PREVENTION AND TREATMENT OF VENOUS THROMBOEMBOLISM

International Consensus Statement 2013
Guidelines According to Scientific Evidence

*(Developed under the auspices of the:)*

Cardiovascular Disease Educational and Research Trust (UK)
European Venous Forum
North American Thrombosis Forum
International Union of Angiology and
Union Internationale du Phlebologie
Prevention of Post-Thrombotic Syndrome

Chapter 22
General Considerations
Post-thrombotic Syndrome

- ~30-50% of patients with DVT develop the post-thrombotic syndrome (PTS)\(^1\)
  - PTS develops despite appropriate anticoagulation therapy
  - Established PTS is a significant cause of chronic incapacity\(^2-5\)
- PTS is the result of venous hypertension from reflux in veins with damaged valves, outflow obstruction or a combination of both\(^6\)
- Venous hypertension is associated with chronic inflammation\(^7\)
  - Excessive capillary leakage
  - Skin nutrition becomes impaired
  - Development of skin ulceration

General Considerations

Signs and Symptoms of PTS

- **Signs and symptoms of PTS may vary**\(^1\)
  - Venous ulcer is the most predictive clinical finding\(^1,2\)
  - Develop as early as 3 months of DVT\(^1,2\)

- **Factors associated with development of PTS include**\(^3-7\)
  - Iliofemoral DVT
  - Chronic iliofemoral vein obstruction
  - Increased BMI
  - Recurrent DVT

- **Elevated inflammatory biomarkers (IL-6, ICAM-1, CRP) are associated with increased rates of PTS post-DVT**\(^8,9\)

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Prevention of PTS
Prevention of Primary and Secondary DVT

- Prevention of DVT should reduce the prevalence of PTS in the general population\(^1\)
- Guidelines aimed to reduce PTS and leg ulcers by 50% by year 2020 have been published\(^2\)

Effective graduated elastic compression has been shown to reduce venous hypertension, edema and minimize the damage to the microcirculation\textsuperscript{1,2}

- Four RCTs (745 patients) have demonstrated that elastic compression for 2 years in patients with proximal DVT reduced the incidence of PTS from 39% to 19% (RR 0.49; 95% CI 0.38 to 0.62)\textsuperscript{3-6}

- Treatment of DVT with LMWH combined with early ambulation and elastic compression further prevents the PTS\textsuperscript{7,8}

Early surgical thrombectomy for iliofemoral DVT may increase iliac vein patency versus anticoagulation therapy alone (67% vs 34%; RR 1.92; 95% CI 1.06 to 3.51)\(^1,2\)

- Incidence of PTS decrease from 93% with anticoagulation only to 58% with thrombectomy (RR 0.63; 95% CI 0.44 to 0.90) \(^1,2\)

- Catheter directed thrombolysis increased vein patency and reduced PTS compared with conventional anticoagulation therapy in a limited number of patients\(^3-6\)

Catheter directed thrombolysis increases vein patency and reduces PTS\(^1-^7\)

- Two RCTs (138 patients) demonstrated a patency rate of 70% in the CDT group and 33% in the standard anticoagulation therapy group (RR 0.48; 95% CI 0.33 to 0.70)\(^5,^6\)

- Another RCT (209 patients) showed iliofemoral patency rates at 6 months of 64% with CDT versus 47% with conventional treatment (RR for patency 1.42; 95% CI 1.09 to 1.85)\(^7\)
  - At 24 months, PTS developed in 41% of patients in the CDT group and 56% of patients with conventional treatment (RR 0.74; 95% CI 0.55 to 1.00; P=0.047)

5. Elsharawy M, Elzayat E. Eur J Vasc Endovasc Surg 2002; 24:209-14
Review of Evidence
Percutaneous Endovascular Venoplasty and Stenting

- Observational studies suggest percutaneous endovascular venoplasty and stenting to relieve chronic venous obstruction may alleviate PTS\textsuperscript{1,2}
- In the largest series published\textsuperscript{1}
  - At 72 months, primary, assisted-primary, and secondary cumulative patency rates were 79%, 100%, and 100% in non-thrombotic disease and 57%, 80%, and 86% in thrombotic disease
  - Severe leg pain (VAS >5) and leg swelling (grade 3) decreased from 54% and 44% pre-stent to 11% and 18% post-stent
  - At 5 years, cumulative rates of complete relief of pain and swelling were 62% and 32% and ulcer healing was 58%

Review of Evidence
Long-Term LMWH Therapy and PTS

- Studies have demonstrated that long-term LMWH produces improved recanalization\(^1\)-\(^6\)
- Meta-analysis of 5 studies reported improved recanalization and a reduced risk ratio of 0.66 (95% CI 0.57 to 0.77; \(P < 0.0001\)) in favor of long-term LMWH\(^7\)
- Pooled analysis of studies yielded an 87% risk reduction with LMWH in the incidence of venous ulcers (\(P=0.019\))\(^8\)-\(^9\)

Recommendations
Prevention of Post-Thrombotic Syndrome

- Early thrombus removal using CDT or pharmacomechanical thrombolysis may be used in expert centers in selected patients with iliofemoral DVT
  - Level of evidence: Low

- If thrombolysis is contraindicated, surgical thrombectomy could be used in expert centers
  - Level of evidence: Low

- Angioplasty and stenting of a proximal stenosis along with early thrombus removal may be required
  - Level of evidence: Low
Recommendations
Prevention of Post-Thrombotic Syndrome

- Although conventional anticoagulation therapy is based on a high level of evidence in terms of VTE recurrence, prolonged therapy with LMWH in patients with proximal DVT is preferable in terms of PTS prevention
  - Level of evidence: Moderate

- In patients with proximal DVT, graduated elastic compression stockings for at least two years in addition to appropriate anticoagulation are recommended
  - Level of evidence: High