



BRIEF ANSWERS
TO SPECIFIC
CLINICAL
QUESTIONS

Q: Which lower-extremity DVTs should be removed early?

SAMIR K. SHAH, MD

Department of General Surgery, Cleveland Clinic

DANIEL G. CLAIR, MD

Chairman, Department of Vascular Surgery, Cleveland Clinic;
Professor of Surgery, Cleveland Clinic Lerner College of Medicine of Case Western Reserve University, Cleveland, OH

A: EARLY THROMBUS REMOVAL for lower-extremity deep venous thrombosis (DVT) is at present only modestly supported by evidence and so remains controversial. It is largely aimed at preventing postthrombotic syndrome.

The decision to pursue early thrombus removal demands weighing the patient's risk of postthrombotic syndrome against the risks and costs associated with thrombolysis and thrombectomy, such as bleeding complications. In the final analysis, this remains a subjective decision.

With these caveats in mind, the best candidate for early thrombus removal is a young patient with iliofemoral DVT with symptoms lasting fewer than 14 days.

■ POSTTHROMBOTIC SYNDROME IS COMMON

Anticoagulation with heparin and warfarin is the mainstay of DVT therapy. Indeed, the safety of this therapy and its effectiveness in reducing thrombus propagation and DVT recurrence are well established. Neither heparin nor warfarin, however, actively reduces the thrombus burden. Rather, both prevent the clot from propagating while it is, hopefully, gradually reabsorbed through endogenous mechanisms.

Up to 50% of DVT patients develop postthrombotic syndrome. A variety of mechanisms are involved, including persistent obstructive thrombosis and valvular injury.¹ But much remains unknown about the etiology, and some patients develop the condition in the absence

doi:10.3949/ccjm.80a.12147

of abnormalities on objective testing.

Symptoms of postthrombotic syndrome can range from mild heaviness, edema, erythema, and cramping in the affected limb to debilitating pain with classic signs of venous hypertension (eg, venous ectasia and ulcers). It accounts for significant health care costs and has a detrimental effect on quality of life.¹ Thus, there has been interest in early thrombus removal as initial therapy for DVT.

■ THROMBUS REMOVAL

Venous clots can be removed with open surgery or, more typically, with percutaneous catheter-based thrombolysis and thrombectomy devices that use high-velocity saline jets, ultrasonic energy, or wire oscillation to mechanically fragment the venous clot. All of these mechanisms help with drug delivery and pose a minimal risk of pulmonary embolism.

Evidence is weak

Patients with DVT of the iliac venous system or common femoral vein are at highest risk of postthrombotic syndrome. Therefore, the Society for Vascular Surgery and the American Venous Forum have issued a grade 2C (ie, weak) recommendation in favor of early thrombus removal in patients with a first-time episode of iliofemoral DVT with fewer than 14 days of symptoms.² Moreover, patients must have a low risk of bleeding complications, be ambulatory, and have reasonable life expectancy.

The recommendation is buttressed by a Cochrane meta-analysis that included 101 patients.³ It concluded that there was a significant decrement in the development of postthrombotic syndrome with thrombolysis (but without mechanical thrombectomy) compared

This controversial therapy is best considered in cases of proximal DVTs in younger patients

with standard therapy: the rate was 48% (29/61) with thrombolysis, and 65% (26/40) with standard therapy.³

More recently, the Catheter-Directed Thrombolysis Versus Standard Treatment for Acute Iliofemoral Deep Vein Thrombosis (CaVenT) study, a randomized prospective trial in 189 patients, demonstrated a lower rate of postthrombotic syndrome at 24 months and increased iliofemoral patency at 6 months with catheter-directed thrombolysis with alteplase (41.1% and 65.9%) vs anticoagulation with heparin and warfarin alone (55.6% and 47.4%).⁴

The Acute Venous Thrombosis: Thrombus Removal With Adjunctive Catheter-directed Thrombolysis (ATTRACT) trial is an ongoing prospective randomized multicenter trial of the effect of thrombolysis on postthrombotic syndrome that also hopes to clarify the relative benefits of different methods of pharmacomechanical clot removal.

