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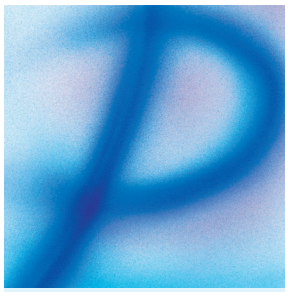

Phlebolymphology

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Phlebolymphology is an international scientific journal entirely devoted to venous and lymphatic diseases.

The aim of *Phlebolymphology* is to provide doctors with updated information on phlebology and lymphology written by well-known international specialists.

Phlebolymphology is scientifically supported by a prestigious editorial board.

Phlebolymphology has been published four times per year since 1994, and, thanks to its high scientific level, is included in several databases.

Phlebolymphology comprises an editorial, articles on phlebology and lymphology, reviews, and news.

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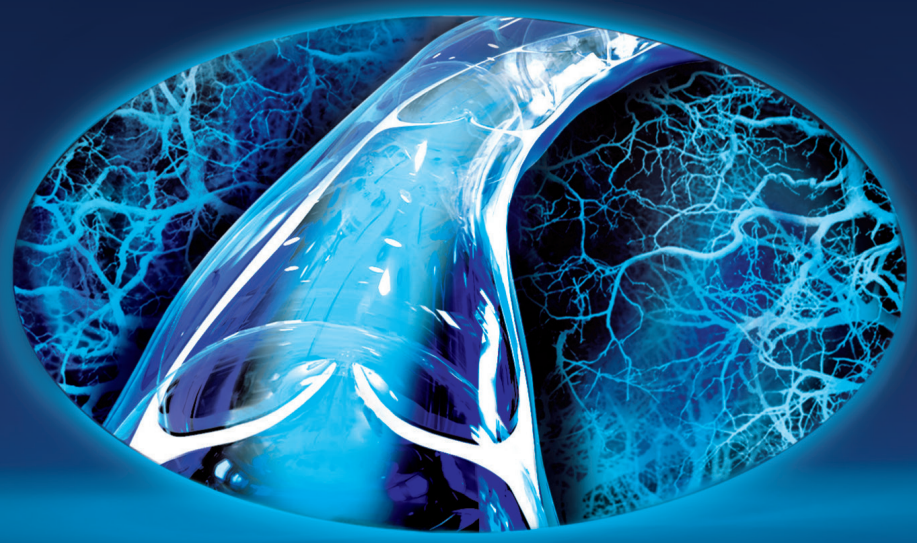

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1 - Pascarella L et al. Mechanisms in experimental venous valve failure and their modifications by Daflon 500 mg. *Eur J Vasc Endovasc Surg.* 2008;35:102-110. **2** - Nicolaides A et al. Management of chronic venous disorders of the lower limbs: guidelines according to scientific evidence. *Int Angiol.* 2014:33(2):126-139.

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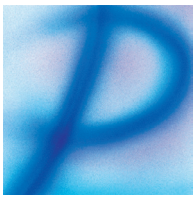

Duplex ultrasound investigation in pelvic congestion syndrome: technique and results

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iliac vein compression; left renal vein compression; pelvic leak point, pelvic varices classification, pelvic varicose vein; ultrasound diagnosis

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Abstract

Chronic pelvic venous insufficiency is a common pathology, but it is overlooked and underdiagnosed as it sits on the edge of two medical specialties: gynecology and vascular medicine. It manifests most frequently as pelvic varicose veins and pelvic venous reflux toward the lower limbs. When symptomatic, it is expressed in the pelvic area as a sometimes-disabling pelvic congestion syndrome and/or in the lower limbs as it supplies the varicose veins. Consequently, the isolated treatment of lower-limb varices without treating pelvic leaks when there is pelvic congestion syndrome may cause early recurrences. The ultrasound exploration allows the positive diagnosis of pelvic venous involvement and the classification by pathophysiological types, which is a key step before any treatment. The echo Doppler is also essential for the diagnosis of superficial points of pelvic venous leaks supplying lower-limb varicose veins. In most symptomatic patients, ultrasound exploration provides sufficient arguments to evaluate the relevance of the pelvic-level venous treatment. It leads to additional imaging techniques, if necessary, or directly to a hyperselective descending pelvic venography. This last investigation provides an accurate mapping of varicose veins and pelvic venous reflux.

Introduction

Chronic pelvic venous insufficiency includes all events related to the dysfunction of the pelvic venous system, whether congenital or acquired. Venous reflux and pelvic varicose veins represent the most common pathological expression. These pelvic varicose veins are very common in multiparous women, and they are most often asymptomatic. When symptomatic, they can be responsible for pelvic congestion syndrome and/or varicose veins in the lower limbs.[1-4] Treating pelvic veins should be considered when they are symptomatic at any level *(Table I)*.

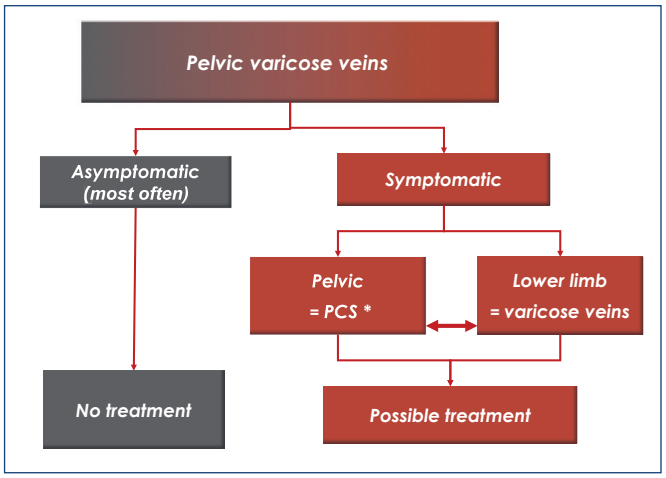

*Table I. Clinical manifestation of pelvic varicose veins. *PCS = pelvic congestion syndrome.*

Type 1: Reflux pathology secondary to valvular or parietal venous anomalies (without pelvic or suprapelvic obstruction to venous flow)

- Valvular diseases:
  - Congenital or acquired valvular incompetence
  - Absence of valves
- Congenital or acquired pelvic venous dilatations, regardless of the sector
- Venous malformations

Type 2: Venous substitute pathology secondary to stenosis or obstruction in a draining vein

Suprapelvic obstruction:

- Abnormalities of the left renal venous return
  - Primary = Nutcracker syndrome
  - Secondary = thrombosis
- Pathology of the inferior vena cava
  - Primary
    - Congenital anomalies
  - Secondary
    - Extrinsic compression
    - Thrombosis

Pelvic obstruction

- Primary
  - May-Thurner syndrome
  - Congenital anomalies of the internal iliac veins
- Secondary
  - Extrinsic compression
  - Thrombosis

Type 3: Local extrinsic cause responsable for pelvic venous anomalies

- Endometriosis
- Abdominal /pelvic tumors
- Benign masses
- Secondary uterine retroversion (postpartum)
- Postsurgery or postinfectious adhesions
- Obstetric destruction of supporting tissue (Allen–Masters syndrome)
- Nonobstetric trauma

Table II. Classification of pelvic venous reflux and pelvic varicose veins (M. Greiner).

Semantic prerequisite

The female varicocele is only a particular form of pelvic varicose veins related to the dilatation of the pampiniform plexus.

Anatomical and hemodynamic prerequisites

The pelvic veins drain into three main collector systems: the internal iliac, ovarian, and rectal veins.[4-6] The common and internal iliac veins are generally valveless, but the visceral and parietal internal iliac tributaries are valved. This fact is clearly demonstrated by using hyperselective retrograde pelvic phlebography. These tributaries come from valveless plexuses that are extensively interconnected. Therefore, pelvic veins are not independent, but interconnected as a network and connected with other networks, particularly with the lower-limb veins. This connectivity explains why an abdominal or pelvic venous reflux can be the origin of a venous anomaly located in another area, ie, a left ovarian reflux can supply the right perineal varices.

Classifications

In 2005, Milka Greiner[5] proposed a classification system based on pathophysiological findings. Three main types of vein damage diagnosed by ultrasound explorations and confirmed by cross-sectional imaging and selective phlebography were identified *(Table II)*. These three types do not depend on the location of the pelvic venous pathology (ovarian or extraovarian coming from the internal iliac tributaries). Each type needs a specific therapeutic plan. Type 1 corresponds to valvular or parietal venous anomalies without pelvic or suprapelvic obstruction to venous outflow, which is responsible for the reflux. It is the most frequent physiopathology, and endovascular treatments are the preferred method of management. Type 2 relates to stenosis or obstruction in a draining vein responsible for symptomatic substitute collaterals. In type 2, the isolated treatment of reflux and varices without treatment of the obstruction can lead to worsening of abdominal, pelvic, and/or lower-extremity–related venous hypertension. It should be considered after a multidisciplinary assessment of the risk/benefit ratio. Type 3 pelvic vein anomalies and pelvic reflux are secondary to a local extrinsic cause. In this context, the treatment of varices could be only considered after the treatment of the cause.

From an anatomical point of view, two locations can be differentiated[6]: (i) genital varices are fed by the ovarian veins and/or the uterine veins; and (ii) extragenital pelvic varices are fed by the other internal iliac tributaries, particularly the extrapelvic parietal tributaries of the internal iliac, ie, the gluteal, obturator, and medial pudendal veins. These two locations can be associated.

Mode of pelvic reflux transmission toward the lower limbs

Two modes of leak transmission have been differentiated *(Table III)*[6]:

1. Direct pelvic leaks occur when the truncal pelvic reflux feeds the lower-limbs varices directly. The inferior gluteal vein and, to a lesser degree, the obturator and medial pudendal veins are involved.

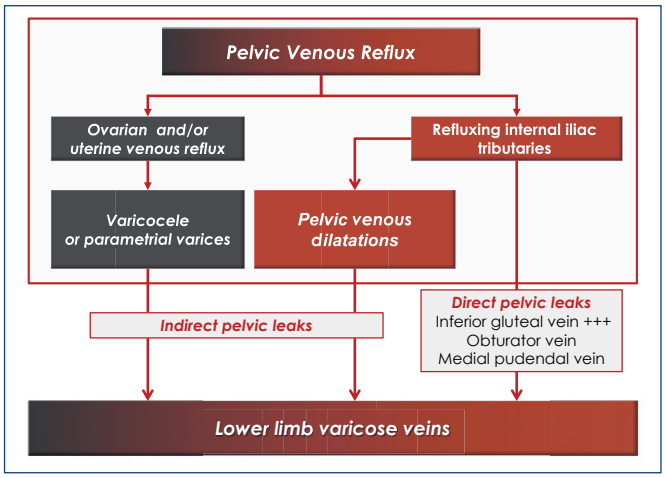

Table III. Mode of pelvis venous reflux toward the lower limbs.

2. Indirect pelvic leaks occur when the truncal pelvic reflux first feeds one or several clusters of pelvic varicose veins, which drain secondarily into the lower limbs. Genital varices are usually indirect leaks. Extragenital venous insufficiency can be expressed in the lower limbs by direct or indirect leaks.

Externalization mode of pelvic reflux toward the lower limbs

Whatever the direct or indirect mode, a venous reflux from the pelvis to the lower limbs requires communication between the two levels, these are called leak points. They can be nonsystematized, in which case, the pelvic venography will show a pelvic venous network that feeds the lower-limb varices. Conversely, the leak points can be systematized. In 2005, Claude Franceschi[7] listed five systematized and symmetrical leak points: the buttock points (superior gluteal [GS] point, inferior gluteal [GI] point), perineal (P) point, obturator (O) point, and inguinal (I) point. A sixth point was described later: the clitoral (C) point. These leak points are different in terms of location and physiopathology because some are located in the anatomical drainage pathways of extrapelvic parietal afferent veins toward the left and right internal iliac veins and their pelvic collectors. Thus, the GS and GI points are located at the intrapelvic passage of the gluteal veins at the greater sciatic notch above (superior gluteal vein) or below (inferior gluteal vein) the piriformis muscle. The O point originates from the intrapelvic path of the obturator vein by the subpubic canal, at the obturator foramen. These three points are anatomically deep and difficult to study using ultrasound methods. The P, I, and C points[7] correspond to the reflux of the extrapelvic infra-aponeurotic veins into the extrapelvic subcutaneous veins *(Table IV)*.

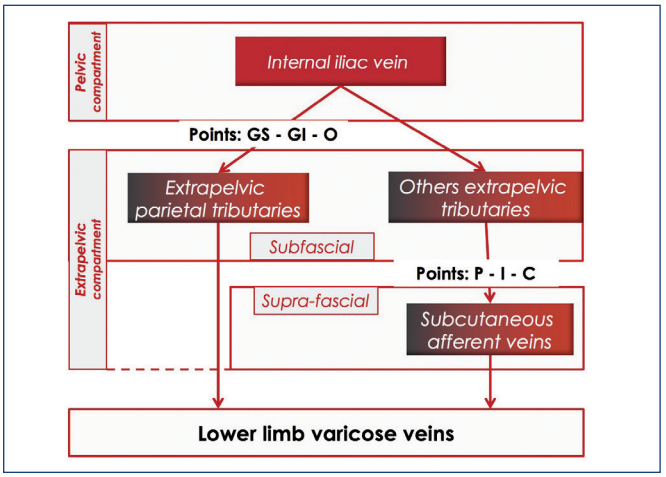

Table IV. The different pelvic leak points.

Perineal point

Superficial perineal veins drain the perineum, receive the anterior and posterior labial veins, and cross the superficial fascia of the perineum by an orifice that has been called the P point. These superficial veins ascend to the medial pudendal vein in Alcock's canal. Refluxing veins follow the same pathway in the opposite direction. The P point is located at the union that is one-quarter posterior and three-quarters anterior to the vulvoperineal fold (near Alcock's canal) *(Figure 1)*. It is fed by the medial pudendal vein, and it could be the result of refluxing small tributaries of the ipsilateral medial pudendal vein and/or truncular pudendal reflux *(Table V and VI)*.

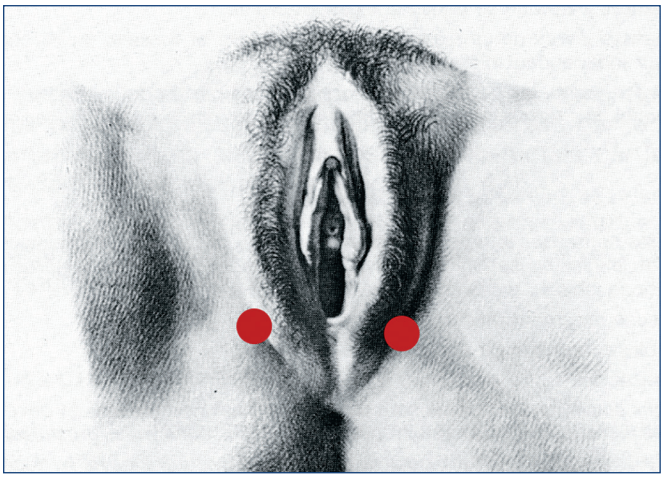

Figure 1. Schema showing the localization of the P point that is three-quarters posterior to the vulvar fold.

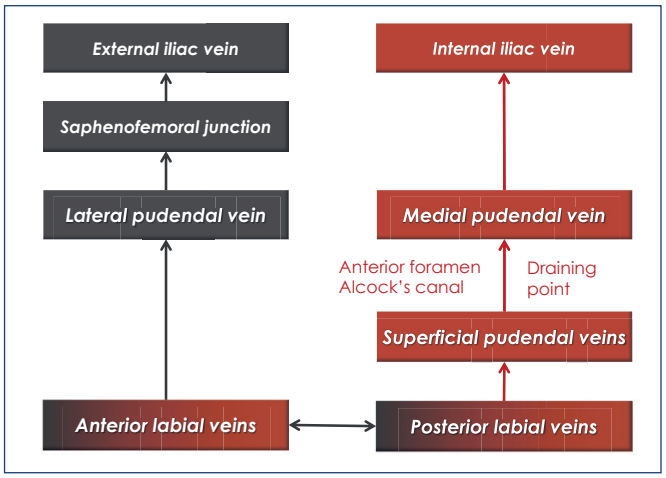

Table V. Draining pathways of the labia majora.

