

POST THROMBOTIC SYNDROME (PTS)



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OBJECTIVES:

- To briefly review the clinical presentation and diagnosis of PTS
- To help identify DVT patients who are at risk of developing PTS
- To review strategies to prevent and treat PTS

BACKGROUND:

- Post thrombotic syndrome (PTS) is a chronic condition that develops in 20% to 50% of patients after deep venous thrombosis (DVT)
- PTS is a burdensome condition in terms of effect on quality of life and costly in terms of lost productivity and dollars spent

HOW DOES DVT LEAD TO PTS?

DVT-related residual venous obstruction and valvular reflux lead to increased venous pressure (venous hypertension), which results in reduced calf muscle perfusion, increased tissue permeability and the associated clinical manifestations of PTS.

CLINICAL PRESENTATION OF PTS (TABLE 1):

Symptoms of PTS may be present in various combinations and may be persistent or intermittent. Typically, symptoms are aggravated by standing or walking and improve with resting, leg elevation and lying down.

TABLE 1: TYPICAL CLINICAL FEATURES OF THE POST-THROMBOTIC SYNDROME

LEG SYMPTOMS	SIGNS
Heaviness or fatigue	Edema
Pain	Peri-malleolar telangiectasiae
Swelling	Venous ectasia, varicose veins
Itching	Hyperpigmentation
Cramps	Redness
Paresthesia	Dependent cyanosis
Bursting pain on walking (venous claudication)	Lipodermatosclerosis
Symptom pattern: Worse with activity, standing, walking; better with rest, recumbency	Healed or open ulcer

HOW IS PTS DIAGNOSED?

- PTS is primarily diagnosed on clinical grounds.
- There is no gold standard laboratory testing, imaging or functional test that establishes the diagnosis.
- The Villalta PTS scale (Table 2) has been adopted by the International Society on Thrombosis and Haemostasis (ISTH) as a standard to diagnose and grade the severity of PTS in clinical studies.
- In some patients, it may take a few months for the initial pain and swelling associated with acute DVT to resolve, hence a diagnosis of PTS should be deferred until after the acute phase (i.e. 3-6 months) has passed.
- Symptoms of PTS usually occur within 3-6 months after DVT, but can occur up to 2 years after DVT.

TABLE 2: VILLALTA PTS SCALE

CRITERIA USED TO DIAGNOSE PTS
<ul style="list-style-type: none">• 5 symptoms (pain, cramps, heaviness, pruritus, paresthesia)• 6 signs (edema, skin induration, hyperpigmentation, venous ectasia, redness, pain during calf compression)• Each symptom and sign rated as 0 (absent), 1 (mild), 2 (moderate) or 3 (severe)• Points are summed to yield total score:<ul style="list-style-type: none">0–4: No PTS5–9: Mild PTS10-14: Moderate PTS15 or more, or presence of ulcer: Severe PTS

WHICH PATIENTS WITH DVT ARE AT RISK OF DEVELOPING PTS?

Approximately 60% of patients with DVT will recover without any residual symptoms, ~30% will have some degree of PTS, and ~5-10% will develop severe PTS. Of note, ~15% of patients with upper extremity DVT also develop PTS. It is not possible to reliably predict which DVT patients will develop PTS.

Specific risk factors for PTS:

- Recurrent ipsilateral DVT: Increases risk of PTS by ~6-fold (via damaging compromised venous valves or aggravating venous outflow obstruction).
- Characteristics of initial DVT: Risk of PTS is 2-4 fold higher after proximal (especially iliofemoral) than distal (calf) DVT.
- Higher body mass index: Increased risk of PTS.
- Quality of oral anticoagulation: PTS risk increases if the initial anticoagulation is inadequate (e.g. subtherapeutic INR >50% time during first three months of treatment), but risk is not affected by the intensity or duration of long-term anticoagulation.
- Residual thrombosis on ultrasound: Modest (odds ratio ~2) increased risk of PTS.

- Persistent elevation of D-dimer: Elevated levels of D-dimer in the weeks to months after DVT may be a modest risk factor for PTS.
- DVT occurring in pregnancy increases the risk of PTS
- Age and sex: No consistent relationships with PTS.
- Inherited thrombophilia: No consistent relationship with PTS.
- Whether the DVT was unprovoked or secondary (due to surgery, trauma or cancer) does not influence the likelihood of PTS.

