>
</tbody>
</table>

Table 3 (Copy from Eberhardt RT, Raffetto JD. Chronic Venous Insufficiency. Circulation. 2014 Jul 22;130(4):333–46.)

**CLINICAL MANIFESTATIONS**

Patient with CVI frequently complain of ‘heavy leg’ as well as evening edema, dilated veins, leg pain, skin irritation, pruritus, tingling, muscle cramps and cutaneous changes in the leg (1,3,15).

Telangiectases, reticular veins and varicose veins are dilated superficial veins, which are the initial stage (C1-C2) of chronic venous disease (CVD) and are not associated with any specific clinical symptom. They are primarily a cosmetic problem for the patients.

The next stage of CVD (C3) refers to the development of varicose vein with leg edema, defined as an onset of CVI (3). Edema begins in the perimalleolar region and ascends up the leg with dependent fluid accumulation. Leg discomfort is described as heavy leg or aching after prolonged standing and is relieved by leg elevation. It is thought to be produced by increased intracompartmental and subcutaneous volume and pressure. Chronic edema may lead to stasis dermatitis, characterized by erythematous, scaly, and sometimes pruritic lesions on the lower legs (Figure 7). It is occasionally mistaken for erysipelas/cellulitis.

Obstruction of the deep venous system may lead to venous claudication (or intense leg discomfort with ambulation) (1).

Continue progression in CVI results in cutaneous changes (C4) include skin hyperpigmentation because of hemosiderin deposition and eczematous dermatitis. Lipodermatosclerosis, a fibrotic process in the dermis and
subcutaneous fat, and atrophic blanches are another form of cutaneous change. They are associated with higher severity of disease and have higher risk of cellulitis, leg ulceration, and delayed wound healing.

A venous ulcer (C5, C6) is the most severe manifestation of CVI (10), the medial malleolus most commonly affected; complete healing of leg ulcers frequently requires prolonged wound treatment (3).


DIAGNOSIS OF CVI

The diagnosis of CVI is based on history, clinical presentation, and noninvasive diagnostic test. Invasive testing may also be used to establish the diagnosis but is typically reserved for assessing disease severity or if surgical intervention is being contemplated (1,3).

- **History**

  As described above, the common presenting symptoms of CVI are vary. The patients may complain of heavy leg, evening leg edema, dilated veins, leg pain, skin irritation, pruritus, tingling, muscle cramps or cutaneous changes in the leg (1,3,14).

  Specific features of the pain should be noted, including, degree of pain that interferes with the patient’s occupation or lifestyle and amount of time that the patient can stand before the onset of pain or swelling. Age of onset also should be asked, as an early onset may suggest a congenital abnormality such as Klippel-Trenunay syndrome. Family history of varicose veins is present in one third of the patient. Finally, past treatments of varicose vein or venous disease should be recorded (15).

- **Physical examination**

  Physical examination of the patient should include a general examination in addition to a detailed examination of the lower extremities. The patient should be examined in the standing position with undressed from the groins to the toes to permit complete examination of entire extremity.

  Visual inspection and palpation may reveal evidence of venous disorders. The location and distribution of all major subcutaneous varicosities should be recorded. The skin is examined for venous abnormalities such as telangiectases, reticular veins or varicose veins. Skin changes, such as hyperpigmentation, stasis dermatitis, atrophie blanche (or white scarring with a paucity of capillaries), or lipodermatosclerosis, also should be concerned.

  The edema and its severity also should be assessed. The edema seen in CVI is dependent and usually pitting and often relative sparing of the forefoot, this might help to distinguish the other cause of edema. Prominent swelling is not a common feature of superficial venous disease, although episodic ankle edema is common. Edema extending beyond the ankle suggests deep venous thrombosis (11). Since the early signs of venous congestion are calf fullness or increased limb girth, calf muscle consistency should be assessed, and measurement of the limb girth should be performed (1). However, it’s not informative unless it’s performed at the same time of the day (11).

