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Aggressive Management of Chronic DVT and the Postthrombotic Syndrome

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Deep vein thrombosis (DVT) is a common and potentially devastating condition that can lead to permanent disability with significant morbidity and even mortality. DVT incidence estimates range from 350,000 to 600,000, with some estimates as high as 2 million, leading to 100,000 to 650,000 deaths.^[1-4]

According to the National Alliance for Thrombosis and Thrombophilia, approximately 60% of patients in whom DVT develops will recover without further symptoms. However, 40% will have some degree of postthrombotic syndrome, (PTS) and in 4%, severe PTS will develop.^[5] The American Venous Forum suggests that PTS will develop in up to two thirds of patients with DVT.^[6] Although the severity of PTS can vary, the signs and symptoms can be lifestyle-limiting and include pain, edema, telangiectasia, hyperpigmentation, lipodermatosclerosis, and ulceration. The more severe symptoms of PTS reportedly occur in 7% to 23% of affected patients, whereas venous ulceration is seen in 5% to 10% of patients.^[4,6]

PTS is thought to occur after earlier venous thrombosis leads to venous hypertension from venous obstruction, valvular damage, and venous insufficiency (reflux).^[6] Venous hypertension can lead to changes in the capillary and lymphatic microcirculation that cause capillary leak, fibrin deposition, erythrocyte and leukocyte sequestration, thrombocytosis, and inflammation. These changes reduce skin and tissue oxygenation, which in turn cause the clinical manifestations of PTS.^[7] Factors that can result in PTS include:

- The extent of DVT;
- The rate of recanalization;
- Episodes of ipsilateral DVT recurrence;
- The extent of venous reflux; and
- Venous valvular function.^[6]

Kahn and colleagues^[8,9] demonstrated that age, previous DVT, more extensive DVT, and severity at 1 month were the best predictors of long-term severity.

Diagnosis of Postthrombotic Syndrome

The diagnosis of PTS is made when the classic signs and symptoms develop in patients with a history of DVT. Two clinical tools may be used to help measure the degree of PTS: the Villalta scale and the CEAP (Clinical manifestations, Etiological factors, Anatomical distribution and Pathophysiological conditions) classification, which will not be reviewed here. Diagnostic testing with compressive venous Doppler examination is useful in identifying PTS in patients with classic signs and symptoms but without a history of DVT.^[4,7] In patients with a history of DVT, Doppler ultrasound is helpful in determining the current extent of DVT, the degree of recanalization as well as collateralization, and whether invasive treatment is of potential benefit.

Venous insufficiency evaluation is important in documenting the presence and severity of venous reflux. In patients with thrombus that extends into the iliac system or whose clinical signs or symptoms are suggestive of a more central involvement (bilateral involvement, history of inferior vena cava (IVC) filter placement, superficial varicosities on the pelvic or abdominal wall), then further imaging with computed tomography or magnetic resonance venography may be advantageous in identifying the central extent of the thrombus. More advanced imaging also gives an overview of the anatomy, identifying anatomic variants and May-Thurner compression and excluding extrinsic compression from a pelvic mass; it is also useful for planning potential access sites (eg, possible internal jugular approach if extensive IVC and pelvic thrombosis are present).

Treatment of DVT

The gold standard in treating chronic venous disease is to control or improve symptoms, reduce edema, venous hypertension and reflux and to promote venous ulcer healing. A traditional method of DVT treatment and prevention of PTS sequelae is adequate anticoagulation of appropriate duration to reduce recurrent DVT. In conjunction with graded elastic compression stockings (ECS), this has been shown to reduce the risk for PTS.^[4,7,10] Early on, it may be necessary to use leg elevation or initiate ECS therapy with lower-grade 20- to 30-mm Hg knee-high stockings. As the pain, edema, and inflammation resolve, the patient can progress to the 30- to 40-mm Hg ECS. The American College of Chest Physicians recommends the use of ECS for a minimum of 2 years from the onset of DVT, or longer if a benefit is seen.^[11,12] Depending on the severity of the PTS and the benefit of the ECS, compression therapy may be lifelong. If venous stasis ulcers are present, persist despite aggressive medical management, or show signs of infection, referral to a lymphedema clinic, wound care clinic, and possibly an infectious disease specialist may be indicated. In addition, evaluation for superficial reflux and for possible endovenous ablation therapy or the use of horse chestnut seed extract could be considered.^[4,7] However, in those patients with chronic and occlusive venous thrombosis who have postthrombotic sequelae resistant to standard therapies, a more aggressive approach to improving venous outflow should be considered.

Thrombolytic therapy. The role of thrombolytic therapy in the prevention of PTS in patients with acute DVT is currently being investigated with the ATTRACT ([Acute Venous Thrombosis: Thrombus Removal with Adjunctive Catheter Trial](#)) study (sponsored by the Society of Interventional Radiology and the National Institutes of Health National Heart, Lung and Blood Institute). Patients with acute DVT are randomly assigned to either anticoagulation alone or anticoagulation with thrombolytic therapy, which may include the use of a pharmacomechanical device to remove the DVT. The reported benefit is to rapidly remove the thrombus and restore patency while preserving venous valve function, reducing venous insufficiency and thus PTS. The incidence of PTS will be evaluated in both cohorts to determine the effectiveness of thrombolytic therapy in reducing PTS.^[13] A review of literature on PubMed showed no studies evaluating the effectiveness of endovascular intervention for chronic DVT.