PREVENTION OF PTS (TABLE 3):

Primary and secondary prevention of DVT

The best way to prevent PTS is to prevent DVT. As ipsilateral DVT recurrence is a strong risk factor for PTS, preventing recurrent DVT by providing anticoagulation of appropriate intensity and duration for the initial DVT is important.

Thrombolysis

- Thrombolytic therapy in conjunction with heparin to treat acute DVT leads to higher rates of vein patency and better preservation of valve function than the use of heparin alone.
- Catheter-directed thrombolysis is likely to be safer and more effective than systemic thrombolytic therapy and could hold promise as a means of preventing PTS, primarily after iliofemoral DVT.
- As yet, there is no high quality, definitive evidence to support the routine use of thrombolysis as a means to prevent PTS.
- Large multicenter trials of standard anticoagulation vs. pharmacomechanical catheter-directed thrombolysis (catheter-directed thrombolysis + mechanical disruption of thrombus) to prevent PTS are ongoing.
- Currently, selection of patients for these techniques is done on a case-by-case basis, and is typically reserved for select patients with extensive (e.g. iliofemoral) thrombosis, recent onset of symptoms, low risk of bleeding, and long life expectancy.

Elastic Compression Stockings (ECS)

- There are conflicting RCT data concerning the long term effectiveness of ECS.
- Two previous small open label trials reported that ECS were effective in preventing PTS, but a recent large multicenter placebo-controlled trial showed no evidence of benefit of active compression stocking to prevent PTS.
- Thus, routine use of ECS to prevent PTS in DVT patients is no longer supported.
- However, in patients with significant DVT-related swelling, ECS can be tried to relieve symptoms.
- If stockings are used, knee-length and thigh-length ECS have similar physiologic effects; knee-length are easier to apply, more comfortable and less costly.

TREATMENT OF PTS:

There are few treatment options for symptomatic PTS (Table 3).

- ECS may reduce leg swelling and discomfort.
- Intermittent pneumatic compression sleeve units can help severe, intractable PTS symptoms or severe edema; however they are cumbersome and expensive.
- The portable, battery-powered Venowave® intermittent compression device benefits some patients with moderate to severe PTS.
- There is no evidence that diuretics or “venoactive” drugs are effective for PTS-related edema or other manifestations.
- Post-thrombotic venous ulcers are treated with compression therapy, leg elevation and topical dressings but can be refractory to therapy and tend to recur.
- Surgical or endovascular treatments for PTS such as venous valve repair, venous bypass and venous stents have only been evaluated in small patient series at single, specialized centers and appear to be of limited value.

TABLE 3: STRATEGIES FOR THE PREVENTION AND MANAGEMENT OF PTS

PREVENTION
<ul style="list-style-type: none"> • Prevent the index DVT with use of thromboprophylaxis in high-risk patients and settings as recommended by evidence-based guidelines • Prevent recurrent ipsilateral DVT by providing anticoagulation of appropriate intensity and duration for the initial DVT and by targeted use of appropriate thromboprophylaxis if long-term anticoagulation is discontinued • Effectiveness of daily use of knee-length, 30 to 40 mmHg ECS for PTS prevention after DVT was recently disproven • The role of thrombolysis in acute DVT to prevent PTS is not yet established • Pharmacomechanical catheter-directed thrombolysis requires further evaluation in properly designed trials
MANAGEMENT
<ul style="list-style-type: none"> • ECS reduce edema and may improve PTS symptoms • Intermittent pneumatic compression devices are effective for moderate to severe symptomatic PTS • Compression therapy, skin care and topical dressings are used to treat venous ulcers

SPECIAL CONSIDERATIONS:

Pediatrics

- The incidence of PTS is reported to be as high as 15% in children with DVT.
- There are no pediatric studies evaluating safety and efficacy of therapy for PTS.
- Symptomatic management of PTS in children may follow adult guidelines.
- Pediatricians with expertise in thromboembolism should manage, where possible, pediatric patients with DVT. When this is not possible, a combination of a neonatologist/pediatrician and adult hematologist supported by consultation with an experienced pediatric hematologist is recommended.

OTHER RELEVANT THROMBOSIS CANADA CLINICAL GUIDES:

- Deep Vein Thrombosis (DVT): Diagnosis
- Deep Vein Thrombosis (DVT): Treatment
- Venous Thromboembolism: Duration of Treatment

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