  The presence of active or healed ulcers, typically in a distribution near the medial aspect of the ankle with GSV reflux or lateral aspects of the ankle with small saphenous vein reflux, may be seen with more advanced disease.
Careful palpitation of the thigh and leg may reveal saphenous trunk varicosities that may be missed by visual inspection and palpation of the leg should also be performed to detect temperature differences between the legs (15).

- **Brodie-Trendelenburg test (1,18)**

  Brodie-Trendelenburg test is used to determine if there is any existing retrograde flow of blood through the saphenofemoral junction (SFJ) or perforator veins, however, it does not indicate the level of the perforator veins incompetent. Therefore, this may determine whether or not high ligation of the saphenous and its branches is indicated, and, secondly, whether or not an additional ligation at a lower level is necessary.

  **Procedures:**

  1. The patient is positioned to lie down with leg elevation to empty blood from the vein.
  2. Apply a tourniquet or manual compression to occlude the superficial vein just below saphenofemoral junction.
  3. The varicose veins are observed with resumption of an upright posture for 30 seconds.
  4. Remove tourniquet or the manual compression and observe the refilling of varicose veins again.

  **Interpretations:**

  1. 1st phase, which the pressure is still applied, indicates the status of perforator veins below the occluded point.
  2. 2nd phase, the varicose veins are observed after tourniquet or manual pressure removal, indicates the status of saphenofemoral junction.

  After standing without removing tourniquet, if the blood is filled within 30 seconds from below, suggests the incompetent of perforator veins, but if the vein is gradually filled over 30 seconds suggests competent of perforator veins.

  After removing the tourniquet or manual pressure, if the vein is refilled rapidly, incompetent of saphenofemoral junction valve is suspected. In the other hand, after releasing the pressure, if the saphenous veins are slowly refilled, incompetent of saphenofemoral valve is unlikely.

  The test is **negative** when there is refilling of varicose veins from below within the period of 30 seconds with tourniquet is on. And after removing the tourniquet, there is no increased rate of filling is observed. This means there is a competent of perforator veins below SFJ, but no SFJ valve incompetent (Figure 8A).

  The test is **positive** when there is no varicose vein filling by 30 seconds after the patient is standing and tourniquet is in place, but rapid filling of the varicose veins from above is observed after the tourniquet is removed. Here, the valve of SFJ is incompetent, while the valves of perforator veins are intact (Figure 8B).

  The test is **doubly positive** when the tourniquet on and there is a filling of varicose veins within 30 seconds, and also a rapid filling of varicose veins takes place after removing the tourniquet. This means there are incompetent of perforator veins and SFJ valves (Figure 8C).

  The test is **nil**, when tourniquet in place and again with the tourniquet removed, there is only slow filling of the veins from below. This would indicate competency of the valves of both the saphenous and perforator veins (Figure 8D).

  The Brodie-Trendelenburg test is highly sensitive for the identification of superficial and perforator reflux (91%), although poorly specific (15%) (19).

![Figure 8: Brodie-Trendelenburg test](image-url)
Differential diagnosis

The common presenting symptoms of CVI are limb swelling and limb discomfort, so, initially, acute venous problem such as acute deep vein thrombosis must be exclude. Then, systemic causes of edema need to be considered, such as heart failure, nephrosis, liver disease, or endocrine disorders, and also the adverse effects of medication, such as calcium channel blockers, nonsteroidal anti-inflammatory agents, or oral hypoglycemic agents.

Critical disorders to consider are lymphedema, lipedema, and the combined disorder of lipolymphedema. Lymphedema causes by the obstruction of lymphatic drainage which leads to fluid accumulation that extends into the foot and toes, in contrast with CVI, which relatively spares the foot. The edema may be pitting early in the course of the disease but as the disease progresses becomes non-pitting. In contrast, lipedema is characterized by fatty tissue accumulation rather than fluid, thus, it is not pitting. It usually spares involvement of the feet, often with a cuff of tissue at the ankle.