Ultrasound-accelerated thrombolysis. More recently, the results of interventional treatment in patients with symptomatic chronic DVT (> 30 days from onset of symptoms) have been reported. The investigator presented single-center outcomes of aggressive therapy in the treatment of symptomatic chronic DVT at the 2009 Veith Symposium on Vascular and Endothelial Issues in New York. The study showed that when completely traversing the chronic thrombus was successful, symptomatic improvement was achieved in all patients. During this retrospective review of 53 patients, the use of ultrasound-accelerated thrombolysis (EkoSonic Endovascular System, EKOS Corp., Bothell,

Washington) was shown to have a positive effect and to improve outcomes when compared with standard catheter-directed thrombolysis.^[14]

The exact mechanism of action of EKOS and what factors may lead to improved outcomes are not completely understood. However, in our practice, the benefit of using standard endovascular techniques to cross the hard, chronic thrombus, and to create "space" for channels of flow with balloon maceration followed by ultrasound-accelerated thrombolysis overnight (Figure) is becoming more evident. In my experience, this can lead to improved venous outflow, and when performed in combination with therapeutic anticoagulation (enoxaparin sodium injection) for 8 weeks and a standard ECS regimen, a significant reduction in symptoms and improved quality of life are achieved. Thus far, we have noted improved outcomes when enoxaparin sodium therapy has been initiated. Patients must undergo therapeutic anticoagulation prior to intervention and anticoagulation must be maintained throughout the procedure. Long-term venous patency and clinical improvement have been seen. There are now patients who are 3 years postintervention who have maintained venous patency as shown on Doppler examination and by continued symptomatic relief. The success of this treatment is in the ability to traverse the hard occlusive clot. This often takes time and perseverance because extensive occlusions involving the IVC, iliac, and femoral veins can take a full day to be successful. Development of newer devices that "chisel away" and allow easier crossing of the occlusions would be a significant advancement in the ability to treat patients with chronic DVT and PTS.

Preprocedural Evaluation:

- History and physical examination with documentation of PTS signs and symptoms
- Confirm occlusive DVT by recent venous Doppler examination
- If signs or symptoms suggest more central involvement, consider CT or MRV
- Maximize medical management with therapeutic anticoagulation, elastic compression stocking therapy if pulses are present, or sequential lymphedema pump therapy if indicated
- If venous ulcers are present, make referral for wound care

Procedure. If significant symptoms persist despite medical management, consider intervention:

- Preprocedural laboratory tests: CBC, electrolytes, DIC screen/coagulation panel
- Initiate therapy with enoxaparin sodium (1 mg/kg twice a day)
- Ultrasound-guided micropuncture access
 - Popliteal vein if femoral-popliteal DVT present
 - Femoral vein if no infrainguinal DVT present
 - Consider IJ if unable to cross DVT from lower extremity access
- Once occlusion is successfully crossed:
 - Balloon maceration of occlusive DVT segments with 8- or 10-mm balloons
 - Initiation of overnight EKOS ultrasound-accelerated thrombolysis
 - Follow-up venography with venous angioplasty of residual stenoses
 - Venous stenting of chronically narrowed segments in iliac and IVC segments
 - Stenting of common or upper femoral segments only if no flow from superficial femoral to common femoral veins
 - Pneumatic compression boots while in hospital receiving lytic therapy and at bedrest

Postprocedural Care

- Discharge on enoxaparin sodium therapy for 8 weeks, and at minimum, provide appropriate knee-high elastic compression stocking therapy
- Follow-up venous Doppler examination and office visits at 1, 3, 6, and 12 months
- Re-evaluate and remeasure for ECS if swelling improves
- Consider adjunctive therapies if indicated (wound care, lymph pump, etc)

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Figure. Algorithm for aggressive management of chronic DVT and postthrombotic syndrome. *CBC* = complete blood count; *CT* = computed tomography; *DIC* = disseminated intravascular coagulation; *DVT* = deep vein thrombosis; *ECS* = elastic compression stocking; *EKOS* = EkoSonic Endovascular System; *IJ* = internal jugular; *IVC* = inferior vena cava; *MRV* = magnetic resonance venography; *PTS* = postthrombotic syndrome

Conclusion

In summary, the aggressive management of chronic DVT and PTS sequelae warrants further investigation. Thus far, this treatment has been shown to be beneficial. When successful channels of flow have been created and improved venous outflow is achieved, improved quality of life can be attained, with the potential ability of the patient to return to the workplace. If positive long-term results can be attained, the socioeconomic burden caused by severe PTS can be reduced. With dedicated interventionalists leading the way, the burden of chronic DVT and PTS can be diminished while providing hope that an improved quality of life can be achieved.