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Update on diagnosis and treatment strategies in patients with post-thrombotic syndrome due to chronic venous obstruction and role of endovenous recanalization



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ABSTRACT

Objective: After a first episode of lower extremity deep venous thrombosis, post-thrombotic syndrome (PTS) develops in 20% to 50% of patients despite adequate anticoagulation. Symptoms of PTS can vary from leg swelling to venous ulceration with disabling venous claudication. It significantly affects the patient's quality of life and has considerable socioeconomic consequences. This review gives an update on diagnosis and current treatment strategies in patients with PTS due to chronic venous obstruction, in particular regarding the role of endovenous procedures.

Methods: This review article is based on a selective literature search in PubMed and the Cochrane Library. The terms "postthrombotic syndrome," "post-thrombotic syndrome," "chronic venous obstruction," "venous outflow obstruction," and "venous stent" were used as keywords. Selected publications addressed the diagnosis of and therapy for PTS. Acute deep venous thrombosis, thrombolysis, case reports, complications as a result of caval vein filters, animal experiments, PTS of the upper extremity, and PTS in children were excluded.

Results: In addition to conservative treatment of PTS, the following invasive procedures are also available: open surgical reconstructions, hybrid procedures, and endovenous recanalization of the occluded ilio caval venous tract with stent angioplasty. Since introduction of dedicated venous stents in 2012, technical success, patency rates, and improvement in quality of life have been at least as good as results of open surgical reconstruction if not better.

Conclusions: First-line treatment should be conservative therapy. In case of therapy-resistant PTS with poor quality of life, the possibility of an invasive treatment should be evaluated. All invasive procedures are recommended with low levels of evidence. Therefore, deciding on an invasive treatment and type of procedure should be made individually. Because PTS is rarely a threat to life or limb, a minimally invasive treatment is preferred. Therefore, endovenous recanalization appears to be appropriate as the therapy of choice. In patients with involvement of the femoral confluence, endophlebectomy of the common femoral vein in addition to venous recanalization is inevitable to ensure an adequate inflow into the recanalized venous tract. It also secures a sufficient drainage of blood from the peripheral venous system. Because this hybrid procedure is burdened with a significantly higher risk of complications, strict criteria must be fulfilled to legitimize the indication for this procedure. For the best possible results to be achieved, the following perioperative and postoperative management must be considered: therapeutic anticoagulation, early mobilization, compression therapy, and systematic follow-up with duplex ultrasound. (*J Vasc Surg: Venous and Lym Dis* 2019;7:592-600.)

Keywords: Post-thrombotic syndrome; Chronic venous obstruction; Endovenous recanalization; Stent angioplasty; Venous stents

Post-thrombotic syndrome (PTS) is a possible long-term complication after deep venous thrombosis (DVT). Symptoms are those of chronic venous disease; they can vary from leg swelling to venous ulceration with disabling claudication. The estimated incidence of DVT is 0.1% per year in the general population.¹ After a first episode of lower

extremity DVT, PTS develops in 20% to 50% of patients despite adequate anticoagulation.^{2,3} DVT of the ilio caval or femoroiliac venous segments has a significantly higher risk for PTS than DVT of popliteal-crural veins as thrombus resolution occurs more slowly and is less complete in proximal venous segments.⁴ Kahn and Ginsberg⁵ reported that

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femoroiliac DVT is the strongest predictor for formation of severe PTS. PTS significantly affects the patient's quality of life and has considerable socioeconomic consequences^{6,7}; the health care costs of PTS are estimated at \$7000 per patient per year.⁷ Because PTS is not curable, the aim of treatment is to alleviate symptoms and to improve quality of life. With conservative methods, treatment of PTS is often ineffective and frustrating. Open surgical reconstructions are invasive with many possible complications, such as bleeding (the reconstructions are performed under anticoagulation therapy) and bypass occlusions. Garg et al⁸ published the largest study of open surgical reconstructions (29 femorofemoral, 17 femoroiliac, 6 complex bypasses). Early graft occlusion occurred in 17%. Because PTS does not threaten life or limb, the surgical risk seems disproportionately high. Therefore, PTS treatment has often been ignored in the past. In 1995, Berger et al⁹ published the successful treatment of iliac compression syndrome with stent placement for the first time. In 2007, Neglén et al¹⁰ published the largest study on stent angioplasty of iliac veins with 982 patients (n = 464 PTS patients). Since then, this less invasive, reduced risk, and effective therapeutic procedure has gained increasing importance.

