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Review Article

A comprehensive study on venous endovascular management and stenting in deep veins occlusion and stenosis: A review study



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ARTICLE INFO	A B S T R A C T
<i>Keywords:</i> Venous stent Occlusion Stenosis	Background: Patients with deep venous disease can be classified into two distinct categories: those with disease resulting from known deep vein thrombosis (DVT), which may subsequently lead to post-thrombotic syndrome (PTS), and those with disease caused by compressive factors or non-thrombotic iliac vein lesions (NIVL). The major factor causing the symptoms in patients with PTS and NIVL is venous hypertension which happens due to venous stenosis or venous obstruction. Nowadays Venous stenting offers a noninvasive approach for treatment of NIVL and PTS demonstrating high patency rate. Methods: We comprehensively reviewed relevant published papers from 2008 to 2023 that surveyed various influencing factors including the site of occlusion and etiology of occlusions, proper diagnostic imaging, ideal characteristics of venous stents, different dedicated venous stents, pre-operative, concomitant, and post-operative interventions and factors that challenge stenting in both PTS and NIVL patients. The papers were identified by searching the keywords "venous stenting", "PTS", "NIVL", "occlusion", and "stenosis" in PubMed central library MEDLINE and Google Scholar. Results: Patency rates, post-stent complications, and relevant data according to the patient's quality of life were
	included and analyzed from 476 identified studies. There is no validated protocol and guideline for using stents in patients with PTS and NIVL.
	<i>Conclusion:</i> As there is no validated protocol and guideline for using stents in patients with PTS and NIVL, our study may provide comprehensive information to assist researchers interested in writing the protocol and give them insight.

Introduction

Patients with deep venous disease fall into two categories, disease caused by a known DVT which may subsequently lead to PTS and disease caused by compressive disease or non-thrombotic iliac vein lesion (NIVL). The severity of the symptoms depends on the etiology of the obstruction. Patients may be asymptomatic or may suffer from a variety of symptoms.

The Villalta score in conjunction with a venous disease-specific quality-of-life questionnaire, is widely considered as the "gold standard" for diagnosis, classification and measuring the quality of life of patients with post-thrombotic syndrome. Moreover, The Venous Clinical severity score and quality of life assessment tool are recognized as reliable and precise instruments for evaluating the quality of care and quality of life [1,2].

Angioplasty with a stent deployment has demonstrated acceptable post-operation results; so, they are the treatment of choice in patients with PTS and NIVL.

We reviewed different factors that improve or diminish post-stent complications and patency rates, to gain the best insight for the management of patients with PTS and NIVL.

Diagnostic imaging

Accurate diagnostic imaging is crucial for assessing occlusion, stenosis, and other factors that influence the effectiveness of venous stenting. Several imaging modalities can aid in the diagnosis and evaluation of venous conditions, including venous duplex ultrasound (DUS),

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contrast-enhanced ultrasound (CEUS), intravascular ultrasound imaging (IVUS), computed tomography venogram (CTV), and magnetic resonance venography (MRV).

- Venous duplex ultrasound (VDUS)

Venous duplex ultrasound (VDUS) is a widely used screening tool and first-line imaging modality for the diagnosis of PTS, chronic venous insufficiency (CVI), and NIVL. DUS effectively reveals venous damages, the extent of obstruction, and valve function. Studies have shown that DUS is more accurate in determining the severity of venous stenosis compared to venography [3–5]. Based on the systematic study of Saleem T et al. DUS determines the severity of venous stenosis as 30 % more accurate than venography [6].

DUS is the most accurate modality to evaluate iliocaval confluence, as determining the location of the confluence is important to prevent contralateral jailing of the stent [7].

However, DUS has limitations in terms of accurate visualization of deep veins and accurate diagnosis due to the limited penetration of ultrasound waves [8]. Therefore, using DUS alone is not recommended, and it should be complemented with other imaging modalities for greater accuracy [9]. Venous duplex imaging exhibits limitations in accurately identifying the caval bifurcation and provides suboptimal quality when evaluating pelvic veins, especially within Western populations characterized by a high prevalence of obesity.

Hong Liu et al. reported low sensitivity and specificity of DUS in detecting in-stent-restenosis (ISR) (63.1 %, 87.8 %), so some cases of ISR would be missed or misdiagnosed by DUS [10]. Moreover, there is no criterion for grading patients based on the degree of stenosis reported by VDUS, although venous blood velocity has been the criterion for grading the severity of in-stent-restenosis [11].

Duplex ultrasound examination of a vessel requires the presence of proper blood flow. However, various factors, such as respiratory modulation of blood flow in the deep leg veins, the veins' compressibility and the mobility of venous valves, must be considered. To assess the direction of flow, vein patency, and valve behavior, provocation maneuvers are necessary to induce blood movement within the veins. These maneuvers enable a comprehensive evaluation of the venous system.

