# Present and future options for treatment of infrainguinal deep vein disease

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## ABSTRACT

**Objective:** Management of chronic deep vein disease focuses on the alleviation of reflux and obstruction. For the suprainguinal veins, the main underlying pathologic process is obstruction, which has been recognized as a significant contributor to chronic venous insufficiency. This is currently being addressed with venous stenting and the development of dedicated stents designed for this segment of the venous system. Treatment of the femoropopliteal vein (FPV) is far more challenging because of the idiosyncratic anatomy, the hemodynamic physiology, and the technical aspects of size mismatch and valve flow dynamics in managing deep venous reflux. This review article discusses traditional and emerging technologies to treat infrainguinal disease.

**Methods:** Previous and current articles addressing this issue were reviewed. Emphasis was placed on emerging techniques and technologies.

**Results:** Significant bench work, in vitro and in vivo studies, have been conducted over the last 40 years addressing the issue of infrainguinal reflux and obstruction. Historically, open procedures to address FPV reflux and obstruction have had variable success in a few centers around the world. The significant increase of emerging endovascular therapies may allow more appropriate, reproducible, widespread treatment of infrainguinal deep venous disease.

**Conclusions:** Adequate and durable therapies for infrainguinal venous disease represent one of the greatest challenges for a vein specialist. Recently, a cluster of interest and techniques/technologies have been developed. The endovascular management of arterial disease is mature. The endovenous management of infrainguinal disease is on the cusp of meaningful innovation. The purpose of this evidence summary is to describe the options for the management of chronic FPV disease, with emphasis on emerging technologies and techniques. (J Vasc Surg: Venous and Lym Dis 2018;■:1-8.)

**Keywords:** Deep venous insufficiency; Femoropopliteal reflux; Post-thrombotic femoropopliteal disease; Venous valve; Valve transplant; Prosthetic vein valve

Chronic venous obstruction (CVO) entails a narrowing or occlusion of the vein lumen caused by extrinsic compression (nonthrombotic), post-thrombotic intraluminal changes, or both. The obstruction can involve the veins above the inguinal ligament (suprainguinal) or below (infrainguinal). The etiology of CVO is predominantly nonthrombotic in the suprainguinal veins[1] and post-thrombotic in the infrainguinal deep veins.[2] Nonthrombotic compression of the iliac veins is a common finding in the general adult population, yet despite different degrees of compression, many people never develop symptoms.[3] Conversely, about 50% of patients with deep venous thrombosis (DVT) develop post-thrombotic syndrome (PTS)[4,5]; in most, symptoms are mild or moderate. It has been postulated that thrombolysis may decrease the incidence of PTS. Early analysis of the Acute Venous Thrombosis: Thrombus Removal with Adjunctive Catheter-Directed Thrombolysis (ATTRACT) trial data indicates that this may not be the case for infrainguinal veins.[6-8] It is more likely that select patients with iliofemoral DVT may have such benefit.

The incidence and severity of PTS are affected by the location and extent of the obstruction.[9] Iliac vein thrombosis is a significant contributor to PTS because this is the main outflow of the lower limb. Similarly, a venous obstruction at the level of the femoropopliteal vein (FPV), which is the main outflow for the leg, can lead to PTS. In many instances, the profunda femoris vein enlarges to compensate for the outflow obstruction in the femoral vein (axial transformation). Paradoxically, such enlargement causes severe venous reflux in some patients that adversely contributes to the symptoms of CVO and PTS.[10] A higher proportion of patients with DVT affecting the iliac vein compared with the FPV develop PTS (60% vs 40%). However, more patients with FPV-related PTS may be seen in clinical practice, as thrombosis in these veins is three times more frequent than in the iliac system.[11]

The common denominator in the pathophysiologic process of PTS is elevated ambulatory venous pressure secondary to residual obstruction or valvular reflux. This

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Author conflict of interest: S.E. receives consulting fees from Hancock Jaffe. A.P.G. receives consulting fees from AV Medical, Hancock Jaffe, and BTG.

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The editors and reviewers of this article have no relevant financial relationships to disclose per the Journal policy that requires reviewers to decline review of any manuscript for which they may have a conflict of interest.