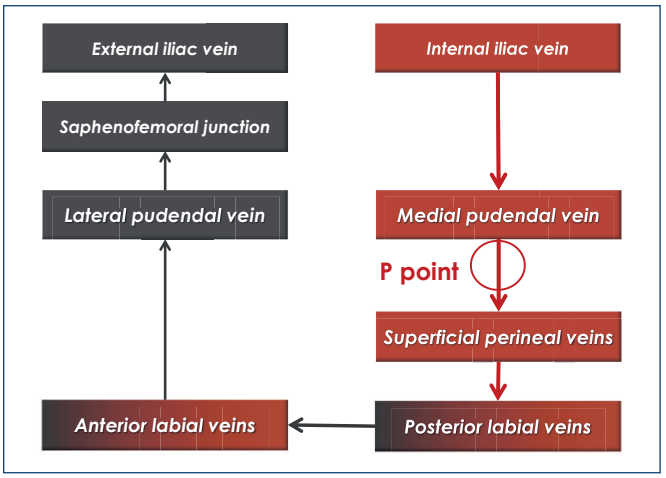

Table VI. Hemodynamic pattern of the perineal point.

Inguinal point

The I point corresponds to the superficial inguinal ring where the vein of the round ligament preferentially drains into the uterine vein. Given the valveless connection between the visceral plexus, the I point can externalize the venous flow from any pelvic area, but preferably from parametrial varices. It is located above the inguinal canal, outside the femoral vessels *(Figure 2)*.

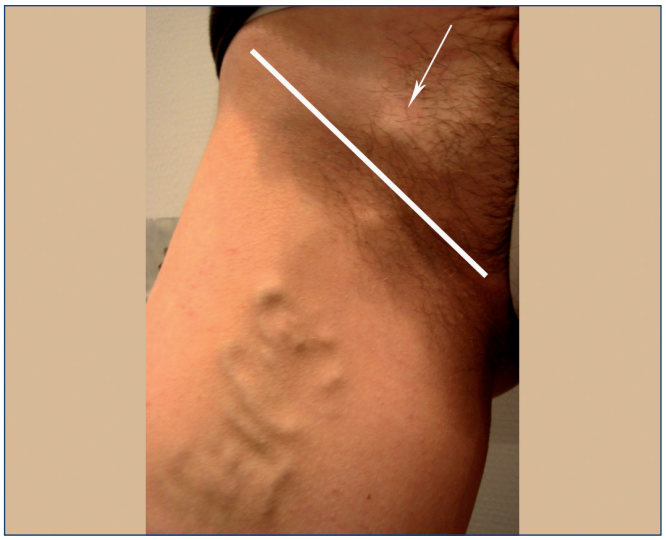

Figure 2. Localization of the I point above inguinal ligament, outside the femoral vessels.

Clitoral point

The C point is related to incontinence of the medial pudendal vein, which generates increased venous pressure in the region of the peri-urethral plexus, followed by a reverse flow from the deep clitoral veins to the superficial clitoral veins. C points are located on each side of the clitoris. In practice, they are rarely identified.

Decisional algorithm

Our management of chronic pelvic venous insufficiency always follows the same decisional algorithm based on four steps *(Table VII)*. Only the second step is related to this article's topic, but it should be set within the global context. Initially, pelvic varices can be evoked in front of pelvic congestion syndrome or lower-limb varicose veins. The problem for the gynecologist is to recognize the venous origin of chronic pelvic symptoms. The vascular physician should recognize the pelvic origin of lower-limb varices. The second step, based on ultrasound exploration, will confirm, quantify, and classify the chronic pelvic venous insufficiency. This is a key step for advancing, in most cases, the decision-making stage by adding investigations, notably mini-invasive, cross-sectional imaging studies, eg,

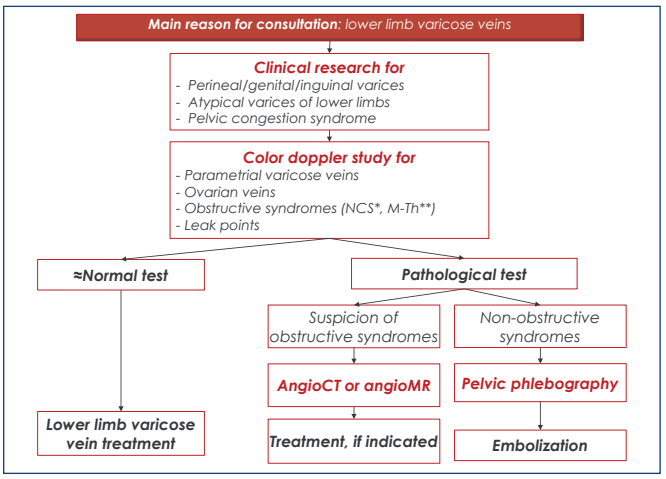

Table VII. Decisional algorithm of pelvic varicose vein management

Abbreviations: M-Th, May-Thurner syndrome; NCS, Nutcracker syndrome.

selecetive retrograde descending pelvic venography. Pelvic venography is the only exploration to provide up a precise mapping of pelvic varicose veins and pelvic venous reflux (P and I points included); therefore, it remains the gold-standard examination. It is a mandatory investigation when interventional treatment is considered.

Principles of ultrasound exploration

Our ultrasound exploration always follows the same approach:

1. Search for varicose veins in the uterine area.
2. Examine the gonadal veins.
3. Search for anatomical and hemodynamic criteria of left renal vein compression.
4. Examine the iliac vessels.
5. Search for leak points.
6. Identify lower limb varices.

Search for varicose veins in the uterine area

The exam must be descriptive; anatomic and hemodynamic criteria must be noted. It begins with a suprapubic exploration using a macroconvex probe (frequency: 5 to 5 MHz). The normal venous plexus appears as a straight tubular structure with a normal diameter (<4 mm). In patients with pelvic varicosities, an ultrasound typically shows dilated and tortuous veins, with reversed and slow flow, that are located on both sides of the uterus, preferably on the left side. Genital varicose veins can form a cluster of little dilated veins; therefore, no specific diameter can be used to diagnose genital varicose veins *(Figures 3, 4, and 5)*. It is important to search for dilated arcuate and/or

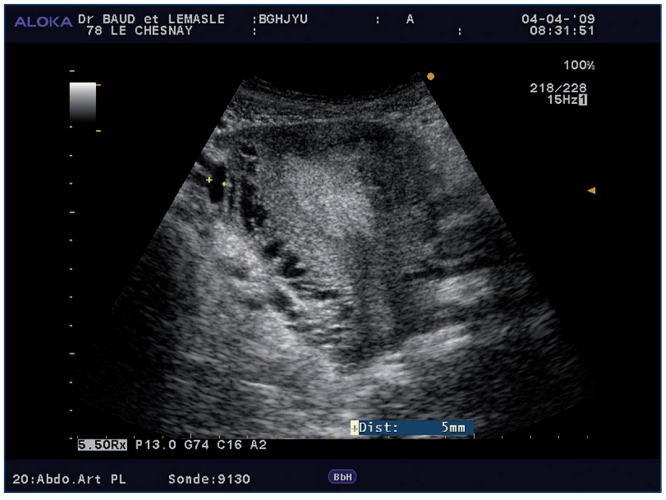

Figure 3. Abdominal approach.
Right lateral uterine varices; right unilateral forms are rare.

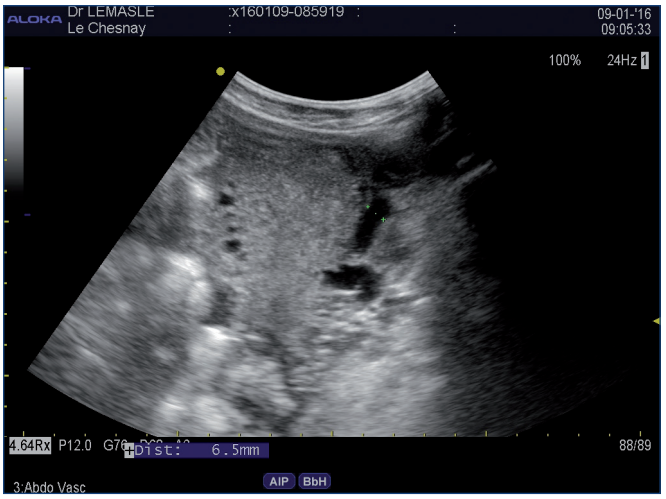

Figure 4. Abdominal approach.
Left lateral uterine varices, with a few dilated varices.

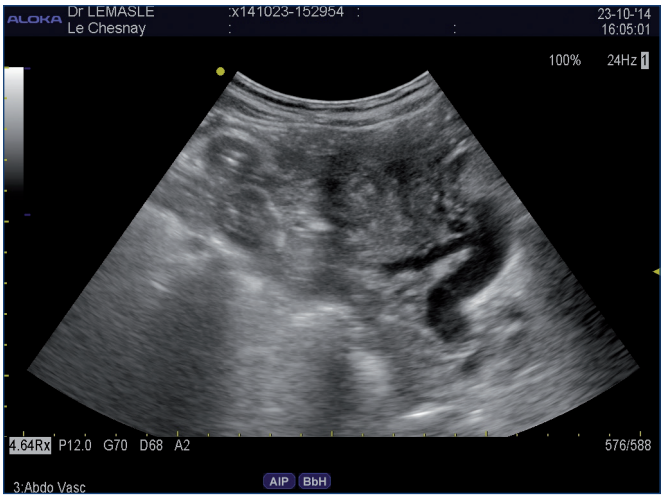

Figure 5. Abdominal approach.
Major left lateral uterine varices.

intramyometrial veins communicating with bilateral pelvic varicose veins.

Flow imaging can confirm the presence of a reflux in lateral uterine venous dilatations and highlight some collateral pathways *(Figures 6 and 7)*. This reflux can be spontaneous with breathing or caused by abdominal compression maneuvers (soft and prolonged) or the Valsalva maneuver.

1. The transperineal approach limits the artifacts related to the mobilization of the abdominal wall during the Valsalva maneuver: the patient is in a supine, gynecological position, and the probe is positioned at the middle perineum. This position

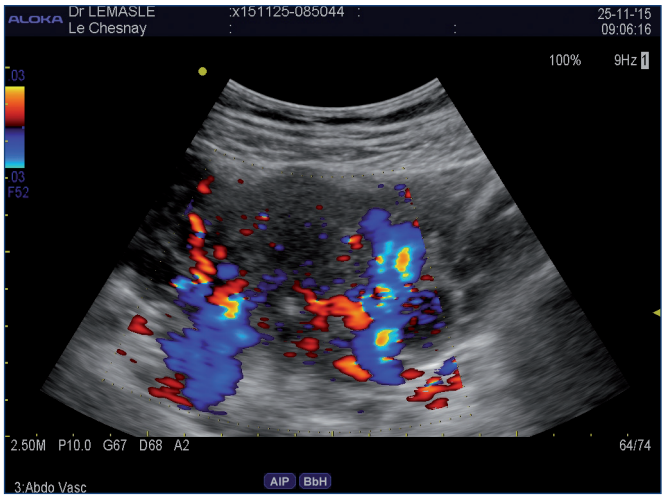

Figure 6. Abdominal approach.

Left lateral uterine varices draining of the lower pole pelvic varicose in right medial pudendal vein.

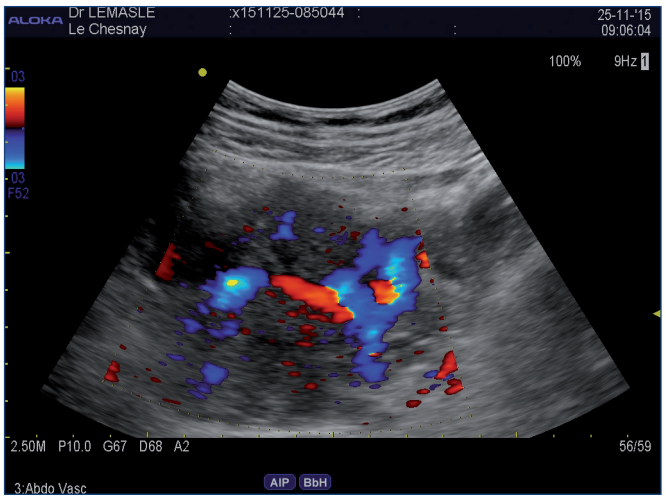

Figure 7. Abdominal approach.

Left lateral uterine varices draining by the right side uterine network via arcuate veins.

has been used in a male patient to study the flow of the medial pudendal artery in the assessment of erectile dysfunction.

2. We do not use the transvaginal ultrasound. It is useless when searching for iliac or renal vein compression and for superficial leak points (P, I, and C), but it provides the best image quality and resolution of lateral, arcuate, and myometrial uterine varices. The transvaginal ultrasound is helpful for assessing endometriosis cysts and tissular pelvic pathology (Type 3). High-resolution transvaginal ultrasound remains indispensable in the etiological evaluation of pelvic symptoms.

Examination of the gonadal veins

The venous territories of the parametrium, mesosalpinx, uterine fundus, and the pampiniform plexus are drained by the ovarian veins. They are formed by separate trunks, which become a single trunk at the level of the 4th lumbar vertebra. The right ovarian vein drains directly into the inferior vena cava and occasionally into the right renal vein. The left ovarian vein drains most often into the left renal vein. Variations are common in the number of trunks (double or triple) and in the mode of termination.[8] These variations make the ultrasound exploration incomplete.

The best anatomical landmark is the psoas muscle *(Figure 8)*. On the left, the upper part of the gonadal vein is located on the anterior side of the psoas muscle. In its inferior part, its way is internal, meaning that it runs along the anteromedial then medial side of the psoas muscle. In the pelvis, the left gonadal vein crosses in front of the common iliac vessels, so it is sometimes possible to see the gonadal vein, artery, and then the iliac vein on the same longitudinal section, from front to rear *(Figure 9)*. The diameter of the vein has to be noted, but this measure is only a guidance element because a dilated gonadal vein can be draining, and conversely, a narrow gonadal vein may be refluxive.

Reflux is analyzed with the pulsed or color Doppler. Several types of reflux can be documented: spontaneous and intermittent retrograde flow; retrograde flow only on

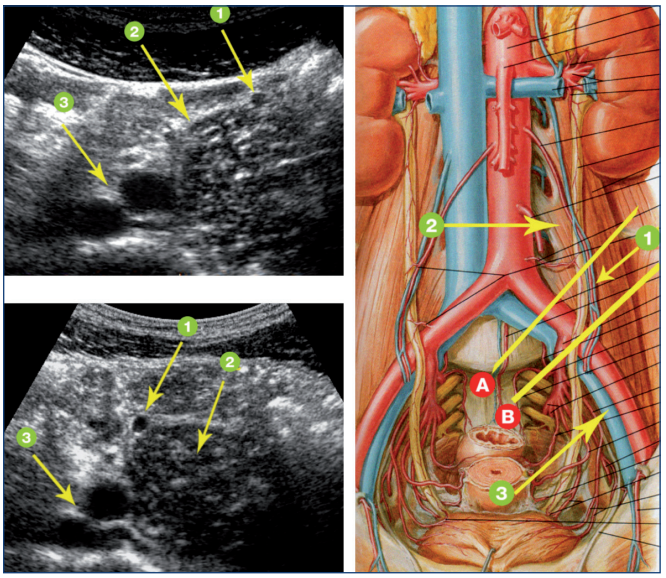

Figure 8. Ultrasound signs of left gonadal vein.

1: left gonadal vein; 2: psoas muscle; 3: iliac vessels; the top image corresponds to section A and the lower image corresponds to section B.

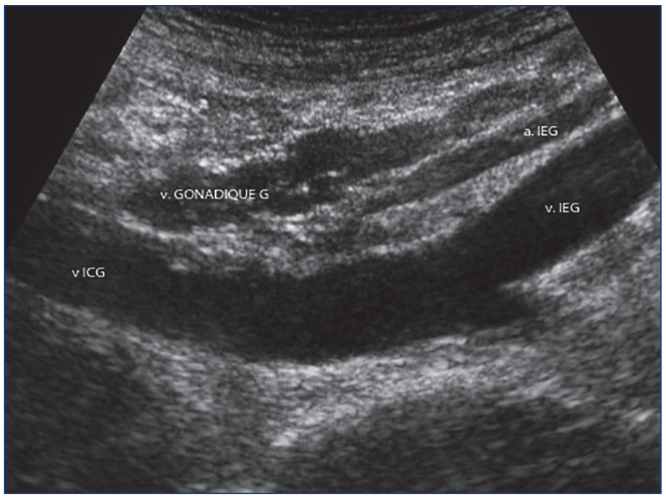

Figure 9. Abdominal approach.

The following veins are visualized, from front to rear: left gonadal vein (v .GONADIQUE G), left iliac artery (a.IEG), left external iliac vein (v IEG), and left common iliac vein (v ICG).

Valsalva maneuvers; and permanent retrograde flow in a standing position and/or in a supine position, and, in this last context, it can be more or less modulated with breathing.