Finally, other regional considerations should be made, such as ruptured popliteal cyst, soft tissue hematoma or mass, exertional compartment syndrome, or gastrocnemius tear. The use of examination findings and noninvasive testing should allow for the proper diagnosis to be established.

INVESTIGATION

Noninvasive testing

Venous duplex imaging

Venous duplex imaging is the most common technique used to confirm the diagnosis of CVI. Its advantages include that it is noninvasive, can be repeated as often as necessary, gives reproducible result, and allows anatomic, physiologic and hemodynamic evaluation of venous system (15). The study is performed with B-mode imaging and spectral Doppler analysis assessment of flow direction with provocative maneuvers (1,14).

Duplex examination of the veins must be systematic and orderly. The deep venous system is evaluated first. The presence of venous obstruction because of chronic deep vein thrombosis or venous stenosis may be directly visualized or inferred from alteration in spontaneous flow characteristics.

Venous valvular competence is evaluated with Valsava maneuver for upper thigh segment and limb compression for the lower limb segment (15). The preferred method to assess for reflux involves the use of a cuff inflation-deflation technique with rapid cuff deflation in the standing position (1). This provides information about the anatomic distribution of reflux disease involving the deep and superficial venous systems, as well as perforator veins.

The presence of reflux is determined by the retrograde flow toward the feet (Figure 9). The duration of reflux is known as the reflux time. A reflux time of >0.5 seconds for superficial veins and 1.0 second for deep veins is typically used to diagnose the presence of reflux. A longer duration of reflux implies more severe disease but does not correlate well with clinical manifestations.

Venous duplex imaging provides information about local valve function to construct an anatomic map of disease in terms of the systems and levels of involvement. This is often sufficient data to help guide therapy, but if the contribution of the reflux to global hemodynamics is required, then further testing, such as plethysmographic techniques, should be considered.

Figure 9: Venous duplex ultrasound demonstrating reflux in the great saphenous vein. Blood flow direction is determined after increasing central venous return with rapid cuff inflation then deflation. Flow in the direction of the feet is because of incompetent valves, as shown in red in the color image and above the baseline in the pulse Doppler. The Doppler spectrum quantifies the duration of reflux, and in the example above it is ≈4 seconds. (copy from Eberhardt RT, Raffetto JD. Chronic Venous Insufficiency. Circulation. 2014 Jul 22;130(4):333–46.)
Air Plethysmography

Plethysmograph is an instrument for determining and registering variations in the size of an organ or limb resulting from changes in the amount of blood present or passing through it. Air plethysmography (APG) is a noninvasive test used to assess pathophysiologic mechanisms of CVI, including reflux, obstruction, and muscle pump dysfunction (1,5). Venous occlusion plethysmography involves the interruption of venous drainage by placing a cuff around the upper leg. Lower-leg circumference is then assessed using a strain gauge, thus providing information about venous capacity and venous drainage. In air plethysmography, a cuff with air chambers is placed around the patient's lower leg, which enables the measurement of volume changes.

Computed Tomographic or Magnetic Resonance Venography

These techniques are useful to evaluate more proximal veins and their surrounding structure to assess for intrinsic obstruction or extrinsic compression. Proper technique allowing for better visualization to assess obstructive disease, varicose veins, perforating veins, and other venous malformations. Both computed tomography and magnetic resonance venography may be used to define complex venous anatomy, such as iliofemoral venous obstruction before intervention (1).

Invasive testing

Contrast Venography

Venography allows directly visualized of the venous system by either an ascending or descending approach (1). Ascending venography provides an objective anatomic and hemodynamic evaluation of the venous system that may be useful with surgical interventions. It involves injection of contrast in the dorsum of the foot with visualization of contrast-traveling cephalad in the deep venous system of the limb (1). Descending venography is used to identify valvular incompetence, involves proximal injection of contrast in a semi垂直 posture on a tilt table with the use of the Valsalva maneuver. However, venography is expensive, invasive, uncomfortable for patients, and associated with a small incidence of phlebitis and other complications related to contrast administration.