The aim of this article is to give an overview of the actual therapeutic options for PTS, especially regarding the role of endovenous procedures. This review article is based on a selective literature search in PubMed and the Cochrane Library. The terms "postthrombotic syndrome," "post-thrombotic syndrome," "chronic venous obstruction," "venous outflow obstruction," and "venous stent" were used as keywords. Selected publications addressed the diagnosis of and therapy for PTS. Acute DVT, thrombolysis, case reports, complications as a result of caval vein filters, animal experiments, PTS of the upper extremity, and PTS in children were excluded. This article is focused on therapy for PTS due to chronic venous obstruction (CVO). Therapy for venous reflux is not the subject of this article.

PATHOGENESIS

After DVT, residual clots or trabeculations cause consecutive outflow obstructions as well as venous valve damage resulting in reflux. Both outflow obstruction and reflux together with impaired compliance of fibrotic vein walls induce an ambulatory venous hypertension, defined as a failure to reduce venous pressure with exercise; ambulatory venous hypertension plays a crucial role in PTS development. Venous hypertension results in dilation of capillaries, disturbance of microcirculation, and increased endothelial permeability for plasma proteins and erythrocytes. This leads to inflammation, edema, hyperpigmentation, and eczema.¹¹⁻¹³

SYMPTOMS AND SIGNS

Typical symptoms of PTS are heavy, tight, tired, and aching legs. Venous claudication occurs as a painful, bursting sensation on walking that is

relieved when the patient stops exertion or after leg elevation.¹²

Common signs are phlebedema, venous ectasia, collateral formation, dermatitis, hyperpigmentation, atrophie blanche, lipodermatosclerosis, and ulceration¹² (Fig 1).

DIAGNOSIS

The diagnosis of PTS is based on the clinical symptoms and signs if the patient experiences persisting symptoms in the affected leg after a DVT. Special scores have been developed (eg, Villalta, Ginsberg, Brandjes, and Widmer scores; Clinical, Etiology, Anatomy, and Pathophysiology [CEAP] classification; and Venous Clinical Severity Score [VCSS]) in which symptoms and signs of venous insufficiency are assigned to corresponding values. The Villalta score is the most commonly used score for the preoperative and postoperative evaluation of PTS severity.^{14,15}

Imaging of PTS is primarily performed by means of duplex ultrasound. If iliac or iliocaval obstructions are suspected, computed tomography venography or magnetic resonance venography should be performed. Both methods are able to detect stenoses, occlusions, external compression, and collateral veins. Using gadolinium-enhanced magnetic resonance venography, it is also possible to detect intraluminal trabeculations and venous wall thickening¹⁶ (Fig 2). Conventional phlebography is rarely used as a diagnostic tool for PTS. Phlebography is mainly used as complementary examination when there is inconclusive information with other modalities. The presence of collateral flow confirms the hemodynamic significance of identified obstructions.

Intravascular ultrasound (IVUS) is the most sensitive examination to detect the extent and type of morphologic lesions in veins. It shows relevant details such as trabeculations, venous wall thickness, external compression, and thrombus formation. The degree of stenosis can be precisely calculated.¹⁷ Morphologic obstruction >50% as measured by IVUS should be considered a potential indication for



Fig 1. Ulcers of the right lower leg with surrounding hyperpigmentation and dermatitis in a patient with post-thrombotic syndrome (PTS).

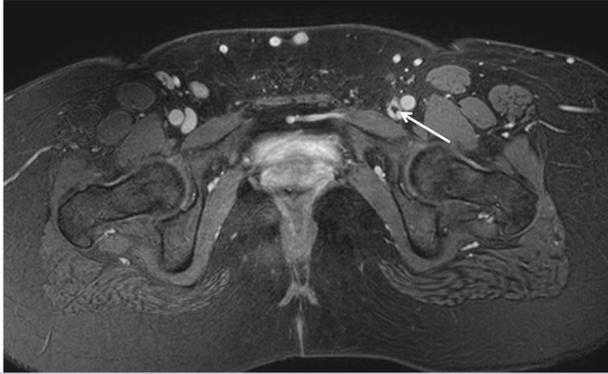


Fig 2. Magnetic resonance venography of a patient with post-thrombotic syndrome (PTS) due to chronic venous obstruction (CVO): intraluminal trabeculations in the left common femoral vein (CFV).

stenting.¹⁷ Therefore, IVUS should be an integral part of the stenting procedure (Fig 3). Furthermore, IVUS does not require any radiographic contrast medium and is therefore a viable diagnostic tool for patients with renal insufficiency. However, the indication for invasive treatment should not be based solely on IVUS findings because an IVUS examination can show a diameter reduction without a hemodynamically or clinically significant stenosis (eg, in case of venous collapse).

