

Update: Contemporary Treatment of Deep Vein Thrombosis

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Patients with deep vein thrombosis (DVT) aren't admitted to the hospital and started on IV heparin very often anymore. Two articles appearing in the same issue of the *New England Journal of Medicine* in 1996, one from Holland, one from Canada, reported success with mostly outpatient treatment of these patients. In the USA, adoption of outpatient treatment has been slower for many reasons, yet today, many USA patients diagnosed with DVT are never admitted to the hospital.

How do patients present?

Approximately 1 in 1000 persons has an episode of DVT every year. Surveys have shown the average duration of discomfort is 4 days before patients finally present to a physician. Physical examination of the leg may show swelling, redness, or very little, and cannot make or refute a diagnosis. Ultrasound is the test most commonly employed (B-mode, usually with Doppler, also called "duplex ultrasound") and is very sensitive, specific, and predictive for DVT in symptomatic patients.

After a positive diagnosis, what next?

Treatment should be started promptly for lower extremity DVT because these clots may embolize to the lung and cause fatal pulmonary embolism (PE). In fact, studies evaluating the lungs in DVT patients have shown that about 50% of patients with proximal DVT (involving the popliteal or thigh veins or above) already have PE, most of the time asymptomatic, when they are diagnosed with DVT.

Initial treatment of symptomatic DVT must be with an injected anticoagulant, not merely an oral one. A convincing study showed an unacceptable risk of important recurrent thromboembolism if acute treatment with the injected anticoagulant was omitted.

For patients with important co-morbid conditions or significant risk of bleeding, hospitalization is best, in order that the response to treatment can be observed. But for many patients with DVT, the next step after diagnosis is prescription of a low molecular weight heparin (LMWH) to be injected in the subcutaneous skin of the abdominal wall (just like insulin). The dosage is adjusted by the patient's actual weight. Some of the LMWHs are dosed in milligrams, some in Units, some come in pre-filled syringes, some in vials. Usually the patient has been examined by a physician before the duplex ultrasound study was ordered. A prescription can be called into a pharmacy for the patient to pick up the drug and start treatment if the patient knows how to self-inject (or has someone to help do that).

What are the components of treatment?

Bedrest is no longer widely considered an important part of treatment, unless the leg is painful. If it is, elevating the sore leg while receiving heparin or LMWH will often reduce the pain.

The risk of a lower extremity DVT embolizing to the lung is no longer considered increased in patients who ambulate.

An injected LMWH (in outpatients or inpatients) is the usual acute treatment and succeeds in preventing recurrence about 95% of the time. The LMWHs are injected sq every 12 or 24 hours (depending on the drug). A CBC with platelet count and screening chemistry are obtained at treatment start because (1) unsuspected renal insufficiency should change dosage and (2) the patient may have other occult disease that can be picked up. LMWHs don't require PTT or PT monitoring and will often raise a PTT a very few seconds or not at all.

Warfarin (Coumadin) is usually started simultaneously, at 4 or 5 mg, without a loading dose. Three conditions must be satisfied to discontinue the LMWH and leave the patient on warfarin alone: (1) The patient should be medically stable with the DVT substantially improved, (2) LMWH should have been given for a minimum of 4 to 5 days, and (3) The INR for warfarin should be between 2.0 and 3.0 for at least 2 days. Since injected anticoagulants are more effective than oral ones, a very large DVT may require longer treatment with injected anticoagulant before relief is obtained. In that circumstance, the warfarin is continued, with a longer overlap period for the two drugs, since one can't predict in advance how many days it will take for a DVT to begin to show improvement. Warfarin is monitored by the INR (which prolongs both the PT and PTT in many labs, but the PT is the relevant test), initially frequently, then less frequently.

Studies appear to show that if the leg (or legs) with DVT are placed in moderate grade knee-high elastic compression stockings (20-30 mm Hg at the ankle), the risk of post-thrombotic syndrome (aching and/or swelling without proven recurrent DVT) is reduced. In these studies the patients were to wear the stockings for 2 years; I recommend these for the affected leg(s) for at least 6 months. They should be worn except while sleeping and bathing. They can be purchased over the internet for about \$50 a pair (Jobst and Sigvaris are two popular brands). The stocking's elastic decays after about 3 months and they require replacement.