Intravascular Ultrasound

Intravascular ultrasound is used in the management of venous disease and is increasingly being used to help guide interventions. The technique uses a catheter-based ultrasound probe to visualize periluminal vascular anatomy to assess for obstructive or stenotic disease of the venous system. It is superior to venography in estimating the morphology and severity of central venous stenosis and in visualizing the details of intraluminal anatomy.

Ambulatory Venous Pressure

Ambulatory venous pressure monitoring is the gold standard in assessing the hemodynamics of CVI. This technique provides information on global competence of the venous system. It is performed by introducing into a dorsal foot vein a 21-gauge needle, which is then connected to a pressure transducer. The mean ambulatory venous pressure and refill time are the most useful parameters. Ambulatory venous pressure has been shown to be valuable in assessing the severity and clinical outcomes in CVI. This technique is seldom used in clinical practice because of its invasive nature, potential limitations, and alternative diagnostic modalities (1,14).
TREATMENT OF CVI

Conservative Management

Initial treatment of CVI involves conservative treatment to reduce symptoms and prevent development of secondary complications and progression of disease. If the conservative is fail or provide unsatisfactory response, future treatment should be considered on the basis of anatomic and pathophysiologic feature.

A referral to vascular specialist should be made for patients with CEAP classes C4 to C6 (or probably class C3), which usually need a specific and invasive treatment. These patients with uncorrected advance CVI are at risk for ulceration, recurrent ulceration, and nonhealing ulcers with progressive infection.

- Compressive Leg Garments

Compression therapy provides graded external compression to the leg and oppose the hydrostatic force of venous hypertension. It also helps to improve the calf muscle pump function and reduces reflux in vein segments. There are several types of compression garments available such as graded elastic compression stockings, paste gauze boots, layer bandage, adjustable layered compression garment. The studies showed that compressive garment improve wound healing and prevent recurrent of ulcer.

Compression therapy is considered first-line therapy for those with symptomatic varicose veins or greater but not a candidate for great saphenous ablation. Compression therapy is also recommended as an adjunct to superficial venous ablation to reduce the risk of ulcer recurrence.

The pressures used for CVI are range between 20 and 50 mmHg, based on the CEAP clinical severity (Table 4).

The most common length is knee length. The stockings needed to be changed every 6-9 months if worn daily to maintain the adequate tension.

- Wound and Skin Care

In advance CVI, the patient’s skin may lose its integrity. The skin is needed to keep moist to maintain skin health and prevent infection. If the patients develop stasis dermatitis, topical steroid may be applied. In case of infection, aggressive wound care is required to minimize infectious complication.

- Pharmacologic Therapy

Four groups of drugs have been evaluated in the treatment of CVI, including coumarins (α-benzopyrenes), flavonoids (γ-benzopyrenes), saponosides (horse chestnut extracts), and other plant extracts such as horse chestnut seed extract, which is effective as compression stockings in the short term at reducing leg edema and pain from CVI, but the long-term safety and efficacy have not been established. These drugs have venoactive properties.

The principle for using these venoactive agents is to improve venous tone and capillary permeability, however mechanism of action for these drugs is not yet fully understood. These venoactive agents provide relief of pain and swelling or accelerate venous ulcer healing when used in conjunction with compression.

The use of other agents, such as aspirin and platelet-derived growth factor, has been reported to promote healing or prevent the recurrence of venous ulceration, but no large randomized studies have been conducted.

- Exercise Therapy

Abnormalities in calf muscle pump functions play a significant role in the pathophysiology of CVI. After 6 months, patients receiving a calf muscle exercise regimen normalized calf muscle pump function parameters but had no change in the amount of reflux or severity scores. Calf muscle exercise may beneficial as supplemental therapy to medical and surgical treatment in advanced disease.
Interventional Management

- **Sclerotherapy**

Venous sclerotherapy is a treatment modality for obliterating telangiectases, varicose veins, and venous segments with reflux.