For all mentioned techniques, the measurements are made at rest in a supine position. Visualized obstructions do not always need to be of any clinical importance, and vice versa, sometimes veins without visualized significant obstructions in a supine position and at rest can have a significant clinical obstruction during exercise or standing. The 24-hour pressure and flow measurements might solve these issues. Therefore, it is important in diagnosis of PTS that the clinical signs and symptoms as well as imaging findings are coherent.

CONSERVATIVE TREATMENT

Because PTS is not curable, the aim of treatment is the relief of symptoms and signs.

Compression therapy. Compression therapy supports the function of the calf muscle pump, reduces vein diameter, and improves venous valve function. As a consequence, venous drainage of the leg increases, whereas venous reflux decreases. This reduces venous pressure with subsequently less edema formation and better microcirculation.^{18,19}

Therefore, a preventive effect of compression stockings is expected. However, in a randomized trial (SOX trial), class II compression stockings did not prevent PTS development.²⁰ In this trial, the effectiveness of compression to prevent PTS was disappointing. It is argued that these results are mainly due to lack of patients' compliance.

For treatment of PTS, Kahn et al² recommended knee-high compression stockings (20-30 mm Hg); compression pressure can be increased to 40 to 50 mm Hg if required. The American Heart Association (AHA) advocates a weak recommendation for compression therapy if contraindications (eg, peripheral artery disease, decompensated heart failure) are excluded (class IIb, level of evidence C).²¹ Intermittent pneumatic compression therapy may also be considered in patients with PTS (class IIb, level of evidence C).^{19,21}

Anticoagulation. Efficient thromboprophylaxis is recommended for patients with increased risk for DVT development as primary PTS prevention (class I, level of evidence C).²¹

A sufficient therapeutic anticoagulation for treatment of DVT and prevention of recurrence is recommended as secondary PTS prevention (class I, level of evidence B).²¹

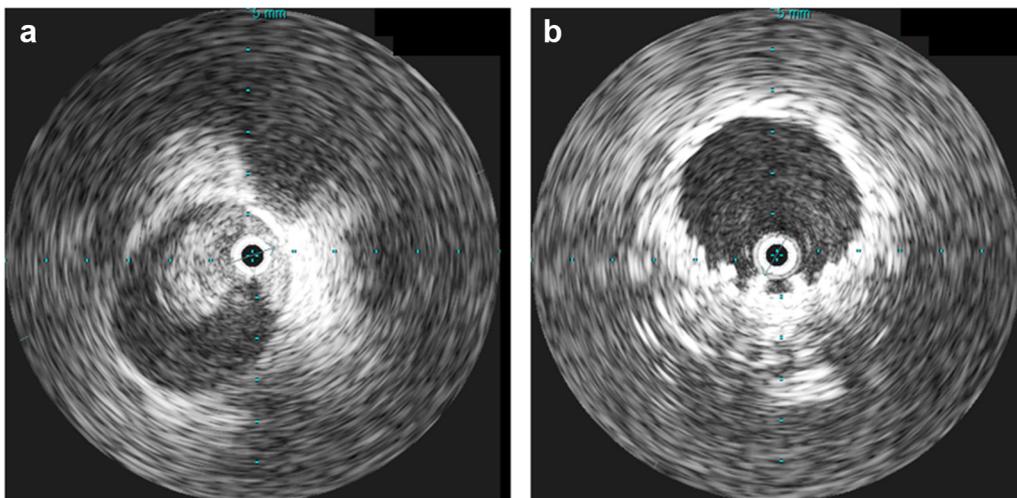


Fig 3. a, Intravascular ultrasound (IVUS) shows trabeculations in the common iliac vein of a patient with post-thrombotic syndrome (PTS) due to chronic venous obstruction (CVO). **b,** IVUS shows widely patent common iliac vein after stenting. The black circle inside the vein represents the inserted IVUS catheter.

However, anticoagulant strategies have not been evaluated for the treatment of patients who have established PTS.

Venoactive drugs. Because of weak evidence of positive effects and possible long-term side effects of venoactive drugs (eg, rutosides), the use of these agents is not recommended by current guidelines.^{2,21,22}

Physiotherapy. Training and physiotherapy, most likely because of improved calf muscle pump function, may ameliorate symptoms of PTS. Two studies evaluated the effectiveness of training vs a control group without training. In the training group, symptoms, leg strength, agility, and quality of life improved. Therefore, the AHA recommends a supervised exercise program (class IIa, level of evidence B).²¹

Weight loss. Studies suggest that obese patients are more likely to exhibit progression of chronic venous disease. Weight loss may assist these patients in controlling PTS symptoms and disease progression.²³

INVASIVE TREATMENT

In patients with severe PTS due to identified CVO and reflux, the obstruction should be treated first. The surgical treatment of reflux is useful only if the outflow of the femoroiliac tract and the caval vein is not impaired.^{10,21,24} Raju et al²⁴ concluded that iliac venous stenting alone is sufficient to control symptoms in the majority of patients with combined outflow obstruction and deep reflux. This publication focuses on the treatment of CVO.