The Valsalva maneuver is one of the provocative maneuvers which is performed by instructing the patient to take a deep breath, hold it, and then increase abdominal pressure by tensing the abdominal muscles, such as through pressing. This maneuver aims to assess the impact of increased pressure in the inferior vena cava on the blood flow within the leg veins.

Parana maneuver is another one which the examiner applies slight pressure to the sacrum, causing the patient to shift their weight forward. As a result, the patient instinctively contracts the triceps surae muscle to maintain balance. This activation of the muscle pump generates a robust flow of blood in the deep leg veins, known as orthograde flow. This maneuver effectively fulfills the need for creating a natural blood flow and can be consistently replicated.

Wunstorf maneuver is the maneuver when the examiner can elicit dorsal flexion of the forefoot by instructing the standing patient to raise their toes or by causing them to "claw" their toes. Conversely, plantar flexion of the forefoot can be induced by increasing pressure on the floor while the patient is standing.

The most commonly utilized maneuver in the standing position involves manual compression of the calf. This maneuver entails applying pressure to a specific area of the leg's soft tissue with the hand and subsequently releasing the grip. While the calf is typically the target area, the maneuver can also be performed on the foot or thigh. Initially, the compression of the tissue induces an orthograde flow in both the superficial and deep venous systems. Following the release of the grip (decompression), venous insufficiency can be detected through sonographically measurable reflux into the examined vein [12].

- Contrast-enhanced ultrasound (CEUS):

Contrast-enhanced ultrasonography offers higher signal-to-noise ratios and deeper penetration of waves into tissues compared to DUS. Hong Liu et al. [10] compared the accuracy of CEUS and DUS in the detection of in-stent restenosis. They reported higher sensitivity and specificity of CEUS than DUS (90.8 % and 97.3 % versus 63.1 % and 87.8 %). So CEUS is more suitable diagnostic imaging in the detection of ISR than DUS.

CEUS is cost-effective, minimally invasive, and carries a low risk of side effects. These qualities make it suitable for follow-up examinations of patients with ISR. However, CEUS may have limitations in evaluating stents implanted in deep veins or overweight patients due to potential imaging challenges caused by obesity [13].

- Intravascular ultrasound imaging (IVUS)

Intravascular ultrasound imaging provides intra-operative diagnostic capabilities, allowing for precise visualization of vessel wall abnormalities (trabeculations, synechia), malfunctioned valves, and extrinsic compressions on the veins [14]. IVUS is considered the gold standard imaging modality for diagnosing chronic venous obstructions and stenosis. It offers high accuracy in measuring the degree of stenosis and detecting a reduction in venous flow. Based on the IVUS, a reduction in the venous flow by >50 % is an indication of the deep stent deployment [4]. Compared to venographic imaging, IVUS is more sensitive in measuring stenosis degree, venous diameter, intraluminal features, the extent of venous lesions, and detection of the etiology [3,15]. IVUS is recommended for removing obstructions in the iliofemoral venous areas and confirming the degree of stenosis in patients undergoing endovascular procedures [4] (Table 1).

While IVUS provides accurate information, it is an invasive procedure and cannot be used as a screening tool or first-line imaging modality [8]. Ultrasonographic (US) imaging is commonly used for diagnosing deep vein thrombosis (DVT) and May-Thurner syndrome, guiding surgeons/interventional radiologists for venous access, evaluating the results of iliac venous stenting in follow-ups, while IVUS is employed for grading and monitoring the severity of venous stenosis caused by extrinsic compressions [16].

- Computed tomography venogram (CTV)

Computed tomography venogram is an imaging modality capable of predicting stent length with a high degree of accuracy by measuring the inflow channel luminal areas similarly to IVUS. CTV has been shown to detect venous obstructions in the common iliac vein, external iliac vein, and common femoral veins with an accuracy of 91 %, 86 %, and 82 % respectively [8]. The accurate correlation between CTV and IVUS, confirms the ability of the 3D CTV to predict the stent diameter.

While IVUS remains the gold standard, using 3D CTV in symptomatic patients can be valuable for diagnosis and treatment planning [8]. Multidetector computed tomography venography (MDCTV) is a noninvasive imaging modality used to evaluate the position of implanted stents and detect changes in stented segments, such as stent compressions [10].

- Magnetic resonance venography (MRV)

Table 1

Raju's recommendations for sufficient venous diameter for stenting, and venous area for IVUS [36].

Venous segments	Diameter of the segment	Area of the segment (mm^2)					
Common iliac vein	16–18 mm	200–254					
External iliac vein	14 mm	150					
Common femoral vein	12 mm	110					

Magnetic resonance venography is particularly useful when other imaging modalities, such as DUS, are unable to provide sufficient information due to factors like the presence of masses, gas in the abdomen, or the depth of the involved segment [17]. MRV helps determine the extent of venous lesions and can reveal occlusions, stenosis, thrombus, extravascular neoplasms, and retroperitoneal fibrosis that cause venous compression and obstruction [3].

Fig. 1 demonstrates an example algorithm for managing patients with PTS and NIVL.