**Indications for venous sclerotherapy**
- Facial telangiectasias
- Vascular malformations
- Congenital malformation
- Unsightly veins of the hands and feet
- Failed segments of endothermal ablation
- Recurrent varicosities
- Telangiectasias
- Reticular veins
- Varicose veins < 8 mm diameter
- Perforator vein incompetence of 4-to 7-mm diameter

There are a number of sclerosing agents, including hypertonic solution of sodium chloride (23.4%); detergents such as sodium tetradecyl sulfate, polidocanol, and sodium morrhuate; and others such as sodium iodide and chromated glycerin. Sclerosing agents such as polidocanol have been shown to be superior to normal saline in both obliterating incompetent varicose veins and improving venous hemodynamics at 12 weeks. Foam sclerotherapy involves the injection of a sclerosant foam into the saphenous veins.

A common complication of sclerotherapy is hyperpigmentation of the surrounding skin from hemosiderin degradation.

- **Endovenous Ablative Therapy**

Ablative therapy uses the thermal injury in the form of radiofrequency or laser to ablate incompetent veins, frequently used for GSV reflux as an alternative to stripping. The heat generated causes a local thermal injury to the vein wall leading to thrombosis and fibrosis. 90% of patients treated with radiofrequency ablation are free from saphenous vein reflux at 24-month follow up, and 95% of patients report satisfaction and improvement of symptoms (regardless of the technical success) (20).

- **Endovenous Deep System Therapy**

Abnormalities in venous outflow, involving iliac veins stenosis and obstruction, contribute to symptoms in 10% to 30% of patients with severe CVI. Previously, they were treated with surgical procedures. However, the use of stents is becoming increasingly common and provides satisfied outcomes with complete pain relief in ≈50%, complete resolution of edema in ≈30%, and complete healing of ulcers in ≈50% (1). The cumulative rates of stent patency at 5 years were 86% in cases of post-thrombotic disease and 100% in nonthrombotic cases (11). Complications included deep venous thrombosis (occurring in 1.5% of patients within 30 days after the procedure) and transient postoperative back pain (in 25% of the patients) (11).

Figure 10: Recanalization of an Occluded Iliac Vein with Stent Placement. Picture on the left shows collateral veins around the occluded iliac vein. Picture on the right showed the collateral vessels disappear with stent placement. (copy from Raju S, Neglen P. Chronic Venous Insufficiency and Varicose Veins. N Engl J Med. 2009 May 28;360:2319–27.)
- **Mechanochemical endovenous ablation (MOCA)**

The newly developed Mechanochemical Endovenous Ablation (MOCA) device uses a technique that combines mechanical endothelial damage using a rotating wire with the infusion of a liquid sclerosant. It is a non-thermal ablation, so heating of the vein and tumescent anesthesia are not required; only local anesthesia is utilized at the insertion site.

Mechanochemical endovenous ablation using the ClariVein in combination with liquid sclerosant is associated with the anatomical success rate of 92% (95% CI 88–95%) 91% (95% CI 86–94%) and After 6 and 12 months. The long-term anatomical success rates at 2 and 3 years were 91% (95% CI 85–95%) and 87% (95% CI 75–94%), respectively. Major complications and especially nerve injury were very rare (21).

- **Endovenous Cyanoacrylate Glue**

Cyanoacrylate glue, a liquid adhesive, delivered endovascularly is a new non-ablative procedure used in treatment of venous incompetence. It does not require tumescence anesthesia. Upon intravascular injection, Cyanoacrylate glue rapidly solidifies via a polymerization reaction and produces an inflammatory vein wall reaction. Granulomatous foreign body reaction is observed at 30 days after treatment and fibroblasts can be seen invading the contents of the tunica intima and tunica media at 60 days (22).