Regarding open and hybrid operations of CVO, there are only small, nonrandomized studies with low case numbers (level of evidence C). For minimally invasive percutaneous endovenous recanalization and stent angioplasty, a higher level of evidence exists (level of evidence B) as a result of studies with larger case numbers.²¹

Open surgical reconstructions

Palma and Esperon²⁵ described a crossover femorofemoral bypass using the contralateral great saphenous vein for patients with unilateral iliac vein obstruction (Fig 4). If there is no suitable great saphenous vein, an 8-mm ringed polytetrafluoroethylene graft can be used. To prevent bypass occlusion, this operation is often combined with the creation of an arteriovenous fistula. In the literature, patency rates of 70% to 85% (follow-up, 6-216 months) for crossover femorofemoral bypasses have been reported.^{8,26-30}

Garg et al⁸ performed femoroiliac or iliocaval bypasses in eight patients and femorocaval bypasses in nine patients. At a median follow-up of 60 months, the patency was 63%.

The largest study of bypass surgery for PTS therapy was carried out in 85 patients.²⁹ Based on the existing small studies, the benefits of these bypasses are not well evaluated (class IIb, level of evidence C).²¹

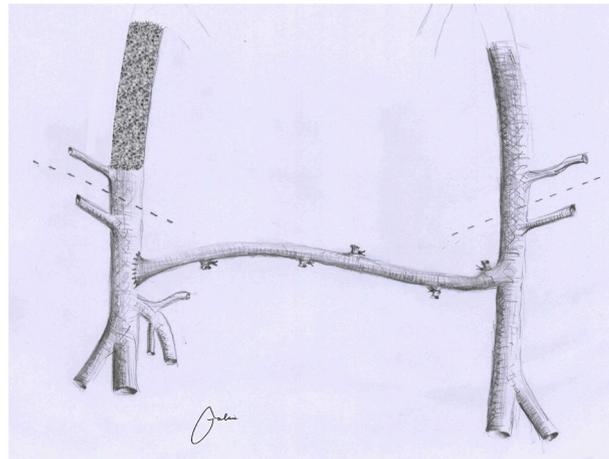


Fig 4. Femorofemoral crossover bypass using the left great saphenous vein to treat chronic venous obstruction (CVO) in the right external iliac vein (Palma procedure).

Endovenous recanalization and stent angioplasty

In 1995, Berger et al⁹ published the successful treatment of iliac compression syndrome with stent placement for the first time. In 2007, Neglén et al¹⁰ published the largest study on stent angioplasty of iliac veins with 982 patients (n = 464 PTS patients). The mortality rate was 0%. The primary and secondary patency rates in PTS patients after 72 months were 57% and 86%, respectively. Neglén et al¹⁰ also showed a significant improvement in limb pain, swelling, and quality of life in patients after endovenous treatment. No aggravation of clinical symptoms was seen in patients in whom a recanalization had failed. Since then, this therapeutic option has been increasingly performed.

Technical details. Recanalization is performed in the supine position with sedation or general anesthesia. Venous dilation and stenting are painful and may take some time. After ultrasound-controlled puncture of the femoral vein in the midpart of the upper leg, a 9F sheath is placed in the vein by the Seldinger technique. The tip of the sheath should be placed caudal to the confluence of the deep femoral vein (DFV) and femoral vein. Thus, the common femoral vein (CFV) can be completely evaluated, and treatment can be adjusted to the extent of the obstructive lesion. Phlebography is performed, first to confirm the obstruction and the existence of collaterals and second to pass the obstructions using stiff hydrophilic wires and supporting catheters. Predilation of the obstructed venous tract is performed next. After balloon dilation without stenting, immediate recoil occurs in the majority of cases. Therefore, stenting is mandatory.³¹ Stenting with a self-expanding stent should be carried out throughout the complete post-thrombotic vein segment (from healthy to healthy). To achieve the best possible alignment of the stent, the balloon used for predilation should have at least the same diameter as the stent (12-18 mm from the CFV to