The hemodynamic status of the gonadal vein allows the type of varicose vein to be defined. In type 1 (reflux pathology without a pelvic or suprapelvic obstacle), the reflux can be spontaneous, major, even almost continuous in case of steal syndrome by the ovarian vein, but it is modulated by breathing. In type 2 (obstruction pathology), the gonadal vein will be the main way for renal drainage flow. In this context, gonadal reflux is spontaneous, permanent, and has little or no modulation by breathing. Type 3 may be suspected by the nonconformity between an important varicocele and little or no gonadal vein reflux.

Search for anatomical and hemodynamic criteria of the Nutcracker syndrome (NCS)

The NCS is characterized by the stenotic compression of the left renal vein (LRV) which is responsible for clinical symptoms. Several anatomical forms have been identified. LRV compression between the superior mesenteric artery and the abdominal aorta (or anterior LRV compression) is the most frequent. The posterior form, when the LRV is in a retro-aortic position and compressed between the aorta and a lumbar vertebral body, is less frequent. The circumaortic LRV with compression of its two branches is rare. Numerous attempts have been made to improve Doppler ultrasound diagnostic criteria. Some quantitative ultrasound criteria for anterior LRV compression has been described, based on small studies.[9-11]

LRV stenosis is detected of the basis of comparing peak velocity ratios and anterior-posterior diameter ratios of the aortomesenteric narrowed and hilar (distended) LRV portions. The sensitivity and specificity of a Doppler ultrasound ranges from 69% to 89%, respectively, for the hemodynamic criteria and from 80% to 94%, respectively, for the anatomic criteria. If we use a combined cutoff value of more than 5, the sensitivity is 90% and the specificity is 100% according to the authors.[10] However, the measurement of LRV diameter is variable depending on systole, patient position, and an inappropriate angle of insonation. It is the same for the measurement of peak systolic velocity.

In practice, the most important criterion is indirect because it corresponds to the spontaneous, permanent, and nonbreathing-modulated flow of the left gonadal vein. The presence of such a reflux must always evoke a supplying flow from a significant stenosis of the LRV, which should lead to a search for direct criteria mentioned above and for other indirect criteria of stenosis, such as the visibility of the collateral pathways *(Figure 10)*.[11] The convergence of these anatomic and hemodynamic criteria suggests

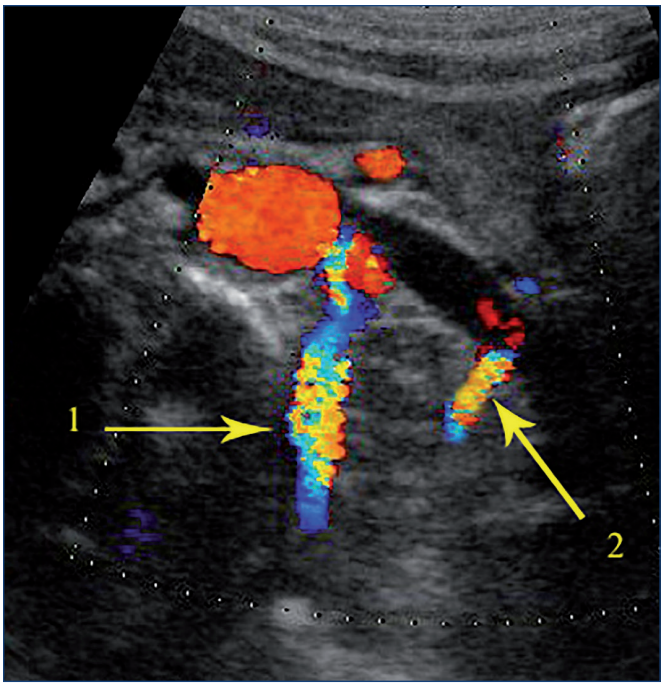

Figure 10. Abdominal approach.

Tight stenosis of the left renal vein in the aortomesenteric space. Visualization speed velocities in the supplying venous ways. 1: lumbar vein; 2: terminal part of the left gonadal vein.

a symptomatic LRV compression that is responsible for a Nutcracker syndrome and must result in an angioCT or a contrast-enhanced MR angiography to help decide which procedure is the most appropriate.

Examination of the iliac vessels

At this step, the angiologist essentially searches for any postthrombotic residual sign or extrinsic venous compression. The most common venous compression is left common iliac vein compression. In its usual form, it is defined as the compression of the terminal part of the left common iliac vein between the right common iliac artery and the 5th lumbar vertebra associated with intraluminal fibrous spur-like bands. The challenge is to differentiate between a simple anatomical impression and a hemodynamic compression. When the later exists, it generates hypertension and stasis in the upstream venous network, thrombotic risk factors, and pelvic venous insufficiency. Symptomatic hemodynamic compressions generate specific ultrasound criteria: (i) slow speeds and decreased respiratory modulation of upstream venous flows, especially at the common femoral vein; (ii) a reversal flow in the ipsilateral internal iliac vein; and (iii) visualization of the draining network.

Search for leak points

The GS, GI, and O points are anatomically deep; therefore, they are rarely identified by direct ultrasound exploration. Conversely, varicose veins in the territory of their afferent veins are easy to identify and represent indirect signs of downstream truncal reflux:

1. The superior gluteal vein mainly drains gluteal muscles. Therefore, a truncal reflux of this vein feeds the buttock varices.
2. The gluteal inferior vein participates in the drainage of the buttocks, but also of the thigh and satellite veins of the sciatic nerve by its deep afferent vein. Gluteal varices associated with varices near the sciatic nerve are highly suggestive of an incontinent gluteal inferior vein.[12]
3. The obturator vein tributaries communicate with the medial circumflex veins that drain into the deep femoral vein or the femoral vein near the saphenofemoral junction. A preterminal reflux at the saphenofemoral junction, caused by Valsalva maneuver and fed by a medial afferent vein (but not by the lateral pudendal vein), should suggest an incontinence of the obturator vein. Of note, a reflux of the obturator vein can also feed the labial varicose veins by its genital afferent vein.

Conversely, the P, I, and C points are superficial and easily identified and localized by ultrasound investigation. Doppler ultrasonography is the most relevant investigation for identifying these leak points. The leak points must be characterized by their size and their hemodynamic status as mentioned above. If drainage is efficient, there will be no pelvic venous hypertension. This concept has two consequences:

1. Significant pelvic varicose veins, in terms of venous dilatation and reflux, can be asymptomatic at the pelvis if they are well drained. In other words, the absence of pelvic congestion syndrome is not a sufficient argument for not treating the pelvic varices.
2. Isolated ligation of a leak point,[13] without treatment of their cause, does not seem an adequate response. This isolated ligation of a draining path can have two deleterious effects: (i) increases the intrapelvic venous pressure; and (ii) transforms asymptomatic well-drained pelvic varices into poorly drained pelvic varices, which become symptomatic varices. If the truncal reflux of the medial pudendal vein can no longer externalize after ligation of the leak point, it will feed Trendelenburg varices, vaginal and labial, and these veins are difficult or impossible to treat.

Conclusion

In the management algorithm of pelvic venous disorders, Doppler examination is the first-line imaging investigation to perform. It cannot identify all reflux, but is a very good tool for identifying pelvic varicose veins and highlights the essential pelvic leak points toward the lower limbs. It allows for the consideration of the main obstructive and supplying syndromes. In those cases, diagnosis will be confirmed by a second-line, cross-sectional imaging examination (angioMR, angioCT). The selective retrograde pelvic venography is the only exam that is able to achieve an accurate anatomic and hemodynamic mapping of the pelvic varicose veins, but it must remain a pretreatment exploration.

Acknowledgments

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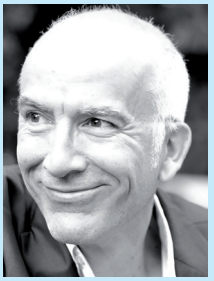

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Stenting as a treatment modality for acute and chronic venous disease

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Abstract

Venous disease is common among the general population, with chronic venous disorders affecting 50% to 85% of the Western population and consuming 2% to 3% of health care funding; therefore, it carries a significant socioeconomic, physical, and psychological burden. The most widely recognized presentation is acute venous thrombosis; however, patients may also experience chronic symptoms related to long-term sequelae, including persistent pain, swelling, and, when severe, ulceration. Due to the high morbidity associated with venous disease and the impact on the patient's quality of life, an effective treatment is a necessity. Stenting has received increased attention as the treatment of choice for patients with iliofemoral venous disease, particularly when there is an underlying compressive pathology. Initially, stenting was attempted for patients with chronic venous disease and postthrombotic syndrome or nonthrombotic iliac vein lesions, such as May-Thurner syndrome, to overcome chronic symptoms by reestablishing venous patency. More recently, stenting has received increased attention in acute venous disease for acute relief of symptoms and potentially reducing features of postthrombotic syndrome. This review summarizes the use of venous stenting in patients with acute and chronic venous disease, and it provides insight into the rationale for use and reviews on the existing evidence and outcomes. Therefore, this article hopes to provide information on the use of venous stents and give recommendations and indications for its use in both acute and chronic venous disease.

Introduction

Venous disease is common among the general population, with venous disorders affecting 50% to 85% of the Western population and consuming 2% to 3% of health care funding; therefore, it carries a significant socioeconomic, physical, and psychological burden.[1] Acute venous thrombosis is the most common and well-recognized presentation of venous disease. Although acute venous thrombosis may affect many different vessels, it commonly affects the deep veins of the leg (ie, deep vein thrombosis), which occurs in approximately 1 person in 1000 in the population,[2] and presents as a swollen and erythematous limb with skin that is warm to the touch.

Chronic venous disease (CVD) is a spectrum of conditions characterized by the retrograde flow of venous blood back into the affected leg. The pathophysiology

of chronic venous disease is attributable to valvular incompetence, venous outflow obstruction, or, most commonly, a combination of both.[3] The causes of CVD that are related to deep vein anomalies may be either primary or secondary. In primary CVD, there is an underlying nonthrombotic lesion compressing the vein and leading to outflow obstruction, which may lead to CVD directly or, alternatively, present with an antecedent acute deep vein thrombosis. The etiologies of this are wide and may include pelvic tumors, retroperitoneal fibrosis, intraperitoneal hematomas, or anatomical variants, such as May-Thurner syndrome.

May-Thurner syndrome is characterized by compression of the left common iliac vein by the right common iliac artery, and this irregularity has been observed in 22% to 32% of cadavers.[4,5] Secondary CVD tends to follow a deep vein thrombosis, and it can be associated with irreversible damage to the valves[6] and a persistent outflow obstruction. Chronically, this damage and obstruction may lead to a postthrombotic syndrome (PTS), which is often associated with pain, itching, restless legs, nocturnal cramps, and, when severe, ulceration,[6] resulting in disability and a significantly impaired quality of life.[7] PTS occurs in approximately 50% of patients within 2 years of a deep vein thrombosis.[8]

Recognizing the impact of venous disease has led to increased research efforts to help identify ways of preventing the development of severe chronic venous disease symptoms, which has resulted in the emergence of deep venous stenting to treat specific groups of patients. The aim of this review is to explore the role of venous stenting in the treatment of both acute and chronic venous disease.

Acute venous thrombosis

The current treatment for acute venous disease can be broadly divided into two categories—conservative and interventional. Conservative treatment options include compression therapy and venoactive medications. Interventional medical treatment includes heparin-related parenteral treatment followed by bridging to a dose-adjusted vitamin K antagonist (VKA), such as warfarin.[9] However, in recent years, newer non–VKA oral anticoagulants (NOACs) have been introduced, and they are becoming a standard treatment in clinical practice.

Parenteral anticoagulation with low-molecular-weight heparin prevents thrombus propagation and reduces the risk of embolization,[10] but it is unable to remove the thrombus from the deep venous system, which instead undergoes remodeling and recanalization in a process reminiscent of wound healing.[11,12] Sometimes this process is incomplete, resulting in a persistent outflow obstruction or stenosis that leads to PTS-related leg ulceration and venous claudication *(Figure 1)*.[8,13,14] In addition, there is a subgroup of patients presenting with acute deep vein thrombosis who have an underlying nonthrombotic ("primary") May-Thurner etiology. This underlying etiology can contribute to venous outflow obstruction, which may lead to a high risk of thrombus extension and recurrence, and it is associated with an increased incidence of PTS.[15,16] Overcoming venous outflow obstruction, whether primary or secondary, has been the basis for the development and use of a venous stent.

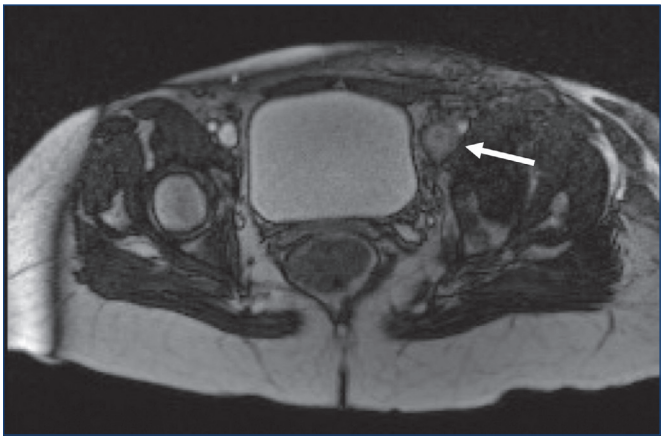

Figure 1. Magnetic resonance venography of a 62-year-old female with acute left iliofemoral deep vein thrombosis (arrow).

Interventional options

In the acute setting of deep vein thrombosis, research has focused on whether invasive management is more effective than anticoagulation alone. The most common technique for the removal of an acute proximal deep vein thrombosis is catheter-directed thrombolysis (CDT). CDT is an endovascular procedure in which a fibrinolytic drug, typically urokinase or tPA, is infused directly into the thrombus (under fluoroscopic guidance), thus theoretically averting the risks associated with systemic thrombolysis.[17,18] Initial data suggested that the procedure was both technically successful in >94% of patients[19-23] and safe in this patient group, with the US National Venous Registry reporting infrequent major bleeding (ie, intracranial bleeding [<1%], retroperitoneal hematoma [<1%], and gastrointestinal/genitourinary/musculoskeletal bleeds [3%])[24] and minor bleeding in 16% of the patients (predominantly at the

venous insertion site and hematuria).[12,25] The best results are seen when the symptoms have been present for <14 days, a thorough history is taken before the procedure, the vein is punctured under ultrasound guidance, and postprocedure observations are taken every 8 hours, and when hemostasis is monitored.[25] A venogram check will be done after 12 to 24 hours to assess the degree of thrombus dissolution, thus helping guide ongoing management.[18] When compared with conventional therapy alone, the use of CDT for the treatment of acute proximal deep vein thrombosis reduced the incidence of PTS from 55.6% to 41.1% at 24 months. At 6 months, the iliofemoral patency was 65.9% in patients treated with CDT and 47.4% in those receiving conventional therapy.[26] The ATTRACT study (Acute venous Thrombosis: Thrombus Removal with Adjunctive Catheter-directed Thrombolysis) is a large, ongoing study that is continuing to address the incidence of PTS in patients with acute proximal deep vein thrombosis treated with CDT.

Stenting, in the context of CDT, has been a secondary measure focused on treating an underlying obstructive lesion revealed by lysis *(Figure 2)*. However, there is a paucity of data to aid in deciding which patients will ultimately occlude without the placement of a venous stent.

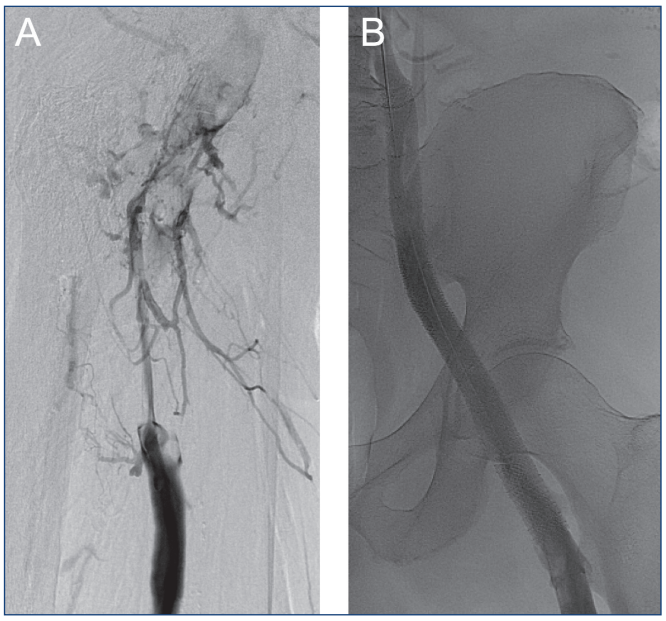

Figure 2. Lower limb venogram of a 62-year-old male with acute right iliofemoral deep vein thrombosis.