Conservative management

Compression therapy is the fundamental pillar and the initial management strategy for patients with chronic venous insufficiency and venous obstructions. However, if compression therapy fails to improve symptoms, deep venous intervention becomes the next therapeutic step [4].

An overview of stents: types, applications, and considerations

- Venous stents vs. arterial stents: key differences and considerations

The venous and arterial systems differ significantly in various aspects, which must be taken into account when selecting stents for occlusion and stenosis. The venous system carries a larger volume of blood with lower pressure and velocity compared to the arterial system. Consequently, venous walls have higher resistance to dilation and are more flexible to external compressions [18].

Moreover, the factors that damage veins differ from those that damage arteries. Venous stressors include constant pulsations of adjacent arteries, causing repetitive trauma, as well as anatomical positions such as hip flexion, which can lead to fibrosis and webs in the vessels. The fibrotic tissue in the veins can result in stent compression [3].

It is worth noting that certain parts of the venous system are more prone to traumas, such as the veins located posterior to the inguinal ligament, the iliocaval junction, and the iliac bifurcation [19].

The Iliac vein bifurcation and the common femoral vein are the anatomical areas that endure the maximum flexion during hip flexion and are located proximal and inferior to the inguinal ligament [20].

When comparing venous and arterial stents, it is essential to consider the specific requirements of each system. Arterial stents aim to restore proper blood perfusion and prevent limb ischemia, whereas venous stents primarily target the elimination of venous hypertension. The stenosis threshold that causes clinical symptoms in the venous system is lower than in the arterial system, making venous stenting more challenging and necessitating accurate pre-operative examination [3].

Venous stents must have larger sizes, increased flexibility, and higher radial force compared to arterial stents [19]. Using arterial stents in venous insufficiencies is not recommended because the high rigidity and the low radial force of the stents decrease the post-stent patency rate and increase the probability of in-stent compressions [21]. Additionally, venous stents require greater stability and long-term resistance to corrosion and fatigue, as patients with chronic venous diseases are typically younger than those with chronic arterial diseases [19]

Performing percutaneous transluminal angioplasty (PTA) alone is the treatment of choice in the arterial system occlusions or stenosis, in contrast, PTA alone in the venous system leads to restenosis of the veins due to the high elastic recoil feature of the venous system, so PTA should constantly be performed with stent deployment to prevent recollapse of the involved vein [22].

Also, performing balloon angioplasty alone does not have a permanent effect on the diseased veins, due to the high rates of recollapse and restenosis of veins and the specific venous features mentioned above [23].

- Ideal characteristics of venous stents.

When it comes to selecting the ideal venous stent, several characteristics must be considered. Firstly, the stent should possess flexibility and rigidity proportional to the anatomy of the involved segment. This is



Fig. 1. An example algorithm of managing patients with PTS and NIVL.

particularly important in stress points such as the origin of the internal iliac vein or the posterior area of the inguinal ligament [24]. The flexibility of the stent is determined by its design and the structure of its struts [25].

Additionally, the stent should have a high radial force to maintain its diameter, especially in veins that are exposed to compressions [18]. The radial force is defined as the external force of the stent or the strength of the stent when compressed to 10 % of the original diameter [26]. Radial force and, flexibility must be balanced in a proper venous stent [19]. Radial force can be improved by oversizing the stent (2–4 mm). Oversizing of stents also improves anchoring of the stent to the vessel wall and prevents stent migration [27]. The stent should also have proper radio opacity for accurate follow-up evaluations [19].

According to the mentioned points and a study by Natalia Beshchasna et al. [28] characteristic of a perfect venous stent is described as follows: 1-high flexibility proportional to the anatomy of the involved segment. 2-high strength of hoop and little recoil. 3-Proper radioopacity for more accurate follow-up evaluations. 4-high resistance to thrombus 5-non toxicity 6-good expandability ratio and 7-drug delivery capacity.

- Stent structures and struts.

The structure of a venous stent is composed of interconnected struts, which play a crucial role in determining the stent's flexibility and strength [29]. The thickness of these struts varies among different venous stents and is highly related to endothelialization, blood flow patterns, local inflammation, stent thrombosis, and in-stent restenosis [26]. Thinner struts have been associated with fewer post-stenting obstructions, higher stability, and better deliverability. However, stents with thinner struts also have less radio opacity, which can pose challenges in post-stenting evaluations [28,30].

To enhance the function and performance of stents, coating the surface with materials such as oxides, nitrides, silicide, carbide, noble metals, hydroxyapatite-based materials, diamond, or diamond-like carbon can be beneficial [31–33].

- Open-cell stents vs. closed-cell stents.

Venous stents can be classified as either open-cell or closed-cell based on the interconnection of their rings and struts. Figs. 2 and 3 demonstrate the interconnected struts in closed-cell and open-cell stents.