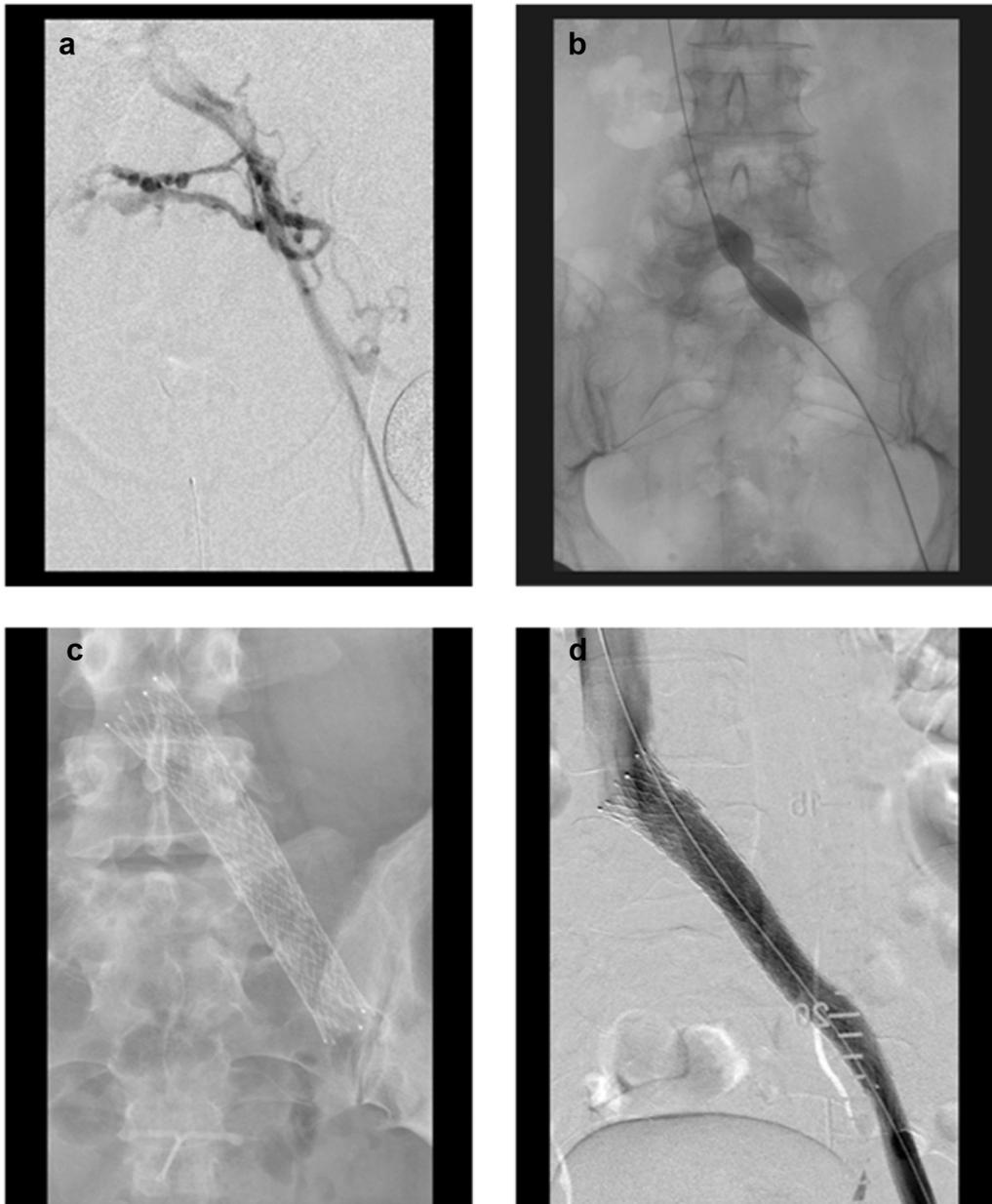


Fig 5. **a**, Phlebography shows post-thrombotic obstruction of the left iliac veins with collateral formation. **b**, Balloon angioplasty of the left common iliac vein with waisting at the maximum point of stenosis before stenting. **c**, Radiograph (anteroposterior plane) after stent-percutaneous transluminal angioplasty of the left common iliac vein (Venovo stent). **d**, Uninterrupted venous outflow after stenting of the common and external iliac veins with disappearance of collaterals.

the common iliac vein). In patients with long-segment post-thrombotic iliofemoral obstructions who need more than one stent, the stents should be placed from the common iliac vein to the CFV, from central to peripheral. According to current practice, there should be 1 to 2 cm of stent overlap. In this manner, the peripheral stent with a smaller diameter will be placed in the distal part of the central stent. A compression of the left common iliac vein (May-Thurner syndrome) should be covered with a stent. Excessive protrusion of the stent into the caval vein with coverage of the contralateral iliac

vein ostium must be avoided. Stenting across the inguinal ligament is allowed as it has not been associated with an increased risk of stent fracture or narrowing.³² Postdilation must always be performed. The operation is completed with final control phlebography in two planes to exclude recoil and thromboembolic complications. Successful recanalization leads to a prompt outflow of contrast material and disappearance of collateral veins^{10,31,33} (Fig 5).