In 2016, Chan et al. conducted the study for the evaluation of efficacy of endovenous cyanoacrylate (saphenous venaseal closure system) for the treatment of primary great saphenous reflux. The study showed that the GSV closure rates were 98.2%, 94.3%, 99.7%, and 78.5% at post-op 1 week, 1 month, 6 months, and 1 year, respectively. And the mean of GSV diameter greater than 8mm was a significant predictor for recanalization (hazard ratio 6.92, 95%CI 1.34–35.67, p= 0.021) (23).

**Surgical Management**

Surgical management of CVI may be considered to complement the compressive stocking in those refractory to medical and endovenous therapy. The choice of surgery is considered based on the venous territories and underlying pathophysiologic mechanisms.

- **Surgery for Truncal Vein or Venous Tributaries**

Interruption and removal of truncal veins prevents the consequences of reflux in the superficial venous system, whereas surgery on vein tributaries is directed toward removal of the resulting varicose veins. Excision of the GSV with high ligation of the saphenofemoral junction (SFJ) can be applied to all of the CEAP clinical classes (C2–C6) with GSV reflux. Recurrence rates are markedly reduced when the GSV is tripped compares with high ligation alone. Ligation and stripping have been shown to improve venous hemodynamics, to provide symptomatic relief, and possibly to assist in ulcer healing, however endovenous ablation is prefer to venous stripping in ulcer recurrent prevention.

Rasmussen et al. studied the short term outcome of endovenous laserablation of the great saphenous vein compared with high ligation and stripping in patients with varicose veins and found no statistical significant different of improvement in quality-of-life scores and VCSS score at 3 months, mean time to resume normal physical activity and work, but infection and Postoperative pain and bruising was higher in the high ligation and stripping group, but no difference in the use of analgesics was recorded (24). Rasmussen et al. also studied the clinical and duplex outcome after 5-year follow-up of venous stripping compared with endovenous ablation and found no statistical significant different between in open reflux (10.1 vs 17.9%, P =0.2145) and in clinical recurrence (37.7% vs 38.6%, P = 0.7209) (25).

- **Perforator Vein Surgery**

Incompetent perforator veins may contribute to the pathophysiology of CVI and its advanced manifestations, primarily ulceration. The interruption of perforator veins which contributed to focal venous hypertension with ligation is performed. The current preferred technique for correction of perforator veins reflux is endoscopic resection (subfascial endoscopic perforator surgery, or SEPS). The choice of techniques to disrupt
pathologic perforator veins remains an area of investigation but has been favoring less invasive methods, such as endovenous ablation and foam sclerotherapy (1).

- **Valve Reconstruction**

  Deep venous valves with reflux due to either a nonthrombotic or post-thrombotic cause can be reconstructed by means of open surgery, but this procedure may not be available outside of specialized centers (11). Venous valve reconstruction of the deep vein valves has been performed selectively in advanced CVI with recurrent ulceration and disabling symptoms (1).

  Complications from valvuloplasty include bleeding, deep venous thrombosis, pulmonary embolism, ulcer recurrence, and wound infections (1).

**CONCLUSION**

Chronic venous disease is one of the most common disease affecting humankind. It affects patient’s quality of life and also healthcare system. Normal function of venous valves and muscle pump are required for normal venous function. Disturbance of these functions leading to venous hypertension and eventually chronic venous insufficiency (CVI). Evaluation of these patients begins with a careful history and physical examination. The duplex ultrasonography used to confirm diagnosis. An additional test may be added in some patients. Patient’s disease can be classified according to CEAP system and venous severity scoring system which serves as a basis for proper treatment and intervention. Sclerotherapy and phlebectomy are primarily used for isolated tributary or perforator incompetence, recurrent varicose veins, as well as in combination with other procedures. In the case of trunk incompetence, classic surgical methods such as saphenofemoral ligation and stripping or the newer endovenous methods should be employed. Combination of surgical or endovenous procedures with adequate compression therapy is a therapeutic mainstay.
REFERENCES