Closed-cell stents have struts that are peak-to-peak connected, with little space between cells. These stents are known for their high radial strength, sufficient scaffolding, uniform surface(which is important in the uniform releasing of drugs during stent bending), and effectiveness in covering damaged segments [23] However, closed-cell stents are less flexible and more rigid compared to open-cell stents, making them more suitable for veins with straight morphologies [34].

According to the study by Chae Hoon Kang et al. [23], rates of stent foreshortening and migration in central veins are higher in patients with closed-cell stents.

On the other hand, open-cell stents have higher longitudinal flexibility, making them more suitable for implantation in angulated veins [34]. They are also easier to deploy and have lower foreshortening rates. Open-cell stents may not be suitable for drug delivery due to variations in drug release at bends. Despite these differences, open-cell stents are often preferred by the specialist due to their lower foreshortening rates,

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Fig. 3. Schematic demonstrating of the closed-cell design of the Boston scientific VENITI VICI VENOUS STENT.

higher patency rates, and ease of implantation [13].

- The optimal size of stents.

Selecting the appropriate size of a venous stent is crucial in eliminating venous obstruction, reducing venous hypertension, and avoiding complications such as contralateral jailing and stent migration [35]. While there is no validated protocol for the ideal size of venous stents, it is generally recommended that the stents should match the caliber of the diseased segment. The caliber can be determined using imaging techniques such as intravascular ultrasound (IVUS) or computed tomography venography (CTV) [36]. Table 1 demonstrates Raju's recommendations for sufficient venous diameter for stenting.

Various studies have recommended different stents based on the location of the obstruction. Mohamed A. et al. [4] reported that Sinus-XL Flex stent (OptiMed, Ettlingen, Germany) is suitable for obstructed segments in the inferior vena cava.

Jeffry et al. [37] studied Wallstents (Boston Scientific, 15 Marlborough, MA) and reported that 12–16 mm and 18–24 mm wallstents are suitable for iliofemoral and iliocaval venous obstructions, respectively. Susan M. et al. [19] recommended that stents with a diameter of 10-24 mm are suitable for cavo-ilio-femoral obstructions. Raju et al. [36] recommended to use of stents that are 2 mm larger than the recommended caliber to reduce post-operative complications. Arjun Jayaram et al. [8], reported that the proper size of stents implanted in common femoral veins and common iliac veins were 14 mm and 16 mm.

- Dedicated stents.

Dedicated stents are a new generation of stents that offer several advantages over non-dedicated stents [38]. Three main types of dedicated stents include bare metallic stents (BMS), drug-eluting stents (DES), and biodegradable stents (BDS). Despite the recent progression in stent manufacturing, post-stent thrombosis and dysfunction of the endothelial layer are still serious challenging complications [39].

Biodegradable stents are particularly interesting as they gradually deteriorate after implantation, eliminating the need for surgical removal [40,41]. These stents are highly bio-safe and avoid complications associated with permanently implanted foreign bodies [42,43]. Biodegradable stents can be coated with both absorbable and non-reabsorbable coating. Resorb-able coatings are constructed of active agents that reabsorb during stent deterioration. In drug-loaded stents with absorbable coating, the drug is released at a proper rate during stent degradation, while in stents with non-absorbable coatings, the drug is absorbed through diffusion [26]. It is recommended to use BDS in children and adolescents because their vessels are immature and are prone to change in size and shape over time. Also, elderly and diabetic patients benefit from the BDS because there is no need for repeated surgeries. This technology avoids local inflammation and reactions due to the lack of a permanent foreign body, but venous stenosis may occur again because of complete deterioration of the implanted BDS [26].

The most common materials used in the scaffolds of biodegradable stents are magnesium, polyanhydride polymers, and polycarbonates (amino acids such as tyrosine) [19,44].

Magnesium-based stents have better performance than polymerbased stents due to the high biodegradability of Mg and its faster reabsorption to the body [26]. Unique properties of the Mg-based stents decrease local vasoreaction inflammation, post-stent thrombosis, and endothelial dysfunction [45]. Bosche et al. [46] found that adding a low dose of lithium to the Mg-based stents stabilizes the endothelium and increases cholinergic endothelium-mediated vasorelaxation.

Drug-eluting stents on the other hand are constructed of biodegradable/metal scaffolds with drug-containing [28]. These stents have been effective in reducing restenosis, thrombosis, local inflammation, and mal-apposition of the stent [47]. They can also be used as drug reservoirs [48]. The drugs in DES can be replaced by other nanoparticles such as sirolimus. It has been reported that implantation of sirolimusloaded PLLA stents in the vessels, reduces the rate of muscle cells and endothelial cell proliferation [44], as Puranik A. et al. [49] reported a reduced rate of restenosis and thrombosis in patients with DES covered with paclitaxel and sirolimus. Generally, bioresorbable stents, geneeluting stents, nanoparticle-eluting stents, and polymer-coated and polymer-free stents are the most common DESs nowadays [44].

- Balloon-expandable and self-expandable stents.