IVUS should be implemented to determine the lesion's extent and the proximal and especially the distal landing

zones of the stent. It is more sensitive than intraoperative phlebography.^{34,35} In addition, IVUS can be used as a completion examination after placement of stents to minimize radiation exposure and use of iodinated contrast agents.

Results of endovenous recanalization and stent angioplasty. In their actual meta-analysis, Wen-da et al³⁵ analyzed 14 studies of stent angioplasty for treatment of chronic obstructive venous disease. The incidence of 30-day thrombotic events was 4%. No pulmonary embolism or embolism-related deaths were reported. Postoperative self-limited back pain was a common complication with a rate of 62.9%. Significant relief of pain and edema was reported. The ulcer healing rate was 70.3%. After 12 months, primary, assisted primary, and secondary patency rates were 90.1%, 92.8%, and 97.3% (after 36 months: 82.3%, 86.9%, and 88.8%).

Seager et al³⁶ published a systematic review of endovenous stenting to treat chronic obstructive venous disease that included 16 studies. Persistent ulcer healing rates ranged from 56% to 100%. Primary and secondary patency rates ranged from 32% to 98.7% and 66% to 96%, respectively (with follow-up between 6 months and 4 years). They concluded that the data were too heterogeneous to perform a meta-analysis.

In both these reviews of 2016, the authors concluded that the quality of evidence supporting endovenous stenting in treatment of CVO is weak. Therefore, current European and American guidelines recommend stenting for severe PTS but also recognize its weakness of evidence.^{37,38} The AHA recommendation on endovenous stenting for treatment of severe CVO is class IIb, level of evidence B.²¹

Venous stents

In all the preceding studies, stents that had been developed for implantation in the arterial system were used. However, arterial stents are not optimal for veins. Veins have a greater diameter than the corresponding arteries; for stenting of the femoroiliac venous tract, stents with 12- to 18-mm diameter are needed. Post-thrombotic veins are often strongly fibrotic or compressed externally (eg, due to May-Thurner syndrome); as a consequence, stents with more radial force are needed. In addition to high radial force, a high degree of flexibility is also required for venous stents to follow the anatomic curves of the veins even during flexion. Therefore, special venous stents with high flexibility and strong radial force have been developed³⁹: sinus-Venous stent and sinus-Obliquus stent (OptiMed, Ettlingen, Germany), Zilver Vena (Cook Medical, Bloomington, Ind), Vici Venous Stent (Veniti Inc, St. Louis, Mo), Venovo (Bard, Tempe, Ariz), and Blueflow Venous Stent (Plusmedica GmbH & Co KG, Düsseldorf, Germany).

Results with dedicated venous stents. To our knowledge, there are currently only four publications on treatment of CVO with dedicated venous stents.⁴⁰

O'Sullivan et al⁴⁰ treated 20 patients (9 of them with PTS) with femoroiliac obstructions with Zilver Vena stents. After a mean follow-up of 55 days, the primary patency rate was 85% (17/20). Three patients suffered from a stent occlusion within the first 30 days. Clinical improvement and decreased leg swelling were observed in the remaining 17 patients.

Stuck et al⁴¹ used sinus-Obliquus stents in 24 patients (10 of them with PTS) to recanalize the femoroiliac venous tract. During a follow-up of 10 ± 3 months, the primary and secondary patency rates were 83% and 100%, respectively. The Villalta score decreased by 6 ± 6 points.

In 40 patients with PTS, de Wolf et al³⁹ performed venous recanalizations with sinus-Venous stents. The follow-up was 5.5 (1-18) months. There was no mortality. The primary patency rates were 97%, 93%, and 85% after 3, 6, and 12 months. In three patients, a rethrombosis occurred, which could be treated successfully with endovascular techniques (thrombolysis, restenting). Postoperatively, the Villalta score decreased from 11.5 to 5.0.

The largest study with dedicated venous stents for reconstruction of the femoroiliac outflow was published in 2017 by van Vuuren et al⁴²; 221 legs (in 196 PTS patients) were operated on. The following dedicated venous stents were implanted: sinus-XL, sinus-XL Flex, sinus-Venous, and sinus-Obliquus (OptiMed); Vici Venous Stent (Veniti Inc); Zilver Vena (Cook Medical); and Venovo (Bard). At 60 months, primary patency, assisted primary patency, and secondary patency rates were 64%, 81%, and 89%; 36 patients had a thrombotic stent occlusion, which was treated by thrombolysis and secondary stenting in 19 patients. Mortality was 0%. No clinical pulmonary embolism occurred. A significant improvement of Villalta score was noticed.⁴²

Hybrid procedure

When post-thrombotic trabeculations are detected in the CFV that cover the ostium of the DFV, an operative endophlebectomy in addition to venous recanalization might be required. This should guarantee an adequate inflow into the recanalized venous tract and sufficient drainage of blood from the peripheral venous system.