Panel A. Pre-catheter directed thrombolysis (CDT). Panel B. Completion venogram after the placement of an intravenous stent and balloon dilatation.

First report of venous stenting

In 1995, Berger et al first reported a case of stenting for acute deep vein thrombosis.[27] A 51-year-old man presented with May-Thurner syndrome. Following treatment with CDT and a subsequent angioplasty, two premounted Palmaz intravascular stents were placed in tandem into the left common iliac vein. At the 6-month follow-up, the patient maintained a good clinical response and the stent was patent. The authors proposed that this intervention warranted further investigation.

Catheter-directed thrombolysis and venous stenting

Stent patency

In studies on venous stenting following CDT for a nonthrombotic iliac vein lesion (NIVL), a widely used primary outcome measure is long-term stent patency. It has been proposed that a residual outflow obstruction will increase the likelihood of further or recurrent venous thrombosis[21] and PTS.[15] Early data on stent patency were limited by small studies and short follow-up times. In patients with iliofemoral stenting for May-Thurner syndrome following an acute deep vein thrombosis, primary patency at 1 year was 83% to 91.8% (n=155).[14,21-23] The primary patency was 84.5% to 90.2% at 2 years,[22,23] and 83% to 85% at 5 years.[14,23]

In a 2015 study by Park et al, 56 patients with an acute iliofemoral deep vein thrombosis were treated with CDT.[22] Completion venography was used to assess the degree of stenosis, and, in patients with a severe stenotic segment or with May-Thurner syndrome, a stent was inserted. This venography data resulted in 37 patients receiving stents. The 5-year primary patency rate was 77.8% in stented patients and 42.1% in nonstented patients (P=0.02). Deep vein thrombosis recurrence was also higher in the nonstented group (57.9% vs 27.1%; P=0.027), with recurrence occurring between 1 and 127 months of follow-up.[28]

Incidence of postthrombotic syndrome

A small number of studies have examined the incidence of PTS in patients receiving a venous stent following an acute deep vein thrombosis. PTS is reported to be as low as 11.5% at 5 years by Xue et al,[23] but the incidence was much higher in a separate study by Alhadad et al, which reported an incidence of 41% at the 6.2-year follow-up (range, 4.6-10.3).[29] In a single-centered, prospective study of 87 patients treated with stenting after a venous stenosis was found following CDT (defined as residual luminal narrowing >50%, absent anterograde flow, or presence

of collateral vessels), 12% and 6% developed PTS at 3 months and 1 year, respectively.[30] In the study by Park et al,[22] 30 patients (54%) were assessed for PTS at 57 months (mean) using the Villalta scale. There was a tendency for a lower score in the stenting group when compared with the nonstenting group, although this did not reach statistical significance.[28]

Surgical thrombectomy and venous stenting

Only a small number of studies have assessed the role of venous stenting following surgical thrombectomy; however, these studies focused on patients presenting with acute deep vein thrombosis, and they had small patient numbers (n=11-29). Of note, thrombolysis was often used along with a thrombectomy, either before treatment[16] or after if there was a residual thrombus.[31,32]

In two studies investigating patients with May-Thurner syndrome, the stent patency rate at 1 year varied widely. In patients with proximal deep vein thrombosis (iliofemoral [n=2]; iliopopliteal [n=1]; iliotibial [n=8]), patency was reported as 64% at 1 year,[16] whereas, in a study of patients with only iliofemoral deep vein thrombosis (n=26), the patency rate was 96%.[15] Where patients with varied etiologies for venous occlusion were included non-discriminately in the study group, patency rate for those with iliocaval deep vein thrombosis was 79% at 1 year,[32] and 74% in patients with iliofemoral clots (mean follow-up, 68 months; range, 3-129 months).[31]

Technical success in all papers was 100%, although there was significant heterogeneity between the different types of procedures.[15,16,31,32] Such heterogeneity also made interpreting postprocedure complications difficult. Except for a 2010 paper by Hölper et al that reported rethrombosis in 20% of patients within 7 days,[31] it was a rare early complication in other studies, only affecting between 3% to 9% of the patients.[15,16,32] The development of PTS was assessed using the Villalta score in a single study (n=11) by Husmann et al. The study showed that, at 3 and 6 months, only a single patient had developed features of PTS, and, in those followed-up after 12 months (n=9), there were no further cases of PTS reported.[31]

Surgical thrombectomy may be associated with a lower rate of stenting than catheter-directed lytic techniques, particularly mechanical techniques, which may be related to the fact that a residual clot after performing these techniques is misinterpreted as a stenosis/disease that requires a stent. Rates of stenting as high as 100% have been reported when purely mechanical thrombectomy was used.[33] Regardless, there is a paucity of high-quality studies examining the long-term efficacy of stenting in this group of patients.

Chronic deep venous obstructive syndrome

Historic treatment

Chronic deep venous obstructive syndrome responsible for CVD or chronic venous insufficiency (CVI) has historically been treated conservatively with compression and anticoagulation alone. However, these treatments provide variable results, and invasive surgical treatment has been suggested as an alternative approach to treating patients with severe venous claudication.[18,34,35] Surgery options include vein-patch angioplasty with excision of intraluminal bands, the division of the right common iliac artery, relocation behind the left common iliac vein or vena cava, and femorofemoral bypass (Palma's bypass) by grafting the contralateral saphenous vein to the ipsilateral common femoral vein with the creation of a temporary arteriovenous fistula. Long-term patency rates vary from 40% to 88%, and experience with these techniques is limited to only a few centers.[36] As a result, over the last 20 years, endovascular stenting has received increased attention for CVD.

Initial reports on stenting for CVD related to deep vein obstruction

The first large study in stenting for CVD was in 2000 by Neglén et al.[37] They investigated patency of 139 consecutive lower extremities in 137 patients after femoral vein cannulation, percutaneous balloon angioplasty, and iliac vein stenting. A total of 68 patients had PTS and 61 had May-Thurner syndrome (52% and 60% 1-year primary patency rates, respectively). They recommended stenting in all venoplasties with wide-diameter stents (16 mm) and found an improvement in pain and swelling with a postintervention thrombosis rate of just 4% (8% for PTS and 0% for May-Thurner syndrome). The authors further noted that 50% of all venous ulcers healed.[37] A follow-up publication, in 2003, featured outcomes of 447 lower extremities that were treated for obstruction alone or obstruction with reflux affected by CVI. They performed angioplasty and stenting without adjuvant treatment for venous reflux disease and found that this treatment led to a marked reduction in CVI symptoms: 50% of their patients were pain-free, 33% of swelling was relieved, and 55% of lower limb ulcers healed. These results suggested an important role of stenting for the treatment of CVI symptoms.[38]

Indications of stenting in CVD

Hartung et al[39] explored patency rates in 89 patients with nonmalignant obstructive iliocaval disease and found that there was a 98% technical success rate for patients treated with balloon angioplasty and stenting. Of these, 52 patients had primary disease with NIVL, 35 patients had disease secondary to PTS, and 2 patients had congenital abnormalities. The combined primary, primary-assisted, and secondary patency rates were 89%, 94%, and 96%, respectively, at 1 year, with restenosis predominantly found in patients with PTS.

The study by Neglén et al reflected on long-term outcomes of stenting in 982 nonmalignant obstructive lesions of femoroiliocaval veins. The study included NIVL and PTS patients and demonstrated a 6-year primary, primary-assisted, and secondary patency of 79%, 100%, and 100%, respectively, in patients with nonthrombotic disease and 57%, 80%, and 86%, respectively, in patients with thrombotic disease. Severe in-stent restenosis was qualified as >50% obstruction and occurred in 1% of NIVL and 10% of PTS limbs. There was also a significant reduction in pain scores and leg swelling, with an ulcer healing rate of 58%; the authors emphasized the benefit of using stent technology in patients with CVD.[40] In this study, stenting was most commonly performed for left-sided lesions, for nonocclusive obstruction, and in women; stenting had better outcomes in patients with NIVL vs PTS. Stent occlusion generally occurred if the obstruction was thrombotic in origin, suggesting that restenosis was likely to be associated with a thrombotic event rather than progressive occlusion. Occlusion was also more common if there was an associated recent trauma, if the stent was extended to the common femoral vein, if the obstruction was complete, and if the stenting was performed at a younger age. History of thrombophilia, additional procedures, and sex were not associated with worse stent outcomes.

A meta-analysis by Wen-da et al in 2015 looked at 14 studies exploring the use of stents in chronic venous disease related to deep vein obstruction.[41] It included a total of 1987 patients, of which, 43.2% underwent stenting for chronic PTS sequelae and 56.8% for chronic symptoms or signs related to NIVL. Of the included limbs, 81.2% involved the left side. They found that the 30-day thrombosis rates were higher (4.0% vs 0.8%) and the rates of ulcer healing lower (70.3% vs 86.9%) in patients with PTS vs NIVL. These findings were consistent with the results of Neglén et al, where it was shown that thrombotic lesions have a higher restenosis rate that is likely associated with a thrombotic event rather than progressive restenosis. This meta-analysis further concluded that occlusions before stenting and long lesions extending into the common femoral vein that damaged the inflow tract were associated with higher rates of restenosis. At the same time, sex (unless in younger patients), thrombophilia, and stents crossing the inguinal ligament did not influence patency. There were minimal complications (fewer in NIVL than in PTS), and the procedure was deemed safe.[41]

An ongoing study in our department is looking at the 1-year patency rates of using dedicated stents for deep venous obstruction. We have studied 347 stents in 140 patients with 57 patients receiving stenting for acute deep vein thrombosis post–CDT and 81 patients receiving stenting for chronic outflow obstruction; 9 of these patients had ulcers. The diagnosis was based on clinical presentation combined with Doppler ultrasound and magnetic resonance venography *(Figure 3)*. Our results show an overall primary, primary-assisted, and secondary patency rate of 67%, 80%, and 82%, respectively, reflecting the potential of using first-generation dedicated venous stents for venous disease. Our data and the studies mentioned above show that, when conservative treatment is not entirely effective, venous stenting is an appropriate and safe alternative therapy for chronic venous disease, resulting in clinical relief of pain and swelling, acceptable ulcer healing and recurrence rates, rare severe peri-operative complications, and good long-term patency.[42]

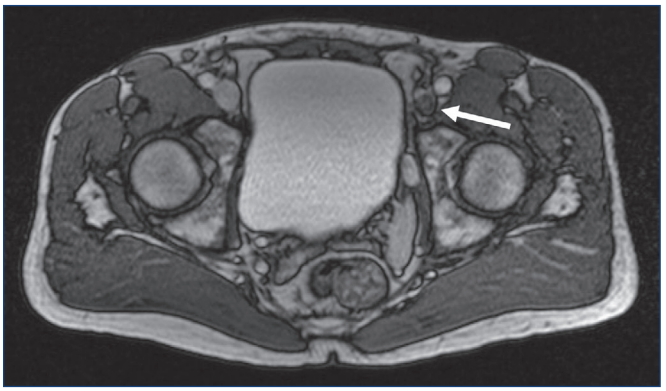

Figure 3. Magnetic resonance venography of a 53-year-old male with postthrombotic syndrome of the left lower limb.

Iliofemoral deep vein thrombosis resulting in vein occlusion (arrow).

Stenting as a treatment for symptoms of CVI

In a large follow-up study by Neglén et al in 2007, adjunct procedures to control saphenous venous reflux were performed, including great saphenous vein ablation and small saphenous vein stripping, in 197 limbs. Additional procedures did not affect patency rates or improve the quality of life scores, suggesting that stenting alone can be used to treat certain groups of patients with symptoms of chronic venous obstruction.[40]

A study by Raju et al in 2010 looked at the use of stenting alone for iliac vein obstruction and deep venous reflux in 528 limbs from 504 patients. Patients who were unresponsive to conservative measures with significant symptoms of pain (VAS ≥5/10), marked swelling, stasis, and skin changes, including ulcers, or a combination of signs and symptoms received stents. Large-caliber stents (14 to 18 mm) were used, and all lesions without skip areas were covered. There was a significant improvement in both pain and swelling in 78% and 55% of patients, respectively. Complete relief from pain and swelling was felt in 71% and 36% of patients, respectively. Cumulative secondary stent patency was 88% at 5 years. The study further suggested a role of iliac vein stenting for symptomatic relief of outflow obstruction and reflux *(Figure 4)*.[43]

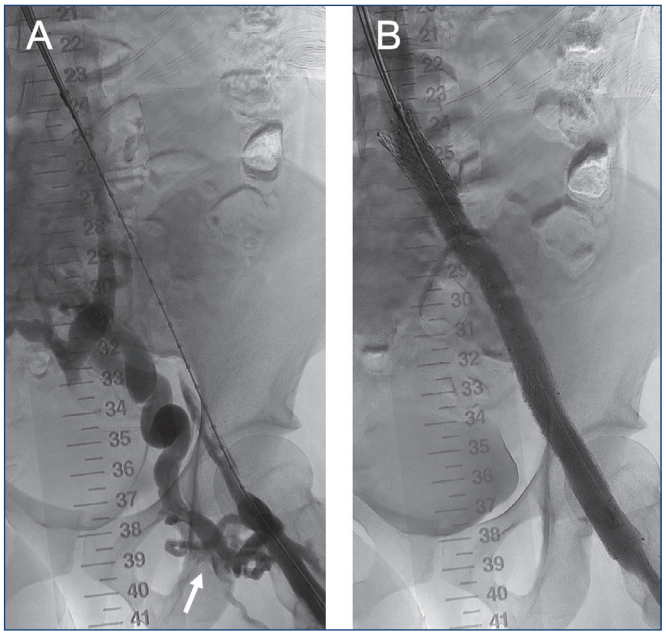

Figure 4. Lower limb venogram of a 37-year-old female with postthrombotic syndrome in the left lower limb following iliofemoral deep vein thrombosis.

Panel A. Preintervention with extensive collateralization observed (arrow). Panel B. Completion venogram after the placement of an intravenous stent and balloon dilatation.

Summary and recommendations

This paper reported on the use of venous stenting in the lower limbs and focused largely on two distinct groups of patients: (i) patients presenting with an acute deep vein thrombosis, where the underlying primary veno-occlusive pathology in the majority of studies was the May-Thurner syndrome; and (ii) patients presenting with CVI, where the etiology was either May-Thurner syndrome or PTS. Therefore, the findings are the most relevant to these specific patient groups.

Irrespective of surgical technique, the technical success of venous stenting appeared high in all studies, with acceptable safety and effectiveness when compared with traditional therapies.[21,22] Stenting for venous disease starts with careful patient selection, and most reported studies suggest that stenting is indicated for chronic venous disease when the obstruction is >50%, when superficial collaterals form, and when there is reflux in the deep and/or superficial veins.[34,36,41] A thorough preoperative preparation in both chronic and acute presentations is required, when possible, to ensure a positive outcome. Preoperative imaging includes ultrasonic angiology with duplex followed by imaging of the deep veins for appropriate planning.[34] Further requirements include patient medical optimization, a thorough anesthetic assessment, and rationalizing of anticoagulant treatment. Anticoagulation with warfarin is usually bridged with treatment-dose heparin.[9]

Intraoperative techniques are essential for a successful outcome, such as selecting an appropriate stent, timing of stenting postthrombolysis or thrombectomy in acute presentations, and considering an arteriovenous fistula.[36] The most common access sites are the femoral vein, the popliteal vein, and the internal jugular vein.[40,41] Ultrasound-guided puncture has shown the safest results, and it is a necessity for lesions in the external iliac and/or common femoral vein. Concerning the most appropriate stent that can be used, preference is usually given to flexible stents with a high radial force. Further preference is given to self-expandable stents rather than balloon-expandable stents to prevent kinking at the confluence of the internal and external iliac vein. The most common stent that has been used is a Wallstent (Boston Scientific, Galway, Ireland) and preference is given to large (14 to 16 mm) and long (>6 cm) self-expanding metallic stents with an overlap where multiple stents are requirement. Some newer dedicated venous stents, such as the Sinus XL stent, Sinus Venous stent (both Optimed, Ettlinger, Germany), the Zilver Stent

(Cook, Limerick, Ireland), and the Veniti Vici System (Veniti, St. Louis, MO, USA), have been launched.[34] Intraoperative intravascular ultrasound or venography has also been shown to improve results.[34,41] There is no consensus on whether an arteriovenous fistula is required for preventing rethrombosis.[31,44]

Postoperative care is equally essential, and it involves a well-defined interval-imaging regime to check for rethrombosis. At our center, we aim to perform a venous duplex scan at 1 day, 2 weeks, 3 months, 6 months, and 1 year postoperatively to ensure high secondary patency. Similarly, a rationalized antiplatelet or anticoagulant approach is also recommended. For NIVL, antiplatelet therapy may suffice; however, for PTS, anticoagulation is generally recommended due to a higher risk of rethrombosis.[45]

Acute venous disease

Stent patency was the most closely studied outcome measure in the literature, with rates reported at approximately 80% or above in the first 5 years following CDT. When patency was assessed in a stented vs an unstented group, the results were significantly better in patients who had iliac vein stenting.[28] These results are encouraging, but have yet to demonstrate whether improved patency rates translate into better patient outcomes.