Balloon expandable stents (BES) are cobalt-chromium stents with closed-cell designs that are commonly used in children due to their sequential dilation capability. However, they are not suitable for the iliocaval area due to their lack of appropriate longitudinal flexibility [23].

Self-expandable stents (SES) are stents that expand automatically after implantation. They can be constructed from metal (self-expandable metallic stents or SEMS) or plastic (self-expandable plastic stents or SEPS). SESs have been associated with increased in-stent restenosis, tissue hyperplasia, and stent migration [44]. Nitinol alloy, a shapememory nickel-titanium alloy, is commonly used in self-expandable metallic stents due to its high flexibility and ability to return to its original shape. These stents modify their shape in proportion to the external force and after the removal of the external force, return to their original shape [23]. However, the structure of nitinol stents is temperature-dependent. According to the ratio of titanium and nickel, at high temperatures, it expands to its predetermined size and becomes more rigid [23].

- The wallstent

Wallstent (Boston Scientific, Marlborough, MA) is a rustproof selfexpanding stent with high radial force and flexibility, commonly used in iliocaval diseased veins [50]. Fig. 4 demonstrates the Elgiloy braided structure of the wall stent. The Elgiloy alloy used in the scaffold of the Wallstent provides it with high flexibility [51]. However, the radial force of the Wallstent is weakest at its ends, which may cause stent migration and insufficient blood flow in certain segments [19]. The Wallstent also tends to shorten during implantation due to its braided structure [50]. To overcome these limitations, the Z stent (Cook Medical, Bloomington, IN) can be implanted on top of the Wallstent, providing sufficient overlap between the stents and preventing narrowing at the ends of the Wallstent. According to the study by Sang et al. [52] Wallstent is particularly suitable for veins crossing the inguinal ligament due to its flexibility and low probability of fracture.

- The Zilver vena stent

Zilver vena stent (Cook Ireland Ltd., Limerick, Ireland) is a selfexpanding stent that according to a recent study by Huimin Xu et al.



Fig. 4. Schematic demonstrating of the structure of The Boston Scientific Wallstent.

has been proven to have excellent 1-year and secondary patency rates in iliofemoral venous obstructions (93.8 %, and 97.9 %, respectively). The study also found that complications such as bleeding and thromboembolic were <1 %, and none of the patients experienced contralateral jailing or foreshortening of the stent. These positive outcomes make Zilver Vena s tents a promising option for treating iliofemoral venous obstructions [53].

- VENOVO stent

The VENOVO (Bard/Becton, Dickinson and Company, Tempe, Arizona, USA) stent is a dedicated, nitinol self-expanding, open-cell venous stent that has some distinct features such as 3 mm flared stent ends designed for anchoring and the largest venous stent diameter range (10–20 mm).

Using the stent in iliofemoral venous obstruction was studied by Michael D. Dake et al.

Freedom from major adverse events through 30 days was 93.5 %, primary patency at 12 months was 88.6 %. Mean quality-of-life measures were statistically improved compared to baseline values at 12 months primary patency at 36 months was 84 % confirming that the stent is suitable for iliofemoral venous obstructions [54].

The factors affecting the success and complications of the procedure

- Stenting according to the etiology of the occlusion.

PTS: Although the main cause of PTS is still unknown, it seems that chronic fibrosis of the venous wall, venous valve insufficiency, and the location of thrombosis are substantial factors in the pathogenesis of PTS. For example, Iliofemoral venous lesions are more prone to develop PTS than distal venous lesions [55,56]. Given that PTS is an incurable disease, the primary objective of its treatment is to alleviate the associated signs and symptoms. Compression therapy serves as the initial phase of treatment that enhances the function of venous valves and promotes efficient venous drainage [5]. If compression therapy fails to yield satisfactory results or if the patient suffers from severe symptoms (According to the CEAP classification, PTS patients with 3 scores and more or patients with 2 scores with significant pain and complications) the subsequent therapeutic action may involve endovascular procedures and stent placement [37].

May Thurner syndrome (MTS): May Thurner syndrome (MTS) or iliac vein compression syndrome occurs when the left iliac vein becomes occluded due to the right iliac artery compression. This phenomenon leads to insufficient drainage of blood flow.

Anti-coagulation therapy is the gold standard treatment in MTS patients with DVT, but anti-coagulation therapy alone does not resolve the venous compression. So MTS patients must undergo both anticoagulation and endovascular therapy [57].

According to the study by Paul J. Gagne et al., the appropriate endovascular intervention is to use a venous stent with a size proportional to the diameter of the external iliac vein, which may be undersized for the most dilated part of CIV. Nevertheless; the undersized stent yet can open the obstruction or stenosis and avoid contralateral jailing of the stent.

- Passion effect in the veins.

The passion effect refers to the tendency of veins to compress in a perpendicular direction to the applied force. This effect is higher in veins compared to arteries and can lead to adjacent vein narrowing when radial force is applied during angioplasty or stenting. Understanding the passion effect is crucial in optimizing the design and performance of venous stents [58]. Fig. 5 demonstrates the passion effect on the adjacent veins.