After longitudinal venotomy of the CFV, intraluminal trabeculations of the CFV and the orifice of the DFV are removed (endophlebectomy). Closure of the incision is performed with or without a bovine patch, depending on the lumen of the CFV after the endophlebectomy. After the inflow into the CFV is restored, stent angioplasty of the already recanalized venous segment will be performed. The caudal end of the stent should be placed below the inguinal ligament at the level of endophlebectomy to ensure stenting from healthy to healthy segments and to prevent collapse of the reconstruction (Fig 6). To further improve inflow, a 6-mm polytetrafluoroethylene loop-shaped arteriovenous fistula can be created between the common/superficial femoral artery and the CFV,

which can interventionally be occluded after 6 to 8 weeks using an Amplatzer occluder (St. Jude Medical, St. Paul, Minn).^{43,44}

In 2010, the technique of endophlebectomy and hybrid procedure was first published by Comerota et al.^{45,46} They treated 16 legs with obstructions of the ilio caval venous segment and CFVs. Within a mean follow-up of 26 months, there were seven postoperative complications: bleeding (n = 3), thrombotic occlusion (n = 3), and lymphedema (n = 1). A significant improvement in quality of life and Villalta score could be demonstrated. de Wolf et al⁴⁷ treated 76 legs in 70 patients in the same manner. At 12 months, the primary, assisted primary, and secondary patency rates were 51%, 70%, and 83%, respectively. Wound infection occurred in 29% and lymphatic leak in 39%. The Villalta score decreased by a median of 7 points at 12 months of follow-up. van Vuuren et al⁴² published the results of treatment of 109 legs (n = 86 patients) by means of hybrid surgery. After 36 months, the primary, assisted primary, and secondary patency rates were 37%, 62%, and 72%, respectively. There was a high incidence of wound-related complications (wound infection, 27%; lymphorrhea, 33%; wound dehiscence, 12%). A significant improvement of Villalta score was seen in 73% of patients. In 83% of patients, venous claudication was absent after a median of 16 months (11-25 months).

Because of the small case numbers, the guidelines give only a weak recommendation for this procedure (class IIb, level of evidence C).²¹

Contraindications to invasive treatment

Stent angioplasty in cases with insufficient inflow due to obstruction of the femoral vein and DFV does not improve the drainage of the leg and is not likely to be successful. Another criterion for exclusion is a contraindication to therapeutic anticoagulation.

Perioperative and postoperative management

The following recommendations should be taken into consideration to achieve good patency rates after venous stenting.

After recanalization, there is an increased risk for thrombosis due to intimal lesions during stent implantation or endophlebectomy and immobility. A thrombotic occlusion of the recanalization route is the most common postoperative complication.¹⁰ Therefore, a *sufficient perioperative and postoperative therapeutic anticoagulation* is crucial.¹⁰ The antithrombotic regimen after stenting is heterogeneous in the different venous centers. In a systematic review, Saeger et al³⁶ included 16 studies on endovenous stenting in chronic venous disease secondary to iliac vein obstruction. In nine studies, combined therapy with anticoagulation and platelet inhibitors was prescribed; in five studies, only therapeutic anticoagulation was given; and in two studies, no statement was made on this topic.