An attempt was made in the literature to measure the incidence of PTS in those with venous stenting. Following a deep vein thrombosis, PTS may occur in up to 50%[7] of patients, and this increases to 70% when the causal factor is May-Thurner syndrome[16,29]; however, the assessment of PTS was not consistent between the studies.[23,29] In the two studies that did use the validated Villalta Scale for assessment of PTS,[46] the sample size was small in one study,[16] and there was a loss to follow-up and a variable follow-up period in the other.[28]

In our experience, stenting for acute venous disease can be done in unison with thrombolysis in the acute period of clot onset (ie, within 14 days). Therefore, in an ideal setting, we recommend conducting stenting with thrombolysis as soon as possible after the diagnosis of acute deep vein thrombosis, guided by the patient's clinical suitability to undergo surgery.

Chronic venous disease

Current experience with the use of stenting for chronic venous disease shows that it is safe, effective, and a reproducible procedure with the right equipment and technique. Study outcomes all show a very good patency rate after 1 year, with low rates of restenosis and major complications. As such, for chronic conditions, such as postthrombotic lesions, elastic lesions, and May-Thurner syndrome, stenting is rapidly becoming the treatment of choice.[41,42]

At the same time, there is clearly a difference in the results between PTS and NIVL patients. Early 30-day thrombotic incidence is reported as 0.8% in the NIVL group vs 4% in the PTS group, and long-term patency is lower in the PTS group vs the NIVL group.[41] These results may be related to the pathogenesis of restenosis, which is likely due to an acute thrombotic event rather than a progressive stenosis. Similarly, the healing rate for ulcers is significantly lower in the PTS group (70.3%) than in the NIVL group (86.9%), with a global recurrence of 8.7%, which may be due to PTS lesions being more extensive; therefore, preventing the progress of ulcer healing. There is, however, no difference between access site complications, stent migration, back pain, retroperitoneal bleeding, and contrast extravasation.[40,41] As such, further research is required to explore the timing of stenting, the type of stent that can be used, and the optimal intraoperative method for PTS.[34,36]

Conclusion

Stenting has been shown to be a safe and effective method of recanalization of veins in both the acute and chronic setting. It has high patency rates and acceptable complication rates. It remains to be seen if the early benefits translate into long-term improvements in morbidity. Although this seems a sensible inference, a large randomized controlled trial is needed. Robust, long-term follow-up is also necessary, and validated assessment tools should be used to assess outcome, particularly for PTS, where the Villalta score, despite its drawbacks, appears to be the gold-standard assessment.

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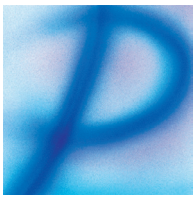

Incidence and location of deep vein thrombosis in the lower extremities: what do we know?

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Keywords:

deep vein thrombosis; incidence; location; lower limbs

Abstract

In the last century, deep vein thrombosis (DVT) plus pulmonary embolism was one of the most frequent causes of death in hospitalized patients. However, the incidence of DVT alone has been difficult to calculate from the entity of venous thromboembolism because the incidence of DVT is provided as either DVT without pulmonary embolism or pulmonary embolism ± DVT, where the latter group does not provide the precise rate of DVT. Therefore, our epidemiological review will focus on the first group, with an emphasis on first-time DVT. In the western world, the incidence of DVT (without pulmonary embolism) is currently around 50 to 80 per 100 000 per year, which increases during the winter, and the incidence increases with age and in females >60-65 years. Until recently, terms, such as distal and proximal DVT, have been used widely, now with suggestions of the anatomical descriptions for proximal DVT. Above-knee DVT is 2- to 3-fold more frequent than is calf-vein DVT, and left-sided DVT is the most frequent. The results from studies and lifetime risk estimates show that more emphasis needs to be placed on prophylaxis with risk assessments in the daily work environment. Prospective, large-scale, epidemiologic studies of patients with DVT verified by ultrasonography are needed with a clear presentation of location and extension. This basic information may reveal location-related rates of postthrombotic syndrome based on well-defined follow-up regimens.

Introduction

Deep vein thrombosis (DVT) is a serious disease, and it is often painful and potentially life threatening due to the occurrence of pulmonary embolisms in the acute phase. Later, DVT carries a varied risk for developing complications, such as postthrombotic syndrome, and surviving a pulmonary embolism event can lead to pulmonary hypertension and cardiac-respiratory failure and collapse. Both diseases greatly affect a patient's quality of life (QOL), and postthrombotic syndrome, the most frequent complication, is responsible for tremendous costs in national health care systems worldwide.[1,2]

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This review highlights the development of symptomatic and mainly first-time DVT and the incidence over a period that is balanced between increasing focus on prevention strategies and increased diagnostic accuracy and effectiveness. This review also explores the location and extension of the venous thrombosis, which is strongly connected to the frequency and severity of postthrombotic syndrome.[3] Furthermore, this review presents the most important epidemiologic large-scale studies published in the last 25 years on mainly first-time DVT in the lower extremities, with some materials even collected back in the 1950's and 1960's for comparison. The entity of venous thromboembolism is mentioned when needed *(Table I)*.

• **Population** nation, county-based, urban-based
• **Special cohorts** elderly people pregnant women
• **Prospective** ultrasound, phlebography (few years)
• **Retrospective** necropsy, medical records, any imaging method, registries (local, national) (several years)

Table I. Method and materials.

History

The recognition of a vein thrombosis probably goes back to the middle ages.[4] Later, the disease gained attention as the most feared disease during pregnancy, and it was treated with bloodletting in the 1700's.[4] In 1793, Hunter hypothesized that the disease was due to veins occluded by clots. He ligated the veins proximally to avoid propagation and, as a consequence, pulmonary embolism, which was unknown at that time.[4] Many years later, the method for vein interruption had been executed in different ways, and, in 1934, it was reinvented by Homans for preventing pulmonary embolisms.[5,6] Virchow demonstrated that there was a connection between DVT and pulmonary embolisms, and, in 1856, his idea of a triad interaction between decreased vein flow, vein wall injury, and blood abnormalities was published as the pathophysiological background of the disease. At the same time, the recognition of the inflammatory response in the vein wall as the pathogenic mechanism was discovered.[4] The clinical condition with phlegmasia alba dolens was described in 1784 and phlegmasia cerulea dolens in 1857

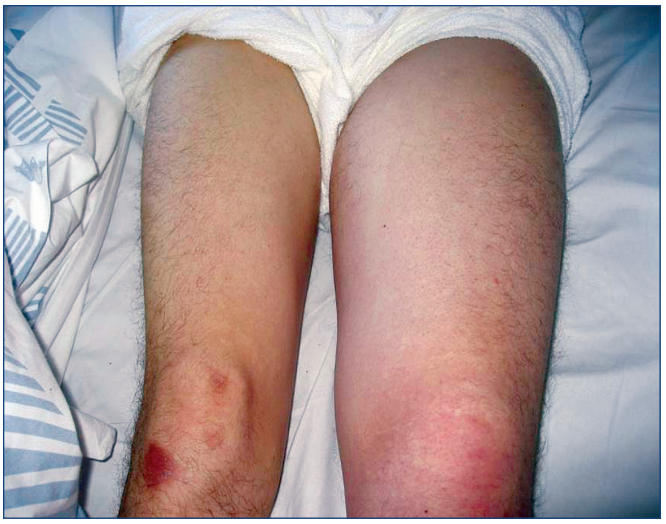


Figure. 1. Left-sided deep vein thrombosis.

When the swelling involves the entire limb, then the deep vein thrombosis involves the pelvis.

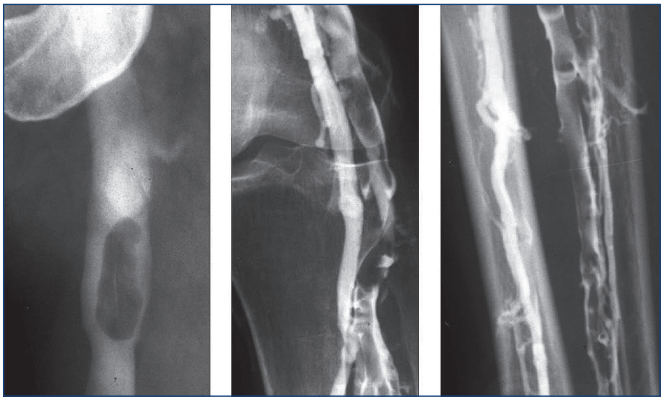


Figure 2. Deep vein thrombosis clots visualized using an "old-fashioned" phlebograph.

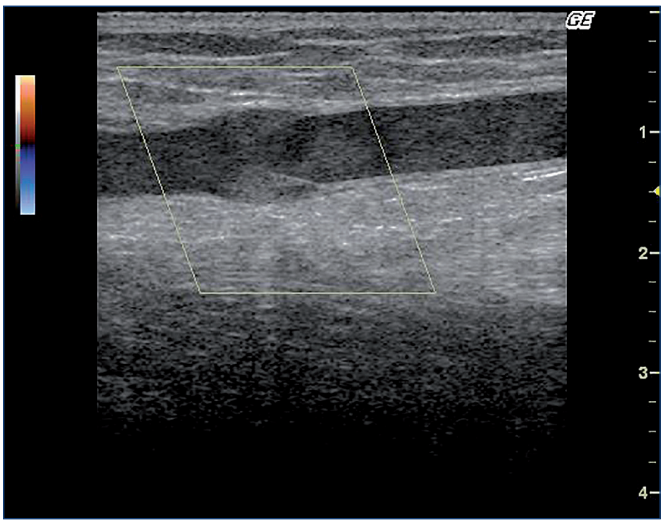


Figure 3. Ultrasonography shows a thrombosis process beginning typically in the valve area.

(Figure 1); the latter is identical with blockage of both deep and superficial veins.[7,8] The sign of Homans from 1944 described dorsal flexion of the foot resulting in calf pain, which was an indication of DVT, but this sign was later questioned.[9,10] For many years, phlebography *(Figure 2)*, plethysmography, and radioactive fibrinogen were used as diagnostic tools until continuous-wave Doppler was applied in the 1960's, and, 10-to-20 years later, continuous-wave Doppler combined with duplex technology became the procedure of choice *(Figure 3)*.[11]

Epidemiology studies

Large-scale necropsy data from the area of Malmö, Sweden emerged in 1991 with DVT being diagnosed via necropsy.[12] Malmö had around 250 000 people in the period from 1957 to 1987 with few yearly variations; this study focused on 4 specific years–1957, 1964, 1975, and 1987. All necropsy reports from the departments of general surgery, infectious disease, internal medicine, oncology, and orthopedics were reviewed, and, of the 26 078 admissions, there were 1293 deaths. Of these 1293 deaths, necropsy was identified in 994, with 347 who had had a venous thromboembolism. While the rate of venous thromboembolisms occurred at a constant rate over the 4 years analyzed, there was a significant decrease in 1987 in patients from the orthopedic departments. This decrease was explained, especially by a fall in DVT, due to more preventive care and mobilization. The rate of necropsy was determined using a uniform necropsy protocol over the entire period to improve the validity of the analysis.

In 1992, a prospective study on the incidence of DVT was published on the 1987 urban population from Malmö). At that time, all patients suspected of DVT were referred to one hospital for phlebography. One-third of the suspected patients were positive for DVT: 170 males and 196 females with a mean age 66 years (range, 28-89 years) and 72 years (range, 13-95 years), respectively. The incidence was similar for men and women and increased considerably in the older groups. The incidence of DVT was 160 per 100 000, and only 5 of these patients had upper-limb thrombosis. Above-knee DVT was 2-fold higher than was below-knee DVT. Malignancy was diagnosed in 20%, a past-history of DVT was found in 26%, and DVT was diagnosed postoperatively in 24% of the men and 31% of the women. Half of the cases in women occurred after surgery for a lower-extremity fracture. The incidence in this study is one of the highest registered, which may be due to a high proportion of previous and asymptomatic DVT.

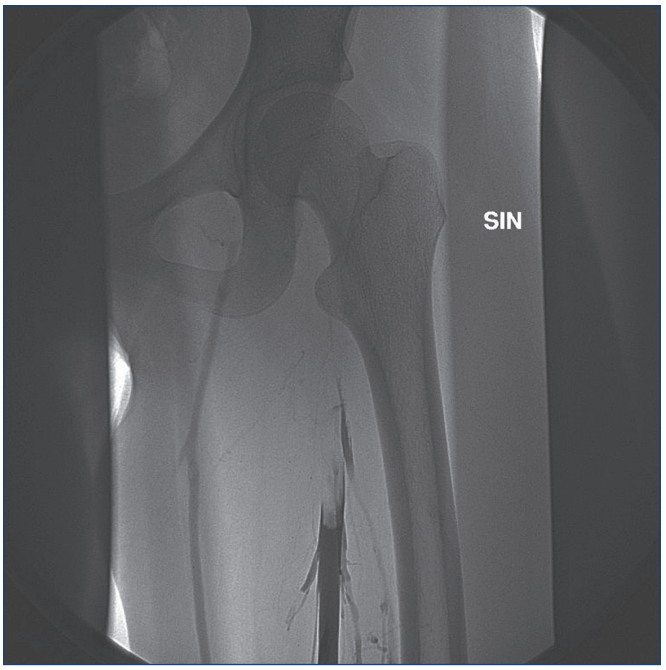


Figure 4. Venogram showing an acute deep vein thrombosis (less than 14 days) from midthigh and upward to the groin and pelvis.

No collaterals are seen pointing out the acute phase.

The results from the Olmsted County study (MN, USA) was published in 1998.[14] Residents presenting with venous thromboembolism diagnosed by any method (n=2218) were retrospectively identified in a 25-year period from 1966 to 1990 (both years included; population in 1990 was 106 470). The mean age of onset was 61.7±20.4 years, and 56% of the patients were female. The incidence of DVT was stable for males in the period and increased for women >60 years old. The overall age- and sex-adjusted annual incidence of DVT alone was 48 per 100 000 and pulmonary embolism with or without DVT was 69 per 100 000. However, the incidence of pulmonary embolism was almost reduced by half during the last 15 years of the period to the same level as DVT without pulmonary embolism. Silverstein et al concluded that a more accurate risk identification of patients was needed for effective prevention.[14]

In a population of 342 000 inhabitants from Brittany, France (the Brest district), the yearly incidence of DVT (verified by ultrasonography) was 124 per 100 000, which was collected prospectively from April 1998 to March 1999, and published in 2000. Almost 63% of the patients were not hospitalized at the time of diagnosis, but 16% had been hospitalized within 3 months before the diagnosis.

The incidence increased in both sexes with age, and around 1000 people were >75 years old. Oger et al highly recommended more attention be given to DVT prevention.[15]

A few years later, another study from Olmsted County, Minnesota, USA compared two groups of residents (n=100 000) with venous thromboembolism in a 10-year period from 1980-1990. Of the 911 residents with venous thromboembolism, 253 were hospitalized for a reason other than DVT or pulmonary embolism and 658 residents were not hospitalized. The average annual age- and sex-adjusted incidence of in-hospital venous thromboembolism was 960.5 (95% CI, 795.1-1125.9) per 10 000 person-years, which was 100 times greater than the incidence of 7.1 (95% CI, 6.5-7.6) in the nonhospitalized group. The incidence rates of DVT and pulmonary embolism in the two groups changed little over the period despite a reduction in the average hospital stay. Heit et al concluded that there is a strong need for better risk stratification and an intensive prevention program for hospitalized patients.[16]

Results from the Olmsted study were published in 2005 on the incidence of DVT during pregnancy and the postpartum period. Between 1966 and 1996, there were 105 cases of venous thromboembolism, including 32 cases of DVT during pregnancy and 44 during the postpartum period (defined as 3 months postdelivery).[17] The incidence of DVT remained relatively constant during pregnancy, but decreased in the postpartum period. The incidence was high, especially in the third trimester and the first week of the postpartum period, with a relative risk for DVT postpartum vs during pregnancy being 4.12 (95% CI, 2.62-6.50; $P<0.001$). The relative risk of venous thromboembolism was 4-times higher for pregnant woman than for nonpregnant women of the same age. Pulmonary embolisms were especially high during the early postpartum period, but they decreased more than 2-fold by the end of the period.