Fig. 5. Demonstrates the schematic effect of passion effect which resultant in retraction of the adjacent vein.

- Factors affecting venous stenting.

Various factors can influence the outcomes of venous stenting procedures. The extension of a stent past the inguinal ligament and a history of DVT before surgical stenting can affect the patency rates of the stents. Gender and age distribution, on the other hand, do not have a significant impact on the results of stenting [16].

A study by Fanilda Souto Barros et al. [16] demonstrated that the 6month patency rate of patients with prior DVT was lower than patients with no history of previous DVT.

Venous lesions that span the entire common and external iliac system may require multi-stent implantation and stent overlapping. Stent overlap can result in rigidity and decreased conformity within the venous system [19].

The degree of iliofemoral venous stenosis does not necessarily correlate with post-stenting clinical outcomes. Even a 20 % obstruction can cause impairment of quality of life, venous hypertension, and severe symptoms. Therefore, stenting decisions should be based on the patient's symptoms and impairment in quality of life rather than the degree of stenosis. In contrast, there is no rule for stenting stenosis in an asymptomatic or even symptomatic patient with no sign of impairment in the QOF. So doctors should move away from "stenting based on the degree of stenosis" to "stenting based on the patient's symptoms and impairment of QOL" [59].

Stenting past the inguinal ligament is a major factor that increases the probability of in-stent stenosis, obstruction, and stent fracture [21,56].

Many studies have reported difficulties in managing stent deployment past the inguinal ligament. Also, according to some studies, Infrainguinal stents compared with supra-inguinal stents, have lower patency rates [24,60].

Black et al. [60] reported that there was no significant difference in outcomes and clinical data in patients who received stents inferior to the inguinal ligament and patients who received stents superior to the inguinal ligament. Moreover, a study by Cheng et al. [61] reported that the point of maximum flexion of the iliac venous system during hip flexion is inferior to the inguinal ligament, and the common femoral vein is several centimeters inferior to the inguinal ligament. So extending stents below this level does not significantly affect patency rates [18].

- Factors influencing stent selection in the iliocaval venous system

When considering venous stenting, it is important to select the appropriate segment for stent implantation. Stent deployment in the iliocaval venous system has shown higher patency rates compared to stent deployment in mobile veins like subclavian veins. This is primarily due to the immobile nature of the veins and the absence of adjacent bones that may compress the stent [18].

Choosing flexible stents with proper extension into the IVC is crucial to prevent contralateral jailing of the stent and preserve blood flow. Extension of implanted stents into the IVC typically ranges from 0.5 to 2 cm, although comprehensive studies on the outcomes of different extensions are lacking [56] Various types of stents are used in the iliocaval venous system, with self-expandable stents being the most popular. A study conducted by Anthony N Hage at al [62] found that the most commonly used self-expanding stents were Wallstent (Boston scientific) and Gianturco (Cook Medical), accounting for 81.8 % (n = 81) and 4 % (n = 4) of cases, respectively. It is worth noting that Wallstent was the most frequently used stent, as reported in numerous cases [62,63]. Also, T. Y. Tang et al. [64] proposed the use of intravascular ultrasound (IVUS) technology to precisely locate the ilio-caval bifurcation and a dedicated bifurcation venous hybrid nitinol stent (sinus-Obliquus, Optimed, Ettlingen, Germany) for proximal iliac lesions near the iliocaval confluence. This stent features a closed-cell section with high radial force at the compression site, an oblique design at the proximal end to prevent jailing of the contralateral iliac vein, and an open-cell distal segment for flexibility.

- Risks and challenges in stenting the iliocaval confluence

According to a study by Myung Sub Kim et al. Stenting distal to the iliocaval confluence has been identified as a risk factor for stent stenosis, especially when the stent does not adequately cover the iliocaval junction. In such cases, fibrotic lesions and arterial pulsations can compress the proximal end of the stent, leading to distal migration and stenosis. Proper insertion of the stent in the iliocaval confluence is challenging, as failure to cover the area adequately can result in distal migration and stent stenosis. Conversely, extending the stenting above the iliocaval junction to the contralateral wall of the IVC can cause contralateral stent jailing and contralateral deep vein thrombosis [65,66].

The paper by Mohammad Esmaeil Barbati et al. [67] discusses the use of a technique called intentional skip placement for stent placement in the iliofemoral bifurcation. The study focuses on patients with chronic bilateral iliocaval venous occlusion. The findings suggest that the intentional skip stent technique can be performed with low risk and high technical success, resulting in favorable midterm to long-term patency rates. The study also suggests that leaving an uncovered area at the iliocaval confluence may not negatively impact the patency rate. The technique involves deploying a stent in the inferior vena cava just above the iliocaval confluence, followed by simultaneous deployment of two self-expandable nitinol stents in both common iliac veins, without extending into the caval stent. Post-dilation is performed using highpressure balloons with matching stent diameters. Completion venography, intravascular ultrasound, and multiplanar venography are used to assess the flow, lumen, and stent geometry after the procedure.