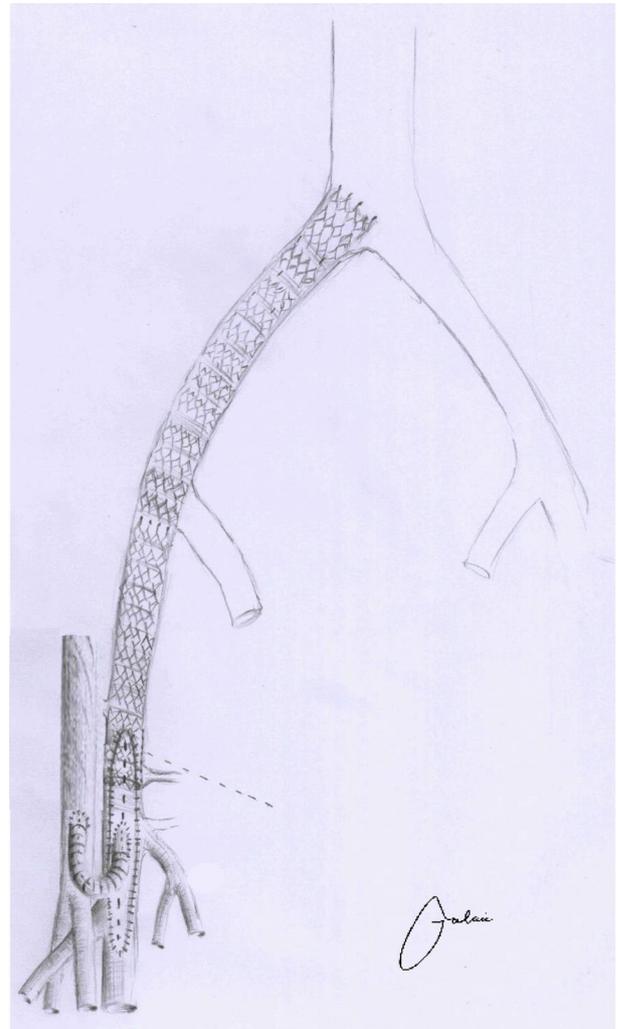


Fig 6. Hybrid procedure: endophlebectomy of the common femoral vein (CFV) and the orifice of the deep femoral vein (DFV), venous recanalization with stenting of the common and external iliac veins and the CFV, and loop-shaped arteriovenous fistula with 6-mm externally supported polytetrafluoroethylene between the common femoral artery and the CFV.

We recommend the following antithrombotic regimen. Preoperative anticoagulation should not be paused. Intraoperative heparin should be applied so that the intraoperative activated clotting time is ≥ 200 seconds. Postoperative therapeutic anticoagulation with vitamin K antagonists (target international normalized ratio, 2.5-3.5) or with directly acting oral anticoagulants should be administered for at least 6 months.³³ We do not prescribe platelet inhibitors.

Early *mobilization* is also essential for the success of interventional therapy. For immobile patients, intermittent pneumatic compression therapy should be used until the patients are mobile. *Compression* stockings

should be worn for at least 1 year postoperatively and life-long in patients with deep venous reflux.³³

A *systematic follow-up* together with duplex ultrasound is recommended. The first follow-up should be performed 2 weeks after discharge to check for patency and geometry of the stents. An early occlusion at this time can be adequately treated with local thrombolysis therapy, and any stent-associated complications may also be corrected.³³

Conclusions

Because of low case numbers and different therapies, there are no large randomized studies regarding the invasive treatment of PTS. Therefore, a clear evidence-based treatment recommendation does not exist. In the latest guideline from 2014, the AHA published equally weak recommendations for all invasive procedures (class IIb, level of evidence B and C).²¹ Recent European and American guidelines recommend endovenous stenting for severe obstructive venous disease but recognize the weakness of evidence.^{21,37,38} Since 2012, dedicated venous stents that are expected to attain better results have been available. There are currently only four single-center studies (with a maximum of 196 patients) on the results with dedicated venous stents. Prospective randomized studies are still missing at present. Therefore, a level of evidence of B and C may be assumed.

The indication for an invasive treatment and the selection of the procedure are mostly individual decisions. Patients should be evaluated critically under consideration of the severity of PTS, underlying pathologic process, venous anatomy, concomitant diseases, and contraindications.

RECOMMENDATIONS

1. First-line treatment should be conservative therapy. In case of therapy-resistant PTS with poor quality of life (because of venous claudication or venous ulcers), the possibility of an invasive treatment should be evaluated.
2. Because PTS is an extremely rare threat to life or limb, a minimally invasive procedure, with the aim of alleviating symptoms and improving quality of life, should be preferred. Therefore, endovenous recanalization appears to be an appropriate therapy. In the majority of cases, it is a minimally invasive, safe, and effective therapy with low perioperative complications, no mortality, and high patency rates. In case of therapeutic failure, there is no progression of disease, and an open surgical reconstruction can still be performed.^{10,31,32}
3. Because hybrid procedures are burdened with a significantly higher risk for complications, even stricter criteria must be applied to the indication for these procedures. Hybrid procedures should be discussed

in particular with the patient, explaining all possible complications.⁴²

4. For the best possible results to be achieved, the following perioperative and postoperative management must be urgently considered: sufficient therapeutic anticoagulation, early mobilization, compression therapy, and systematic follow-up.³³
5. Because the outcome of open and endovascular surgery is dependent on the surgeon's expertise, treatment should be carried out in dedicated venous centers.²¹

Randomized, prospective studies on venous recanalization and optimal stent configurations are required to improve the level of evidence of these procedures.

AUTHOR CONTRIBUTIONS

Conception and design: KS, IT, CW, HJ

Analysis and interpretation: Not applicable

Data collection: KS, MB, JG, KH

Writing the article: KS, HJ

Critical revision of the article: MB, JG, KH, IT, CW

Final approval of the article: KS, MB, JG, KH, IT, CW, HJ

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Overall responsibility: KS

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