In 2007, a study from Nord-Trøndelag, Norway, which was based on all residents ≥20 years (n=94 194), identified the incidence of venous thromboembolism between 1995 and 2001 from diagnosis characteristics retrieved from medical records.[18] A total of 740 patients with a first-time venous thromboembolism event were identified (incidence rate, 1.43 per 1000 person-years; 95% CI, 1.33-1.54), with a DVT incidence rate of 0.93 per 1000 person-years (95% CI, 0.85-1.02). More women were overweight than were men (411 women vs 329 men; mean age, 75 and 71 years for women and men, respectively). Proximal DVT was 3-fold more frequent than was distal DVT, and it was mostly located on the left side. The incidence increased exponentially with age and it was higher in cancer patients. The ratio of idiopathic and secondary thrombosis was 1:1. The risk of dying was highest in the first month; after which, the mortality rate approached the rate in the general population.

A prospective community-based study from Perth, Australia investigated multiple overlapping retrospective sources, such as searching hospital morbidity and mortality databases using the ICD-10 codes ("cold pursuit") published in 2008. The study period was 13 months and included 151 923 residents with a mean age of 64.4 years, of whom 1.4% were Indigenous Australians. The annual DVT incidence was 52 per 100 000 residents (95% CI, 0.41-0.61) with a minor male preponderance, and an almost exponential increase was noted in patients >50 years old. Ho et al concluded that 17 000 Australians would suffer from venous thromboembolism annually, calling for an effective prevention program.[19]

Data published in 2008 concerning venous thrombo-embolism in the elderly population from the Worcester metropolitan area (MA, USA) in 1999, 2001, and 2003 (n=477 800) showed that, of the 1897 validated events included in the study, 55% occurred in patients who were >65 years old. The DVT incidence in this category of patients increased from 59 per 100 000 in the population <65 years to 334 per 100 000 in patients between 64 and 74 years. The same tendency was observed for pulmonary embolism, which was found in one-third as many patients. The events in this elderly group were less unprovoked than in younger patients. The rate of recurrence did not differ significantly between the age classes. However, major bleeding from anticoagulation increased 2-fold in older patients. While age is not a predictor of recurrent venous thromboembolism, major bleeding is increased in older patients; therefore, treatment decisions should be tempered by this observation.

In 2009, another prospective study between 1998 and 2006 from Malmö, Sweden (n=280 000 inhabitants) was published.[20,21] Patients >18 years, who were recruited from the only hospital in the region to treat venous thromboembolisms, were included after an objective diagnosis of (probably first time) DVT or pulmonary embolism. Mean age was 61 years in both sexes, with slightly more women included. DVT occurred in 71% of the patients without a pulmonary embolism and in 6% with a pulmonary embolism. The annual risk was 51 per 100 000 for DVT and 19 per 100 000 for pulmonary embolism. The

left leg was the most affected limb, and the femoropopliteal location was the most frequent site involved. Iliac DVT occurred in only 13% of the cases. Hormone therapy, immobilization, previous surgery, and malignancy were the most acquired risk factors. A positive family history for venous thromboembolism was obtained from 25% of the DVT patients.

A nationwide, Swedish, large-scale, family study was performed in 2013 to assess the age-and sex-specific seasonal variation of venous thromboembolism in hospitalized patients.[22] The study included 150 416 individuals who were registered with a first-time event in 288 months between 1987 and 2010, and, of these, 4.9% had at least one first-degree relative with a venous thromboembolism. The incidence of DVT peaked in February in individuals without a family history of venous thromboembolism (peak-to-low ratio, 1.24). In patients >50 years old, the seasonality was more prominent. These results support the data from a prospective study published 9 years earlier on 1154 Italian patients over a 6-year period.[23] The seasonal analysis showed a significantly reduced frequency of DVT events in the summer and an increased frequency in the winter, for the total population (P<0.0001), for men (P=0.003), and for women (P=0.007). The exact mechanisms of this variability are not well understood, although seasonal changes in the coagulation activity may play a role.[24]

A Swedish, retrospective, population-based registry included all adults ≥18 years old residing in the Västerbotten County in northern Sweden during 2006 (n=204 836), and 22.6% of the population were ≥65 years old.[25] The mean incidence of venous thromboembolism was 167 individuals per 100 000 person-years (155 for men and 180 for women), the incidence increased with age, which was highest among older women (≥85 years old), and a first-time event occurred in 82% of the patients. The incidence of lower-extremity DVT without pulmonary embolism was 76.6 per 100 000 individuals per year. The most prevalent risk factors were a recent hospitalization and a concurrent malignancy. Only 3.9% of the patients with a first-time venous thromboembolism were taking pharmacological prophylaxis at the time of diagnosis.

Instead of looking for the incidence of venous disease per individuals per year, estimates of lifetime risk have recently been calculated.[26] Participants in different age groups were recruited from two known prospective cohort studies from the US: (i) the CHS study (Cardiovascular Health Study) (n=5414 individuals >65 years old followed at baseline visits from 1989–1990 and 1992–1993); and (ii) the ARIC study (Atherosclerosis Risk in Communities) (n=14 185 individuals 45 to 64 years old followed at baseline visits from 1987–1989). An incident venous thromboembolism was defined as the first DVT or pulmonary embolism from baseline through the end of follow-up in 2011 for ARIC and 2001 for CHS. At 45 years, the remaining lifetime risk of venous thromboembolism was 8.1% in ARIC, which was 2-fold higher than the incidence rate in CHS. This result was explained by differences in the period of venous thromboembolism ascertainment, which became more frequent in recent years. As expected, the remaining lifetime risk decreased across increasing index ages. Obesity was identified as a high risk factor (lifetime risk, 10.9%; 95% CI, 8.7-12.3). Bell et al concluded that at least 1 in 12 middle-aged adults will develop venous thromboembolism, which may be more useful than the annual incidence studies to promote awareness of the diseases and guide decisions at both clinical and policy levels. Unfortunately, this publication did not assess DVT and pulmonary embolism separately.

A prospective, 1-year study compared venous thromboembolisms from 2013 in the same area in Western France to the study performed in 1998, and the incidence of symptomatic DVT decreased significantly to 0.76 per 1000. The numbers concerned distal and proximal DVT, especially in patients >60 years. Delluc et al concluded that these results might be due to an easier access to pharmacological thromboprophylaxis, early mobilization, and a reduction in the length of the hospital stay. On the contrary, an increase was found in the incidence of pulmonary embolism, which may be due to the availability of more sophisticated diagnostics.[27]

Finally, the results from a 1-year, retrospective, Chinese study (2010–2011), which was based on 7.1 million Han Chinese people, showed that the incidence of DVT was 30 per 100 000 people. DVT occurred in up to 0.2% after intermediate and major surgery. While it is known that, in this region of the world, venous thromboembolisms occur less frequently than in western countries, the reasons for this are unknown.[28]

First-time DVT studies

An estimation of the location of DVT has been made from large discharge cohorts of patients from the two biggest

urban areas in Denmark-Copenhagen and Aarhus.[29] Almost 160 000 men and women aged 50 to 64 years were identified from the Diet, Cancer, and Health study that was conducted between 1993 and 1997. Patients from the Danish National Patient Registry were identified with the codes for venous thromboembolism at discharge diagnosis, and this diagnosis was confirmed from the medical records. In 358 patients, 12.3% had distal DVT, 36% proximal DVT, 7.1% pelvic DVT, and 2.6% upper-extremity DVT. Of the confirmed events, approximately 50% were idiopathic and the other 50% were nonidiopathic events. The authors concluded that data on venous thromboembolism obtained from administrative registries are a valuable source of information, but this must be used with some caution.

The above-mentioned Swedish, retrospective, population-based registry presented numbers for the location of first-time DVT in the lower extremities: 43% had iliac DVT, 36% femoropopliteal DVT, and 21% crural DVT. Classified by age, iliac DVT occurred more frequently in the oldest group, whereas femoropopliteal DVT occurred more frequently in the youngest group.[25]

A new, retrospective, single-center study on ultrasound-verified DVT has illustrated the large diversity of thrombus distribution.[30] The analysis concerned patients >18 years old presenting with unilateral DVT who were referred to one hospital in Antwerp between 1994 and 2012 (n=1338). The anatomical site and extension was registered into five segments: (i) calf veins (segment 1); (ii) popliteal vein (segment 2); (iii) femoral vein (segment 3); (iv) common femoral vein (segment 4); and (v) iliac veins with or without the inferior vena cava (segment 5). The median age was 62 years (range 18 to 89 years) and the male/female ratio was 50/50. There was a left-sided dominance (57%) in all segments that increased from segment 1 to segment 5, including the iliofemoral segment. The reason for this dominant side location is due to the left-sided iliac vein compression syndrome, which explains the starting point of DVT from this location *(Figure 5)*.[31] Calf-vein DVT (distal DVT) occurred in 28% of the cohort, femoropopliteal DVT in 33%, and iliofemoral DVT (proximal DVT) in 38%; data on 23 patients were excluded from the analysis due to nonadjacent segments. The femoropopliteal DVT involved segments 2 and/or 3; whereas, iliofemoral DVT involved segments 4 or 5.[30] Prospective studies are needed with more attention about the thrombosis of the profunda femoris vein. It could be argued that many thrombosis events in the common femoral vein belonged to the femoral vein, which decreases the severity of postthrombotic syndrome.

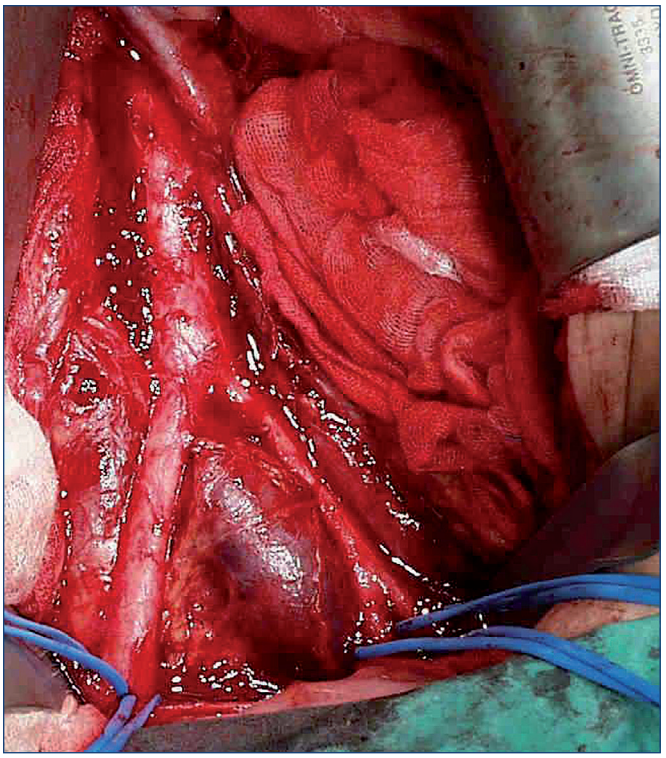


Figure 5. The left iliac vein compression syndrome, seen from the outside.

Pulmonary embolism

From some of the papers in this review, it seems that the incidence of pulmonary embolism has fallen during the past 50 years. However, the number given is inconsistent, ranging from 20 to 50 per 100 000 annually. The number includes a high rate of asymptomatic pulmonary embolisms, which are found due to an increased screening for cancer. However, pulmonary embolisms occur more frequently in connection with iliofemoral DVT than with calf-vein DVT.[32] In addition, the rate of DVT (50 to 80 per 100 000) is an underestimation because the presentation of venous thromboembolism includes pulmonary embolism ± DVT, where the rate of DVT is not presented individually.

Cost studies

A recent cost analysis from the Olmsted County study in an 18-year period from 1988–2005 showed that the adjusted mean predicted costs were 1.5-fold greater for venous thromboembolism incidents in 355 patients undergoing major operations vs controls and 2.5-fold higher for 286 patients with acute medical illness vs controls. Cost differences between cases and controls were the greatest within the first 3 months.[33,34]

Could the incidence be lower?

Heit et al examined the reasons for the trends in venous thromboembolism over the last years.[35] The population-based cohort study from Olmsted county (MN, USA) showed that, while the annual venous thromboembolism incidence did not change significantly, the prevalence of obesity, major surgery, active cancer, trauma, and paresis has increased. Obesity has the greatest influence on the risk of a venous thromboembolic event. These conditions have challenged the preventive anticoagulation strategies. We have the medicine and mechanical devices for prophylaxis, risk scores, and national and international guidelines, but we have to provide education pertaining to the entire available armamentarium.

Conclusion

It seems that the incidence of DVT without pulmonary embolism during the past 50 years has been decreasing to about 50 to 80 per 100 000 annually *(Table II)*. All studies are based on well-defined areas and populations, but with many different methods of registration. The 2-fold higher incidence from the Malmö study (year 1887) might be explained by patient referral from uptake areas outside the district of Malmö, and patients with a pulmonary embolism with simultaneously diagnosed asymptomatic DVT might be an explanation. Lower-extremity DVT is, in all studies, mostly left-sided, 2- to 3-fold more frequent for above-knee DVT, and, in general, occurs equally between men and women. The incidence increases with age, especially in people aged >60-65 years and in females. Other risk factors are malignancy, hospitalization, acutely ill medical patients, postsurgical condition, hormone therapy, and pregnancy. Descriptions are missing in older studies on the precise location and extent of the DVT *(Table III)*. The constancy in the incidence emphasizes the need for an increased emphasis on prophylaxis based on education and the use of existing risk assessments and guidelines. Prospective studies to predict the precise location and extent of the thrombosis are warranted *(Table IV)*.

• DVT (without symptomatic pulmonary embolism) incidence is 50 to 80 per 100 000 annually
• Almost equal sex distribution
• Increasing >60-65 years especially in females
• Mostly left-sided DVT
• Iliofemoral DVT is 2- to 3-fold more frequent than calf-vein DVT
• Unprovoked DVT counts for almost half of the cases

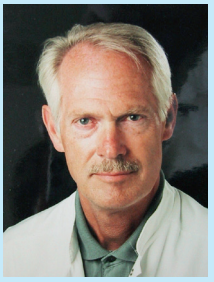
Table II. Summary.

• Age
• Malignancy
• Increasing >60-65 years, especially in females
• Hospitalization
• Immobilization
• Acutely ill medical patients
• Postsurgical patients
• Trauma
• Hormone therapy
• Pregnancy

Table III. Main risk factors.

• Prospective studies including DVT with and without pulmonary embolism
• Population based on well-defined county/community areas
• Avoid the term proximal DVT
• Description of the anatomic localization according to existing definitions with ultrasonography
• Include the profunda femoris vein in the diagnostic phase
• Follow-up regimes for postthrombotic syndrome with ultrasonography and Villalta score for the different anatomic locations

Table IV. What we need.



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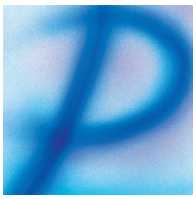

Anatomy of foot and ankle perforator veins

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Keywords:

ankle and foot perforator veins; chronic venous disease; foot venous pump; plantar veins; saphenous system roots; venous anatomy

Abstract

Background: The foot venous pump is located in the plantar veins, where both its anatomy and connections with the saphenous roots and the foot perforator veins are not well known, and therefore, they are underinvestigated in daily practice. The aim of this paper is to describe the unique anatomy and the functional role of the foot perforator veins and emphasize their key role during the activation of the foot venous pump. Ankle perforator veins also play a crucial role in the venous blood return, giving rise to the anterior tibial and fibular veins.

Materials and methods: A total of 400 cadaveric feet from the "don des corps" of the Descartes University (Paris, France) were injected with green Neoprene latex, which was followed by an anatomical dissection and a colored segmentation of the venous system. Duplex color sonography and CT venography with 3D modeling were used to investigate the foot perforator veins and their connections with the foot venous pump and the saphenous systems in patients with venous disease.

Results: Some foot perforating veins are characterized by flow that is oriented from deep to superficial veins, due to the presence of one-way valves, a unique feature in the venous system of the lower limbs. From a hemodynamic point of view, the foot veins should not be classified into deep and superficial systems, but into medial and lateral functional units. The medial unit is comprised of the medial plantar veins, the medial marginal vein, and the medial foot perforator veins. The lateral unit is comprised of the lateral plantar veins, the lateral perforator veins, and perforator veins of the calcaneus. Ankle perforator veins are mainly the dorsal perforator veins that are connected to the initial segment of anterior tibial and fibular veins and the lateral perforator veins along the distal fibula.

Conclusion: Despite the small volume of blood ejected at each step, the foot venous pump plays a key role in the venous blood return of the lower limbs. The foot perforator veins are the main outlet of the foot venous pump into the superficial venous system, working from deep to superficial; therefore, they are responsible for the systolic ascending flow in both the great and small saphenous systems during foot venous pump activation.