Concomitant interventions

In some complex cases, venous occlusion may occur in both the femoral and deep femoral veins or massive thrombosis may occlude the external iliac and femoral veins. In these situations, stenting alone may not be sufficient, and a hybrid procedure of endophlebectomy (removal of the inner lining of the vein) and stenting is required to open and clean up the involved segments. Surgeon/interventional radiologist decide whether a patient is indicated for the endophlebectomy procedure based on various factors such as magnetic resonance venography (MRV), intravascular ultrasound (IVUS), collateral veins, luminal stenosis, and patient risks [62].

A study by Mert Dumantepe et al. [57] demonstrated the effectiveness of the hybrid procedure of common femoral vein (CFV)

Table 2

Anti-coagulation therapy of various studies.

Study	Type of study	Number studied	Participants	Anticoagulation therapy
Arshpreet Singh Badesha et al.	Systematic review	16 studies	1688 patients (70.5 % PTS 29.5 % NILV)	LMWH were prescribed post-operatively followed by Vitamin K for 6 months in NIVL patients and 6–12 months in PTS. LMWH for 1–3 weeks followed by VKA for 3 months or LMWH for 3 months was recommended in patients with active malignancy
Rolf P. et al. [68]	Prospective single-center cohort	1	87 patients (100 % PTS)	Initial use of oral anticoagulation therapy with rivaroxaban (15 mg twice daily for three weeks followed by 20 mg per day) or with vitamin K antagonists (target INR 2–3) was recommended the day after the procedure with a minimum duration of three months.
Thomas Zeller et al. [75]	Prospective multicenter cohort	1	108 patients with 119 ISR lesions	Clopidogrel was administered at least 24 h before the procedure or as a loading dose during the procedure. Following treatment, clopidogrel therapy was continued for 60 days and aspirin therapy was continued indefinitely.
Atsushi Tosaka et al. [76]	A multicenter, retrospective observational study		116 patients with ISR	Dual-antiplatelet therapy (aspirin 100 mg/day plus clopidogrel 75 mg/day or ticlopidine 200 mg/day) from 2 days before the procedure was prescribed. 3000 to 5000 of Unfractionated heparin was injected IU before the intervention and during the intervention to maintain the active clotting time (>200 s)
Bei Wu, et al. [77]	Retrospective study		57 patients with cancer- associated venous obstruction	Administration of 4100 U of LMWH for 5 days after surgery and then using anticoagulation agents (rivaroxaban or warfarin tablets) as a replacement was recommended.
Peng Qiu [56]	Systematic review	7 studies	489 patients (100 % PTS)	Recommended the regimen of warfarin for two or six months with or without lifelong aspirin
Nicolas Langwieser et al. [78]	Retrospective		9 patients (100 % PTS)	Recommended that a combination of Rivaroxaban and Clopidogrel post- operatively is safe and effective.
Arjun Jayaram [8,59]	Prospective cohort study	2	22 patients plus 480 patients with CIVO	Administration of prophylactic enoxaparin 30–40 mg and bivalirudin 75 mg preoperatively, and therapeutic enoxaparin (1 mg/kg/dose subcutaneously every 12 h until discharge) was recommended. Warfarin, cilostazol (50 mg twice daily), and aspirin (81 mg once daily) were prescribed for 6 months after stenting and lifelong for Aspirin.
Joseph L et al. [79]	Retrospective study		137 patients	Administration of enoxaparin 1 mg/kg twice daily followed by warfarin as a replacement for at least 1 year was prescribed. Clopidogrel 300 mg loading dose, then 75 mg daily for 2 months, and aspirin 81 mg daily lifelong was prescribed when patients were discharged from the hoepital

endophlebectomy and stenting in 157 patients with PTS. After three months, the symptoms and quality of life (QOL) of the patients improved, with primary and secondary patency rates of 81 % and 89.5 % after 12 months. However, the study also highlighted the serious complications associated with this hybrid procedure, such as a high rate of groin infection (up to 30 % [4]) and hematoma. Therefore, it is crucial to reserve this procedure for patients with poor QOL and venous limb ulcers.

Thrombolysis, a procedure that dissolves blood clots, is indicated for patients with life-threatening deep vein thrombosis (DVT). However, it is not recommended for use in patients with chronic DVTs, as thrombolysis cannot remove synechiae (adhesions) and septae that replace the thrombus in these cases [4]. An alternative approach is ultrasound-assisted catheter-directed thrombolysis (USAT), which combines catheter-directed thrombolysis with low-power, high-frequency ultrasound waves to improve thrombus permeability for thrombolytic drugs. Currently, there is no validated recommendation for using USAT to treat acute iliofemoral DVTs [68].

The creation of an arteriovenous fistula, in conjunction with endophlebectomy and stenting, is an uncommon procedure used to maintain blood flow rate through the stented vein and prevent potential stenosis caused by low inflow blood pressure [4,69].

