

Advances in Hematology

Section Editor: **Craig M. Kessler, MD**

*Current Developments in the
Management of Hematologic Disorders*

Catheter-Directed Thrombolytic Therapy for the Treatment of Deep Venous Thrombosis

Pamela A. Flick, MD

Chief, Vascular and Interventional Radiology

Department of Radiology

Georgetown University Hospital

Could you give some historical perspective on the use of catheter-directed therapy for the treatment of DVT?

In the initial studies comparing intravenous (IV) streptokinase to heparin therapy for the treatment of deep venous thrombosis (DVT) of the lower extremities, those patients who were treated with IV therapy had a better overall outcome. In addition, the risk of developing chronic venous insufficiency were lower for patients receiving IV therapy than for patients who received anticoagulation alone.

A number of studies have shown similar results. Dr. Anthony Comerota of the Jobst Vascular Center in Ohio analyzed 13 different series in order to compare IV therapy with heparin alone. In this large study, only 4% of patients receiving heparin alone experienced significant or complete lysis, compared with 82% of patients receiving IV therapy.

Another study evaluated popliteal reflux at the popliteal valve level in patients receiving IV anticoagulation versus IV systemic thrombolytics. Patients who had received IV thrombolytic therapy experienced resolution or improvement at a higher rate than those who received anticoagulation alone with no thrombolytic therapy. These patients were followed for 5–10 years and were evaluated for popliteal reflux and restoration of valvular function at this level. The outcomes were significantly better for patients who received IV thrombolytic therapy.

In the 1980s, Drs. Dake and Semba of Stanford University published the first series of patients receiving catheter-directed therapy. Twenty-one patients were enrolled, with a total of 21 limbs being treated. According to the study findings, if the catheterization was successful, the rate of symptomatic and clinical improvement was approximately 95%.

How is improvement defined for DVT patients?

Improvement is defined as resolution of thrombus, either partial or complete, and/or improvement of reflux, and/or no development of postthrombotic syndrome or chronic venous hypertension.

Is catheter-directed therapy a standard approach for treating DVT?

No. The standard therapy is still anticoagulation with either heparin followed by warfarin (Coumadin, Bristol-Myers Squibb) or enoxaparin (Lovenox, Aventis). It is difficult to educate patients and clinicians about the benefits of catheter-directed DVT. Often, DVT patients are overlooked because it is not life threatening, even though most patients will develop chronic venous insufficiency within 3–10 years of their initial acute event.

Why does chronic venous insufficiency develop?

Especially in iliofemoral DVT, the clot burden cannot be broken down by heparin, warfarin, or enoxaparin. These agents simply prevent propagation of thrombus from forming on the clot that is already present. The body's own fibrinolytic cascade mechanism must dissolve the clot. Large clots are not able to be dissolved by the body, later resulting in chronic occlusion. The incidence of DVT after an acute event is quite high, approximately 36%. With catheter-directed therapy, the thrombolytics dissolve the clot, relieving the obstruction and preventing venous hypertension, which is caused by blockage of outflow.

Why is catheter-directed therapy not a standard approach for treating DVT?

There are risks and requirements associated with this approach. The risk of intracranial bleeding associated with any thrombolytics is approximately 1–2%. Bleeding at the puncture site and bleeding outside the area of the catheter, whether retroperitoneal or gastrointestinal or other bleeding, may also be associated with this approach. In addition, catheter-directed therapy requires a hospital stay, which is often not as attractive to patients as outpatient treatment. Also, while prices have come down over the years, thrombolytics were initially quite expensive.

Are DVT patients generally not being treated as effectively as they could be?

I think that the overall outcome for these patients could be improved and that complications associated with DVT could be alleviated if catheter-directed therapy were offered as an alternative to anticoagulation alone.

Has there ever been a prospective trial comparing catheter-directed therapy with anticoagulation?

There has never been a clinical trial comparing the long-term benefits of these approaches. The ongoing TOPAZ study is comparing catheter-directed thrombolytic infusion versus anticoagulation for lower extremity DVT. The study should be completed within a year or 2 and will hopefully provide firm data for treatment decision making, beyond the speculation and anecdotal reports to which we are currently limited.

What is the connection between catheter-directed therapy and radiology?

Traditionally, interventional radiologists and vascular surgeons have been most interested in the treatment of DVT using this approach. Vascular surgeons initially performed surgical thrombectomies for DVT in the US, an approach that was found to be not very effective.

A number of mechanical devices are available. The development of combination therapies has enabled the process to occur in a shorter amount of time while also reducing the risk of bleeding, because lower doses can be used. The devices help break up the thrombus, creating a channel that allows the thrombolytics to remove any remaining thrombus. Treatment can now be completed in 24–48 hours, rather than 4–5 days, although this improvement increases the expense.

Has the rate of recurrence been compared between DVT patients treated with catheter-directed therapy versus anticoagulation alone?

There has not been a direct comparison made. One study found that 10–29% of patients receiving anticoagulation will develop more clots. Proximal venous thrombosis is associated with a 20–50% risk of recurrence in iliofemoral thrombus.

Could you describe the technique for administered catheter-directed therapy?

Catheter-directed therapy is usually approached using ultrasound guidance and a micropuncture, 22-gauge needle. When the patient is lying prone, the catheter is passed not

against the valve but with the valve, so that it easily passes through the thrombus area into an area of normal flow. Once the catheter is inserted, infusion continues for approximately 24 hours. Patients are reevaluated every 12–24 hours with a repeat venogram in order to assess whether or not lysis has occurred. Treatment is stopped if no change has occurred in 12–24 hours. Such a situation indicates significant chronic disease or a long-term presence of a clot, which would then be treated accordingly.

Once the clot is dissolved, the underlying vein is evaluated. Often, there is a narrowing or indentation of the vein, particularly where it is crossed by the artery, a situation known as May-Thurner syndrome. The compression of the vein triggers the artery to cross over toward the other leg. This movement can slow the flow of blood by causing it to thrombose. When the underlying venous narrowing or lesion has been identified, it is effective to stent the area with a metal stent in order to keep the vein open so that flow will remain normal, without thrombosis. Patients are followed with ultrasound at 3, 6, and 12 months, and are often given compression stockings. Anticoagulants are given for 3–6 months after the procedure.

Patients presenting with cerulea dolens, a state in which the blood flow is blocked because the DVT is so extensive within the leg, require emergency treatment. Such patients are at risk for losing the affected limb, but flow can be reestablished fairly easily using a catheter.

Is ultrasound the standard diagnostic approach?

Ultrasound is the current standard for diagnosis of DVT. False negatives do occur, and a recent study found that computed tomography could effectively be used, although the expense would be greater. If the ultrasound is questionable, a venogram could be done to confirm the findings.

Suggested Reading

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