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Anatomical technique and protocol

The injection technique has been described previously in our anatomical study of the foot venous pump.[1,2] This study used 400 feet from 200 nonselected, nonembalmed cadaveric subjects from the department of the "don des corps" of the Descartes University (Paris, France), with an average age of 84. After exposing the medial marginal vein, a No. 19 butterfly venous catheter was inserted and directed toward the toes (countercurrent to the physiological blood flow). The common femoral vein was approached, and a tube was inserted to perform lavage-irrigation with soapy water, which was repeated several times, followed by a massage of the muscles to obtain a clear liquid. After ligating the common femoral vein, it takes about 30 minutes to fill the entire venous network by injecting 120-150 mL of green neoprene latex in each limb. Dissection was performed on the following day, and color segmentation was done by painting veins with different dyes to simplify their identification.

Color Doppler ultrasound was used to assess the anatomy of the foot perforator veins, their connections with the foot venous pump, and their hemodynamics. Multislice CT venography (also known as phlebo CT) was used to obtain the 3D modeling of the foot's venous system, which strongly correlated with the dissection findings. Multislice CT venography was specifically indicated for patients with a complex venous disease or recurrent varices after surgery (REVAS). The multislice CT venography acquisition and reconstruction protocol and results *(Table I)* have been described previously.[3-5] This technique provides an accurate depiction of the foot veins, with an interactive 3D assessment, including virtual dissection. These new imaging tools also provide access to virtual reality techniques,[6,7] which is mainly the virtual dissection of the limb, and it is useful for making decisions in complex cases, for educational purposes, and to improve our knowledge of the venous anatomy.

Foot pump anatomy

The venous blood reservoir of the foot, also called the foot venous pump, is located deeply in the plantar veins, between two plantar muscles, the quadratus plantaris, and the Hallux flexor longus *(Figure 1)*.[1,2] The medial (or internal) plantar pedicle is short (5 cm), rectilinear, and it is comprised of 2 to 3 veins that are often plexiform with several anastomoses. The lateral (or external) plantar pedicle is longer (12 cm), curved, and larger. It is located

Protocols	Acquisition	Reconstruction	Postprocessing	Contrast injection
16 detectors 600 slices in 25 s	120 kV 150 mAs Slice collimation: 16 × 1.5 mm Field: 512 Field of view: 380 mm	Slice width: 2 mm Slice increment: 1.5 mm Filter: B30 Matrix: 512 × 512 Zoom factor: 1.7	1998-2012 Volume rendering Fast & automatic with tissues transparencies	Medrad MCT injector system Uniphasic injection with 20 mL of iodine contrast medium in 180 mL of serum
64 detectors 1000 slices in 20 s	120 kV 150 mAs	Slice width: 1 mm Slice increment: 0.75 mm Matrix: 512 × 512 Zoom factor: 1.7	Volume rendering	Puncture of a dorsal foot vein or, rarely, the varices of the thigh
128 detectors 1000 slices in 10 s	100 kVp Slice collimation: 128 × 0.6 mm	Rotation time: 300 ms using a continuous helical scan MinDose® technique Pitch: 0.16-0.22	Volume rendering with phase contrast using multiprocessors Osirix using fast graphic card	Proximal and bilateral injections to visualize pelvic veins

Table I. CT venography: multislice and multidetector spiral CT protocols

between the two muscle layers of the sole; therefore, it is compressed during the systolic phase of the foot venous pump. The lateral plantar pedicle is comprised of 2 to 3 veins (2 to 4 mm in diameter), which are connected to each other by several anastomoses *(Figure 2)*. These two plexiform pedicles join posteriorly to form the calcaneus confluent of the plantar veins, where the blood is ejected upward into the posterior tibial veins, which are the main exit pain of the foot venous pump.[1,2]

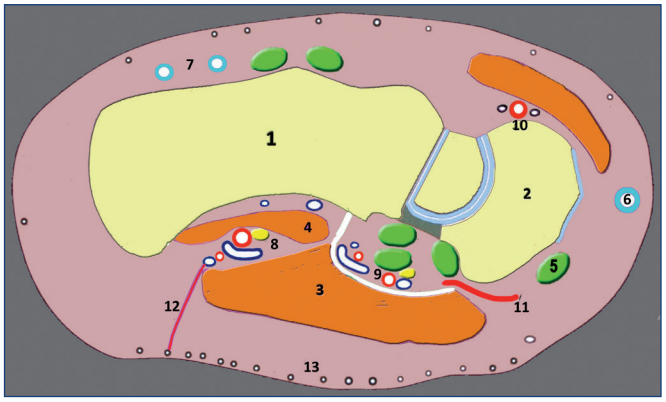

Figure 1. Paramedial longitudinal section of the foot.

This section shows the intermuscular topography of the lateral plantar veins (8) located in the slit that separates the fleshy body of the quadratus plantaris (4) from that of the abductor hallucis (3). The medial plantar veins (9) have fibrous and tendinous relations.

Abbreviations: 1, calcaneus bone; 2, navicular bone; 3, abductor hallucis; 4, quadratus plantaris; 5, tendon of the posterior tibial muscle; 6, medial marginal vein; 7, lateral marginal plexus; 8, lateral plantar veins; 9, medial plantar veins; 10, pedal artery; 11, navicular perforator vein; 12, perforator in fatty tissue; 13, subcutaneous venous plexus of the sole.

Figure 3 shows the complete anatomy which explains foot venous pump function. The pump (shown in green), which is comprised of plantar veins, has three parts (listed from front to back)–a suction pole (A), a reservoir (R) in the plantar veins, and an ejection pole (C) at the calcaneal confluent. Anteriorly, at the aspirational pole, blood enters the pump during relaxation of the plantar muscles during the foot's plantar flexion. The ejection pole is represented by the calcaneal confluent or calcaneal crossroad (C). During foot venous pump systole, blood is ejected directly toward the posterior tibial veins and the great and small saphenous veins through the foot perforator veins.

For a more detailed description, please see our previous paper: *Phlebolymphology.* 2010;17:151-158.[2]

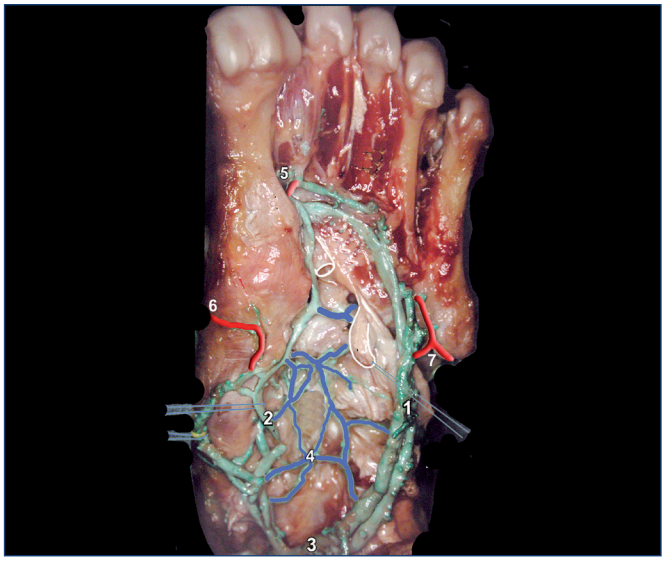

Figure 2. Anatomical dissection of foot veins (inferior view).

Latex injection and colored segmentation.

Abbreviations: 1, lateral plantar veins (double); 2, medial plantar veins; 3, calcaneal crossroad of the plantar veins; 4, plexus-shaped network of the sole; 5, perforator of the first intermetatarsal space; 6, navicular perforator; 7, perforator of the fifth metatarsal bone.

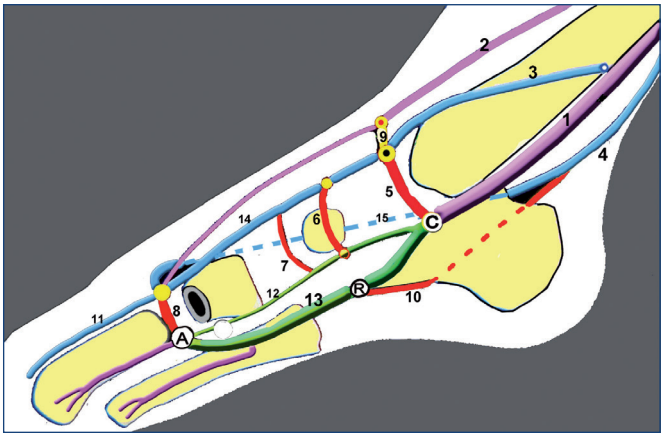

Figure 3. Hypothesis about venous pump function.

The three parts of the foot venous pump include a suction pole (A), a reservoir (R) in the plantar veins, and an ejection pole (C) at the calcaneal confluent.

Abbreviations: 1, posterior tibial vein; 2, anterior tibial vein; 3, great saphenous vein; 4, small saphenous vein; 5, submalleolar perforator; 6, navicular perforator vein; 7, cuneal perforator vein, 8, perforator vein of the first intermetatarsal space; 9, dorsal perforator vein; 10, calcaneal perforator vein; 11, dorsal vein of the hallux; 12, medial plantar vein; 13, lateral plantar vein; 14, medial marginal vein; 15, lateral marginal network (dotted line).

Anatomy of the foot perforator veins

Foot perforator veins provide direct connections between the plantar veins and the roots for both saphenous systems. These foot perforator veins are split into two well-separated functional units (medial and lateral), connected to each plantar vein. The medial foot perforator veins are connected to the medial plantar veins and the roots for the great saphenous vein. Lateral and posterior or calcaneal foot perforator veins are connected to the larger lateral plantar veins and the roots for the small saphenous vein. The anterior foot perforator veins also connect the dorsal foot network to the origin of the fibular and anterior tibial veins at the ankle.

Medial foot perforator veins

The perforator veins of the first intermetatarsal space, generally with a large diameter (4 mm), is at the anterior aspect of the dorsal foot. It originates from the medial marginal vein, which is the main root for the great saphenous vein below the medial malleoli *(Figures 4 and 6)*. The three medial perforator veins of the foot include: (i) the inframalleolar perforator, which is the second root for great saphenous vein; (ii) the navicular (or scaphoid) perforator, which is close to the navicular bone; and (iii) the cuneal perforator, which is located next to the first cuneal bone. The dorsal medial perforator communicates anteriorly with the anterior tibial veins, and it often forms laterally to the third root for the great saphenous vein *(Figures 3 and 4)*.

Lateral foot perforator veins are cuboid or tendinous perforators

Lateral foot perforator veins are comprised of two veins crossing the lateral fibular tendons that are also called intertendinous and subtendinous perforator veins *(Figures 5 and 8)*. These two perforator veins frequently join into a common trunk, which connects to the lateral marginal network, giving rise to the main root for the small saphenous vein.

Calcaneal foot perforator vein is a posterior foot vein

The calcaneal foot perforator vein originates from the calcaneal plexus and usually feeds the Achilleal tributary vein, which runs upward and medially to the Achilles' tendon, and it commonly joins the small saphenous vein at the lower third of the calf *(Figures 6, 7, and 10)*. To the best of our knowledge, the Achillian tributary has not been previously described. It is important because it establishes a direct connection between the lateral plantar veins and the small saphenous vein.

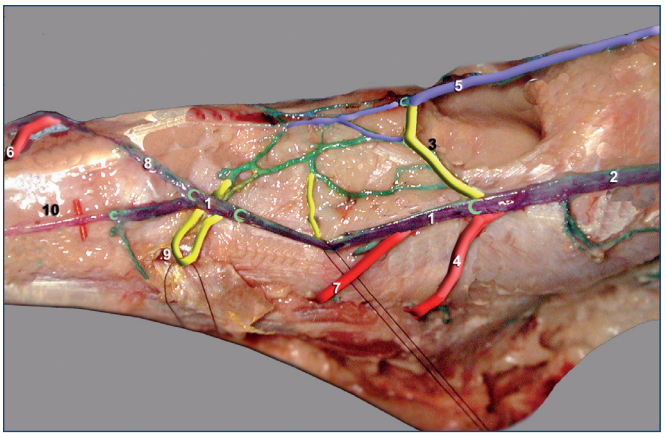

Figure 4. Anatomical dissection of the foot perforating veins (medial view).

Latex injection and colored segmentation (1, 3, and 4 are the three roots for the great saphenous vein).

Abbreviations: 1, medial marginal vein; 2, great saphenous vein; 3, dorsal perforator vein that is communicating with the anterior tibial vein; 4, submalleolar foot perforator vein; 5, anterior tibial vein; 6, perforator vein of the first intermetatarsal space; 7, navicular perforator vein; 8, dorsal arcade of the foot; 9, dorsal perforator vein; 10, dorsal vein of the Hallux.

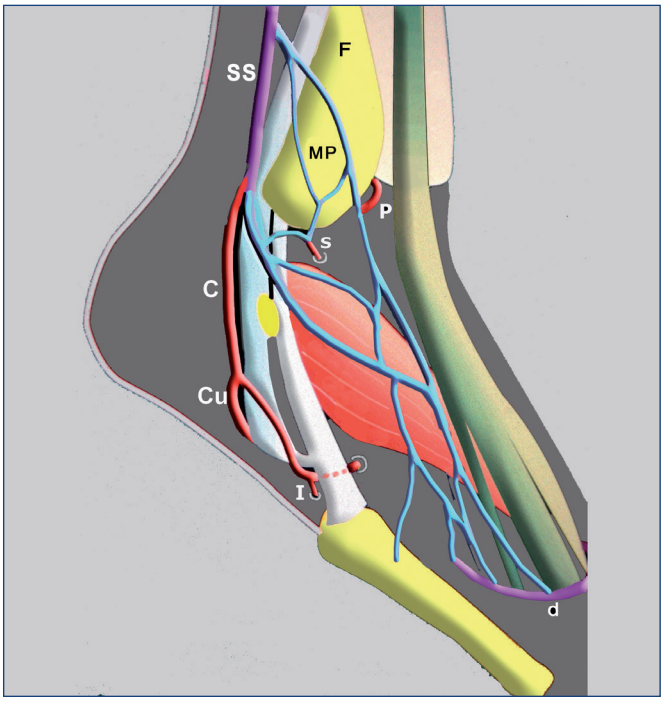

Figure 5. An illustration showing the roots for the small saphenous vein.

The lateral marginal vein, absent in the majority of cases, is often replaced by a lateral marginal plexus.

Abbreviations: C, common trunk of the lateral perforator vein; Cu, cuneal perforator vein; d, dorsal foot arcade; F, fibula; I, intertendinous perforator vein; MP, malleolar plexus; P, dorsal perforator vein for the anterior tibial veins; s, dorsal perforator vein for the fibular veins; SS, small saphenous vein.

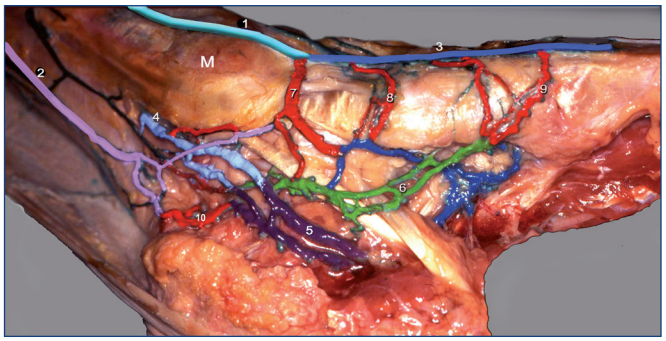

Figure 6. Anatomical dissection of the foot perforating veins (medial view).

Latex injection and colored segmentation.

Abbreviations: 1, great saphenous vein at the medial malleolus; 2, Achillean tributary of the small saphenous vein; 3, medial marginal vein; 4, posterior tibial veins; 5, lateral plantar veins; 6, medial plantar veins; 7, submalleolar perforator vein; 8, navicular perforator vein; 9, cuneal perforator vein; 10, calcaneal perforator.

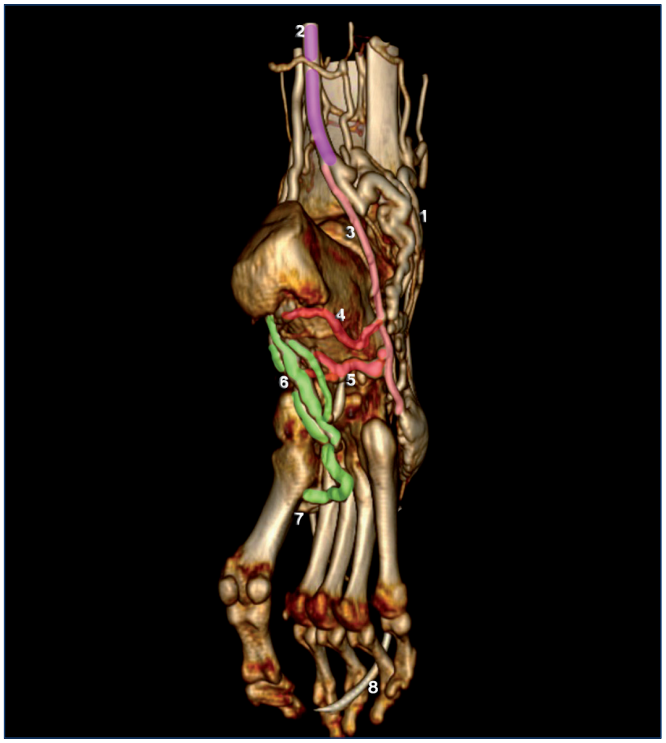

Figure 7. Three-dimensional reconstruction of the foot by CT venography.