M. A. F. de Wolf et al. studied the effect of endophlebectomy and venous stenting, followed by arteriovenous fistula creation in patients suffering from PTS. They reported that the primary patency rate of this procedure is lower compared to iliofemoral stenting alone (primary patency rate of 51 % versus primary patency rate of 70–80 %), but it still offers positive results in terms of assisted primary and secondary patency rates(70 % and 83 %, respectively) [69].

Post-operative interventions

After venous stenting, post-operative interventions are necessary to ensure proper venous flow and prevent complications. Elastic compression stockings and bandages are the recommended treatments for venous post-operative ulcers, and they should be worn regularly for a duration of 3 months to 2 years [56]. Post-stent angioplasty and venography should be performed after complete stent implantation to confirm adequate venous flow [37].

Ultra sonographic examination is the key imaging in the postoperative follow-ups, which is recommended to be performed 1 day, 1 and 6 months, and 1 year after the endovascular intervention and yearly thereafter [16]. Intravascular ultrasound (IVUS) should be utilized in patients experiencing new or worsening signs and symptoms [3,16].

Post-stent balloon angioplasty is performed in patients suffering from in-stent restenosis or compression of the stent. Isolation balloon angioplasty means using a balloon of the same size as the diameter of the inserted stent [3].

Hyperdilation balloon angioplasty means using a larger balloon than the inserted stent. Hyperdilation is limited because many stents, such as wall stents, recoil immediately after angioplasty. Nevertheless, hyperdilation balloon angioplasty is possible in patients who underwent wall stent implantation for >8 weeks.

Anticoagulation therapy

Post-stent contraindications, such as in-stent stenosis and obstructions, are often associated with recurrent thrombotic events. Proper post-operative anticoagulation therapy can prevent venous thrombus formation and improve post-stent outcomes [15]. The recommended duration of anticoagulation treatment varies among different vascular units, and the choice of anticoagulant may also vary [70]. Practice guidance on iliocaval stenting from CIRSE highly recommends the prescription of at least 3 months of warfarin in patients with extensive and complex occlusions, underlying thrombophilia, suprarenal occlusions, and previous long-term anticoagulation regimen [17,38]. However, Xing Zhang et al. reported that consuming rivaroxaban is more effective in reducing GI bleeding, intracranial hemorrhage, recurrence of DVTs, and improving ulcer healing [71].

Table 2 summarizes the anticoagulation therapy recommendations from various studies.

Post-operative complications

Although venous stenting is an effective treatment for occlusion and stenosis, there are potential complications that may arise. The most common post-stent complications include in-stent occlusion, stenosis, bleeding, and venous thromboembolism (VTE). The prevalence of instent occlusion is often related to the severity of the disease and the number of recanalization procedures performed [70].

In-stent restenosis, characterized by the proliferation of smooth muscle cells and narrowing of the lumen, is another complication that can occur [72]. This cellular migration of smooth muscles is called neointimal hyperplasia. The etiology of cellular migration is unknown, and more therapeutic approaches are needed to solve the issue [73].

Also, previous DVT and long thrombotic lesions, especially those that extend into the common femoral vein, are the major risk factors of instent restenosis that restrict blood flow [15].

Nevertheless, inaccurate and insufficient pre-operative assessments of the occluded vein, such as using undersized stents increase the risk of stent migration even to the heart valves; whereas using oversized stents increases contralateral jailing of stents [21].

Arjun Jayaraj et al. reported that 74 % of patients with iliofemoral stents, showed in-stent restenosis. However, only 51 % of the patients were symptomatic (ISR > 50 %) in 5 year-follow ups. Most of the restenosis occurred in the CIV or EIV venous segments [74].

If follow-up imaging reveals in-stent restenosis >50 %, percutaneous transluminal angioplasty is performed to reduce the symptoms and maintain the patency [10].

Additional complications associated with stent placement encompass stent fatigue/fractures, and neuropathic pain attributed to stent expansion within vessel wall, presenting as a gradual onset of C-fiber type pain.

Conclusion

Proven benefits of using stents to successfully treat occlusions include more predictable outcomes and less likelihood of recurrence of the lesion, less risk of complications in the future, and a more predictable course of the stent. However, these benefits must be weighed against potential complications, including stent-related complications such as migration and stent stenosis as well as potential safety issues such as increased risk of infection or bleeding. Nevertheless, venous stenting is an acceptable and effective therapeutic intervention for patients with post-thrombotic syndrome and nonthrombotic iliac vein lesions.

Accepted patency rates in stented patients can be expected by: 1-accurate pre-operation examination, 2-choosing a sufficient stent with accurate size and length, 3-determining the optimal anti-coagulation therapy, and 4-proper post-operative follow-ups.

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Review articles do not require any original research and are not subject to ethical approval.

Clinical trial registration

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Informed consent

As no participant was investigated in our study, there was no need to provide informed consent requirements.

CRediT authorship contribution statement

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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