2213-333X



https://doi.org/10.1016/j.jvsv.2018.01.010

leads to increased capillary permeability and a cascade of inflammatory events resulting in edema and skin damage.[12] Patients with both reflux and obstruction have the highest morbidity.[9,13]

Typical PTS signs and symptoms include pain, swelling, venous claudication, heaviness, itching, skin damage, and ulcers. Claudication and edema are more likely to be associated with obstruction, whereas venous leg ulcers are predominantly seen in those with reflux with or without obstruction.[14] The symptoms of PTS are typically progressive and significantly reduce quality of life.[15,16] Higher degrees of the quality of life impairment are seen in patients with previous proximal DVT presenting with leg claudication and advanced clinical stages. Patients' perception of physical functioning, general health, social function, and mental health has been demonstrated to be worse than previously thought.[17]

Treatment options for PTS are limited and often ineffective. The recommended conservative and interventional options are aimed at alleviation of venous hypertension. Most patients are managed conservatively with leg elevation and compression.[18] Unfortunately, many do not experience a substantial relief of symptoms because of the inability to tolerate adequate high compression, poor compliance, and severe obstruction.

Presently, several procedures designed to alleviate venous reflux and obstruction are available. These procedures are usually reserved for patients who fail to respond to conservative management. Options for PTS affecting the iliofemoral veins focus on obstruction, mostly using an endovascular approach: thrombolysis, recanalization, balloon angioplasty, and stenting. Treatment of the FPVs is far more challenging because of the idiosyncratic anatomy, the hemodynamics pertaining to these veins, and the technical aspects in addressing deep venous reflux. Historical open procedures to address FPV reflux and obstruction have variable success in a few centers around the world. Promising endovascular therapies are being developed. The purpose of this evidence summary is to describe the options for the management of chronic FPV disease, with emphasis on emerging techniques and technologies.

## CONSERVATIVE OPTIONS

Conservative measures are designed to relieve symptoms, to delay disease progression, and to improve quality of life. Options include compression, leg elevation, weight loss, skin care, and exercise training. Most studies evaluate the use of compression garments and exercise training.

Compression garments are used for both primary and secondary PTS prevention. A small interventional study published >20 years ago found that 60% of patients with a first episode of proximal DVT developed PTS within 2 years and demonstrated a 50% incidence reduction of PTS with the use of graduated compression stockings (GCS).[19] Subsequently, comparable findings were reported by a handful of small trials,[20,21] and the recommendations for wearing GCS after a fist episode of DVT to prevent PTS were adopted by the pertinent society guidelines.[22,23] However, a more recent, larger, multicenter randomized placebo-controlled trial found that GCS did not prevent PTS; therefore, it did not support routine use after DVT.[24] Based on this trial, the newest guidelines suggest, with a moderate quality of evidence, that GCS not be used routinely to prevent PTS.[25] On the other hand, strong evidence about the role of GCS for patients with established PTS is lacking. Some experts recommend their use on the basis of low risk of harm and a possible beneficial effect in terms of symptom relief.[18]

There is evidence from two small trials that exercise training may be useful in treating PTS. A randomized controlled study of patients with chronic venous insufficiency revealed a significant improvement in venous hemodynamics after 6 months of structural exercises that aimed to increase the strength of the calf musculature. Half of the patients in the study had a previous history of DVT, and 30% had deep venous postthrombotic changes on Doppler ultrasound.[26] Similarly, a feasibility trial at two medical centers investigating the clinical effectiveness of supervised exercise training in patients with PTS demonstrated improvement in disease severity and quality of life. The program consisted of leg strengthening, leg stretching, and aerobic exercises for a 6-month period.[27] Larger prospective studies are needed to demonstrate the reported benefits.

## INTERVENTIONAL OPTIONS: GENERAL APPROACH

Endovascular or hybrid procedural techniques have emerged in recent years. Recanalization with balloon venoplasty and stenting of the suprainguinal veins has proved to be an effective and safe procedure and is now the method of choice in the treatment for iliocaval disease.[28] However, the management of postthrombotic disease of the infrainguinal veins remains more diverse. Whereas the main goal of therapies for iliocaval CVO is to restore axial blood flow, in addition to this, valvular incompetence may also need to be addressed in the treatment of CVO affecting the FPV.

A variety of procedures for the management of both obstruction and reflux of the infrainguinal veins have been suggested over the years (Table).[12,29-31] The level of evidence on the efficacy and safety of most of these procedures is low, and as previously stated, some are technically challenging. Therefore, selection of patients and expertise of the physician with the procedure are crucial. Patients at low surgical risk with venous leg ulcers or PTS symptoms causing substantial disability and who have failed to respond to conservative therapies may benefit the most. The patient's expected life span and