How long does the patient require treatment?

This remains controversial. Idiopathic DVT (no apparent risk factor identified) is often treated for 6 months. DVT in which a risk factor was identified and removed (e.g., peri-operative after hernia surgery, oral contraceptive pills, etc.) is sometimes treated for only 3 months. One concept gaining favor, which I employ, is to re-image the thrombosis with a repeat ultrasound examination at the time I contemplate stopping treatment (3 or 6 months). On average, the normalization rate at 3 months is 30%; it is about 50% at 9 months. Normalization rates will vary depending on the location and extent of the clot, with proximal clots involving the popliteal and femoral veins having the lowest rates of 6-month normalization.

The overall recurrence rate for DVT is about 20% over 5 years. The fact that warfarin, even when carefully managed, has a major hemorrhage risk of about 4% per year in the community at large is the primary reason patients aren't left on the drug indefinitely.

If I had contemplated stopping treatment (at 3 or 6 months) and a fully occlusive or significantly occlusive clot is still present despite wearing of moderate pressure knee-high stockings, I ask if the patient has had considerable trouble with warfarin. If not, I suggest continuing 3 more months and repeating the ultrasound exam.

Can lower-intensity warfarin be used?

In a recent study, patients with idiopathic DVT were randomized after 6 months of treatment to receive either placebo (no warfarin) or warfarin with an INR of 1.5 to 2.0, so-called "low intensity warfarin". The results showed a significant decrease in recurrent DVT without a significant increase in major bleeding in the low intensity warfarin group. However a simultaneous study (New England Journal, 8/14/03) compared the usual INR of 2.0 to 3.0 to this lower-intensity INR and found equal bleeding but more recurrent DVT in the lower-intensity group. The latter results would suggest that lower-intensity warfarin bleeds no less but does lead to more DVT than usual intensity warfarin. How to handle these patients remains unsettled.

Should LMWH be continued for the entire treatment period, rather than giving warfarin?

When used for chronic treatment, LMWH requires an injection, usually once daily during the chronic treatment period, and costs more at the pharmacy than warfarin does, although INR monitoring of warfarin adds additional expense. LMWH is more effective in preventing recurrent DVT and likely provokes less bleeding than warfarin in cancer patients with DVT over 3

or 6 month follow-up, so a recent New England Journal editorial recommended it as preferred treatment for DVT for these patients.

Does DVT limited to the calf veins or superficial (for example, saphenous) vein thrombosis require the same treatment?

Available evidence does not allow firm answers to these questions. Most experts would treat symptomatic calf vein thrombosis for 3 months at least (asymptomatic calf vein DVT discovered in a venogram for a clinical trial may be another matter). Treatment of symptomatic calf DVT is identical to that of other DVT: an injected anticoagulant, followed by warfarin. Superficial vein thrombosis is another matter: many experts would use warm compresses and non-steroidal drugs and observe for resolution or progression to DVT.

Should hypercoagulable states be searched for in DVT patients?

Passions abound on this issue but stripping them away, nearly all experts would agree that blood testing for an antiphospholipid antibody, especially a lupus anticoagulant, would influence management (i.e., lead to prolonged anticoagulation until/unless it goes away). Limited, target testing for other thrombophilic states can be useful, tailored to the patient's demographic and family history information.

Summary

The treatment of DVT has evolved a great deal from the era of automatic hospitalization and heparin iv drips while warfarin was begun. Further evolution (e.g., twice-daily oral anticoagulant warfarin substitutes that don't require monitoring, once-weekly sq injections of synthetic heparin derivatives) are also under development. However, patient care must be individualized—in the treatment of acute DVT, "one size" still does not fit all.

(The opinions and recommendations expressed in this article are those of the author and do not necessarily reflect the position of Pacific Vascular or any of its Associated Physicians.)

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