Inferior and lateral view of a right foot.

Abbreviations: 1, varicose network of the lateral marginal plexus; 2, small saphenous vein; 3, common trunk of the lateral perforator veins; 4, calcaneal perforator vein; 5, cuneal perforator vein; 6, lateral plantar veins; 7, perforator vein of the first intermetatarsal space; 8, venous catheter for contrast injection.

Anterior perforator veins of the foot and ankle

There are commonly three anterior perforating veins. One is connected to the medial marginal vein, and it is the dorsolateral component of the three great saphenous vein roots. The two other perforating veins come from the venous network of the dorsal foot. They constitute a separate entity, which is not connected directly to the plantar veins, and gives rise to the fibular and anterior tibial veins *(Figures 8 and 11)*.

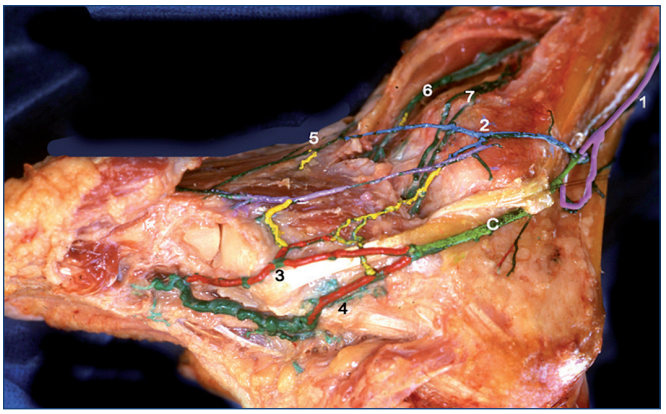

Figure 8. Anatomical dissection of foot perforating veins (lateral view).

Latex injection and colored segmentation.

Abbreviations: 1, small saphenous vein; 2, dorsal plexus; 3, intertendinous perforator vein; 4, cuneal perforator vein; 5, dorsal perforator veins; 6, anterior tibial veins; 7, fibular veins; c, common trunk of the lateral perforator veins.

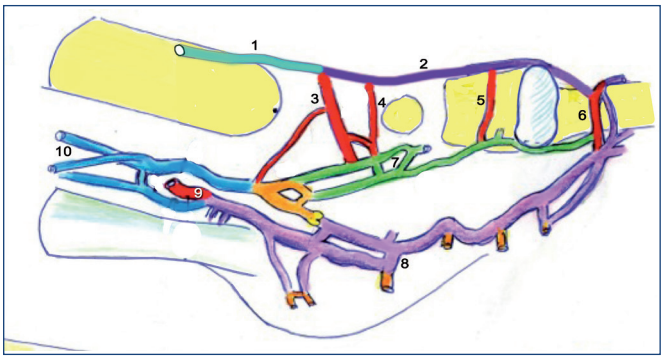

Figure 9. An illustration of foot perforator veins.

The medial functional unit is composed of the medial marginal vein (2), which continues as the great saphenous vein (1), and the submalleolar (3), scaphoid (4) and cuneal (5) perforating veins. The previously mentioned perforator veins (3, 4, and 5), together with the first intermetatarsal space perforator vein (6), are connected to the medial plantar veins (7). The lateral functional unit is composed of the lateral plantar veins (8) and the calcaneal perforator vein (9). In the rear the plantar veins join the calcaneal which gives rise to the two confluent (yellow), originating both plexiform posterior tibial veins (10).

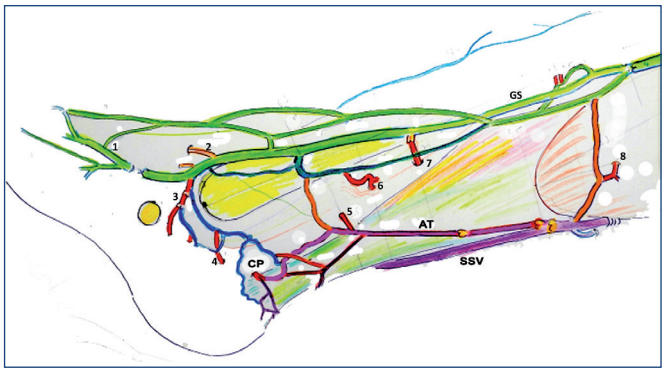

Figure 10. Anatomical dissection, medial view of the Achillean tributary of the small saphenous vein. Right lower leg.

Abbreviations: 1, medial marginal vein; 2, dorsal perforator vein to the anterior tibial veins; 3, submalleolar perforator vein; 4, foot perforator vein; 5, lower posterior tibial perforator vein; 6, middle posterior tibial perforator vein; 7, higher posterior tibial perforator vein; 8, medial gastrocnemius perforator vein; AT, Achillean tributary; CP, calcaneal perforator vein (connected to the lateral plantar veins); GS, great saphenous vein; SSV, small saphenous vein.

Perforator veins of the ankle and lower leg

At different levels, horizontal or oblique anastomoses (deep communicating veins) between the posterior tibial, anterior tibial, and fibular veins may be present *(Figure 11)*. These horizontal anastomoses between the three deep veinous axes are not randomly distributed, but located at several levels, which define the hemodynamic levels, explain the fixed location of the leg perforator veins,[8] and allow for venous blood flow exchange when needed.

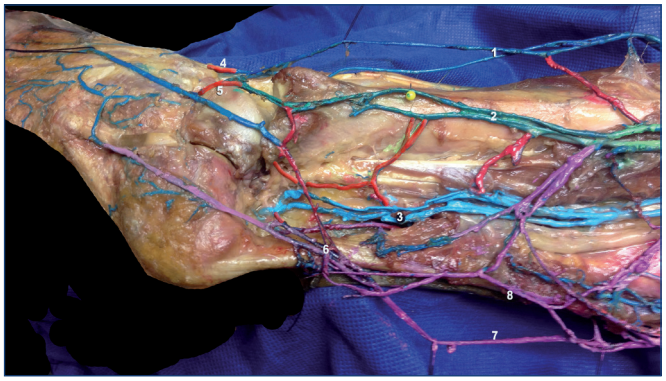

Figure 11. Anatomical dissection of right foot after removing the fibula (lateral view).

Latex injection. In this image, the three deep venous axes of the leg are simultaneously shown, with multiple transversal anastomoses (deep communicating veins).

Abbreviations: 1, anterior tibial veins; 2, fibular veins; 3, posterior tibial veins; 4, dorsal foot perforator vein to anterior tibial veins; 5, dorsal foot perforator vein to the fibular veins; 6, roots of the small saphenous vein; 7, Achillean tributary; 8, trunk of the small saphenous vein.

Hemodynamic characteristics of foot perforator veins

A unique feature for some foot perforator veins is that they are commonly provided with one-way valves to explain their unidirectional flow, from deep to superficial, which is unique in the venous system of the lower limbs. *Figure 12* shows the valves present along all of the medial perforator veins, which explains the ascending flow in both saphenous veins during systolic activation of the foot venous pump. In fact, during calf systole, the posterior tibial veins are closed, and the main outlet could only be the two saphenous systems, in particular into the medial marginal vein via the perforator of the first intermetatarsal space. However, it is important that, rather than dividing the foot veins into deep and superficial, the foot veins should be divided into two functional units–medial and lateral.

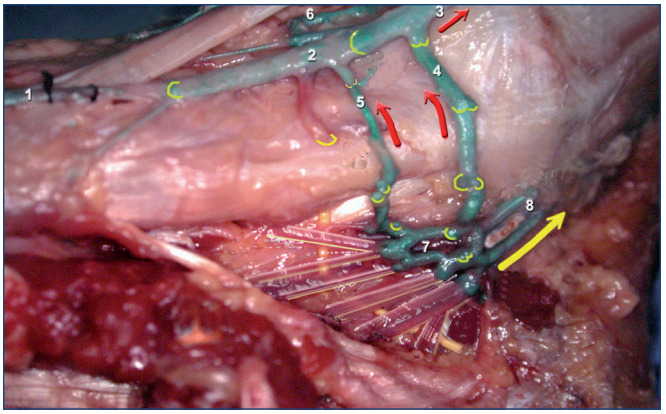

Figure 12. Anatomical dissection of the right foot.Medial perforator's valves (medial view).

Latex injection. This image shows confluence (7) plexus of the plantar veins (not injected) with the origin of posterior tibial veins (8). The blood is ejected upward in the leg during plantar systole (yellow arrow), but the deep venous blood is also injected toward the superficial system (red arrows) via the medial foot perforator veins inframalleolar perforator vein (4) and navicular perforator vein (5), where the valves are oriented from deep to superficial.

Abbreviations: 1, dorsal vein of hallux; 2, medial marginal vein; 3, great saphenous vein; 4, inframalleolar perforator vein; 5, navicular perforator vein; 6, anterior communicating vein (origin of the anterior tibial veins); 7, calcaneal confluent veins; 8, posterior tibial veins.

The medial functional unit is comprised of the medial plantar veins, the medial marginal vein, the dorsal perforating vein (or dorsal communicating vein), which gives rise to the anterior tibial vein and all of the medial foot perforator veins–inframalleolar, navicular (or scaphoid), and cuneal. The lateral functional unit is comprised of the lateral plantar veins and the calcaneal perforator vein,

which forms the posterior root for the small saphenous vein. Therefore, during the systolic phase of the foot, venous return is shunted when the posterior tibial veins are not open, the blood is pushed up into both saphenous systems, ie, medially into the medial marginal vein, the main root for the great saphenous vein, and laterally via the calcaneal perforator vein, which is commonly connected to the Achillean vein and joins the small saphenous vein in the lower third of the calf.

During contraction of the calf muscle pump, while walking, the passage of blood through the posterior tibial and fibular veins is not possible.[10] Consequently, during calf muscle pump systole, venous blood return from the foot must take alternative routes. This goal is achieved thanks to "physiological shunting" through foot perforator veins, from the deep plantar veins toward the superficial veins,[11] including both saphenous axes. Outward blood flow through the lower posterior tibial perforator vein (Cockett I) is common in subjects without venous insufficiency, probably

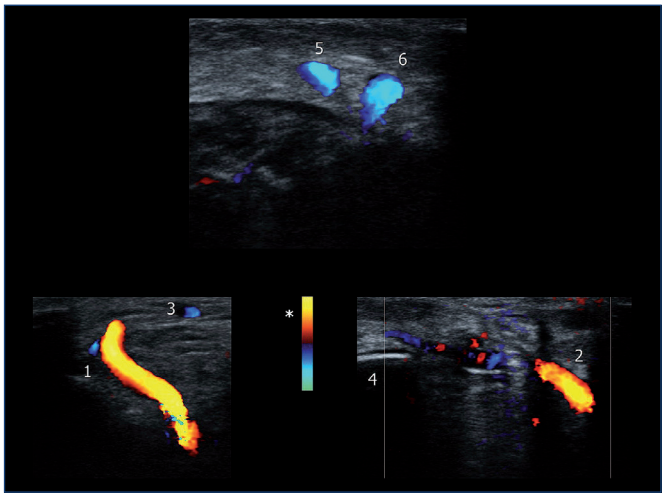

Figure 13. Ultrasound images of the right foot in a person without venous disease.

Inverted flow through the first intermetatarsal (1) and premalleolar (2) perforator veins during provocative maneuvers. Flow towards the probe is coded in red (*). Ultrasound demonstration of inverted flow within foot perforator veins is a common finding in individuals without evidence of chronic venous insufficiency. In the same subject, a transverse scan of the right lower leg shows flow augmentation through both the Achillean tributary (5) and the small saphenous vein (6) during foot's venous pump systole, which is induced by body weight displacement from the contralateral limb toward the limb being studied.

Abbreviations: 1, first intermetatarsal perforator vein; 2, premalleolar perforator vein; 3, superficial dorsal venous arch; 4, lateral malleolus; 5, Achillean tributary; 6, small saphenous vein.

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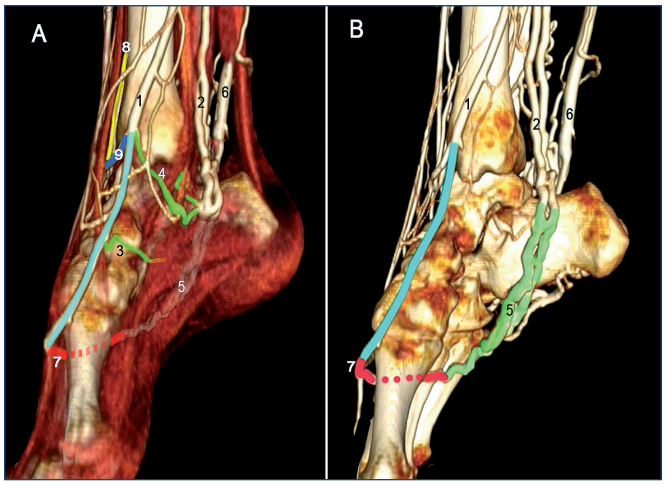


Figure 14. Three-dimensional modeling of medial and lateral foot perforator veins.

Direct CT venography with the muscles and tendons (Panel A) and without (only veins and bones) (Panel B).

Abbreviations: 1, great saphenous vein; 2, posterior tibial veins; 3, navicular perforator vein; 4, inframalleolar perforator vein; 5, lateral plantar veins; 6, small saphenous vein; 7, perforator vein of the first inter-metatarsal space; 8, anterior tibial vein; 9, dorsal perforator to the anterior tibial vein.

accomplishing the same functional purpose. Since foot perforator veins and lower leg perforator veins are located at the lower end of limb's venous system, ie, below the calf muscle pump, inverted flow during muscle activity should not be interpreted as either abnormal or physiological "reflux," but as a "physiological shunting." Real-time ultrasound assessment during provocative maneuvers is a dynamic, noninvasive, diagnostic tool that can show inverted flow through these perforator veins in people without venous disease *(Figure 13)*. Our anatomical data were confirmed with 3D modeling of CT venography data. *Figure 14* shows the plantar veins with their connections to the superficial system, particularly the roots for the great saphenous vein.

Clinical consequences

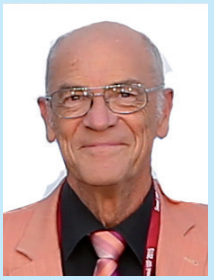
The role of the foot venous pump and foot perforator veins should not be underestimated. Despite the small volume of blood ejected with every step, foot perforator veins play an essential role in the lower limb's venous return,[9] which is the reason why any foot static disorder (flat or hollow foot) will impair the foot venous pump, and the clinical condition of a patient with chronic venous disease could worsen. As shown in our previous study, foot static disorder could be considered a major risk factor for chronic venous disease.[12,13] In daily practice, it is mandatory to check for foot static disorder in our patients and correct the problem

with an insole, which will improve the symptoms related to chronic venous insufficiency and foot static disorder. In fact, we should keep in mind that about 60% of the so-called venous symptoms do not have a venous origin.[14]

The clinical consequences of the foot venous anatomy are also interesting because varices of the foot could be related to a zone of weakness at the ankle.[15-16] When submitted to a reentry flow caused by a great saphenous reflux, the local venous hypertension is increased by the peaks of pressure created by the foot venous pump systole, and transmitted by the foot perforator veins into the superficial venous system.

Conclusion

Foot perforator veins are characterized by a distinctive feature in the lower limb: the blood can flow from the deep to the superficial veins due to the presence of valveless or "inverted-valve" perforator veins, which act as shortcuts between the foot venous pump and the superficial venous system. During calf muscle pump contraction, these perforator veins shunt the foot's venous return, which explains the augmentation in systolic flow that is observal in both saphenous axes.



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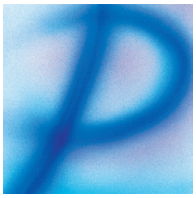

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Web-based material: Nicolaides AN. Investigation of chronic venous insufficiency: a consensus statement. American Heart Association, 2000. http://www.circulationaha.org. Accessed October 17, 2005.

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