While CaVenT has not been criticized extensively in the literature, other studies supporting early intervention for iliofemoral venous thrombosis generally have been noted to have a number of shortcomings, including a lack of randomization, and consequent bias, and the use of surrogate end points instead of a direct assessment of postthrombotic syndrome.

Reflecting the weakness of the evidence, the American College of Chest Physicians has issued a grade 2C recommendation *against* catheter-directed thrombolysis and against thrombectomy in favor of anticoagulant therapy.⁵

A subjective, case-by-case decision

The decision on standard vs interventional therapy must be made case by case. For example, thrombus removal may be more appropriate for a physically active young patient who is more likely to be impaired by postthrombotic syndrome, whereas standard warfarin therapy may be preferable for a sedentary patient. We

are also more inclined to offer thrombus removal to patients who have worse symptoms.

Complicating the issue, many patients present with a mix of variables that support and oppose intervention—eg, a moderately active elderly patient with an unclear life expectancy and a history of gastrointestinal bleeding. At present, there is no way to quantitatively evaluate the risks and rewards of thrombus removal, and the final decision is essentially subjective.

Additional facts warranting consideration include the possibility that thrombolysis may require several days of therapy with daily venography for evaluation. Monitoring in the intensive care unit is normally required during the period of thrombolysis. Patients should be apprised of these elements of therapy beforehand; obviously, those who are unwilling to comply are not candidates.

Not a substitute for anticoagulation

It is important to recognize that thrombus removal is not a substitute for standard heparin-warfarin anticoagulation, which must also be prescribed.⁵ Thus, patients who cannot tolerate standard post-DVT anticoagulation should not undergo thrombus removal. Furthermore, the current evidence supports the use of standard anticoagulation over early thrombus removal of DVTs that are more distal in the lower extremity, such as those in the popliteal vein.⁵

PHLEGMASIA CERULEA DOLENS IS A SPECIAL CASE

Phlegmasia cerulea dolens—acute venous outflow obstruction associated with edema, cyanosis, and pain that in the worst cases may lead to shock, limb loss, and death—constitutes a special case. Although we lack robust supporting evidence, phlegmasia is a commonly accepted indication for early thrombus removal as a means of limb salvage.^{2,6}

REFERENCES

1. Kahn SR. The post thrombotic syndrome. *Thromb Res* 2011; 127(suppl 3):S89–S92.
2. Meissner MH, Gloviczki P, Comerota AJ, et al; Society for Vascular Surgery; American Venous Forum. Early thrombus removal strategies for acute deep venous thrombosis: clinical practice guidelines of the Society for Vascular Surgery and the American Venous Forum. *J Vasc Surg* 2012; 55:1449–1462.
3. Watson LI, Armon MP. Thrombolysis for acute deep vein thrombosis. *Cochrane Database Syst Rev* 2004; 4:CD002783.
4. Enden T, Haig Y, Kløw NE, et al; CaVenT Study Group. Long-term outcome after additional catheter-directed thrombolysis versus standard treatment for acute iliofemoral deep vein thrombosis (the CaVenT study): a randomised controlled trial. *Lancet* 2012; 379:31–38.
5. Kearon C, Akl EA, Comerota AJ, et al; American College of Chest Physicians. Antithrombotic therapy for VTE disease: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. *Chest* 2012; 141(suppl 2):e419S–e494S.
6. Patterson BO, Hinchliffe R, Loftus IM, Thompson MM, Holt PJ. Indications for catheter-directed thrombolysis in the management of acute proximal deep venous thrombosis. *Arterioscler Thromb Vasc Biol* 2010; 30:669–674.

ADDRESS: Samir K. Shah, MD, Desk 100, Cleveland Clinic, 9500 Euclid Avenue, Cleveland, OH 44195; e-mail: Samirshah.0@gmail.com