

Pro: Calf Deep Venous Thrombosis Should Be Treated with Anticoagulation

Joseph A. Caprini, MD, Jennifer G. Sarayba, MD, Dejan Maksimovic, BS, Catherine J. Glase, BS, Andrew C. MacDougall, BS, Juan I. Arcelus, M.D.

Physicians in the past assumed that calf vein thrombosis (CVT) was a benign, self-limited disease that rarely posed any clinical risks and did not require treatment with anticoagulants. Physicians embracing this philosophy felt that the bleeding risk to the patient from the use of anticoagulants was more likely to cause harm than a calf vein thrombosis. As more research has been done, it turns out that these assumptions are probably not true. Lohr et al¹ conducted an interesting study in 75 patients with isolated CVT monitored at 3-4 day intervals with duplex scans. In her study, 32% of patients with CVT suffered propagation including 5% with pulmonary emboli. Based on her data, the option of doing nothing with CVT seems “illogical and poorly contemplated.” She feels the 4%-10% risk of anticoagulation is safer for the patient than the 32% risk of propagation and 5% risk of pulmonary emboli.²⁻⁴

With the advent of low molecular weight heparin (LMWH), the risk/benefit ratio moves further in the direction of treating calf vein thrombosis with anticoagulation as complications from heparin treatment are minimized. In addition, with the development of outpatient home monitoring and the self-administration of subcutaneous LMWH, anticoagulant therapy is far more cost effective than serial duplex scans. Lohr was unable to identify any specific risk factors that were associated with proximal extension of CVT. The factors examined included obesity, trauma, estrogen use, malignancy, varicose veins, smoking, surgery, activity level, leg pain, swelling, tenderness, discoloration, and leg mass.

Some investigators have found that recurrence of isolated untreated CVT occurs in 20-29% of patients within three months.^{5,6} Hirsh and Lensing⁷ calculated that post thrombotic manifestations would develop in 4% of patients with CVT. Kaakar⁵ has reported that 20% of those with untreated CVT develop recurrent thrombosis which may contribute to the development of valvular incompetence.⁸ Lohr¹ has shown that calf vein thrombi may propagate in up to 32% of patients but also calf vein thrombi that propagate are more likely to result in pulmonary emboli than those CVT that do not propagate.⁹ In addition, studies that use routine lung scanning have documented pulmonary emboli in 33% of patients with CVT, 44% of which were estimated to involve greater than 20% of the lung volume.¹⁰ Of major concern to this author is the fact that calf vein thrombosis was the source of 15-25% of fatal pulmonary emboli in autopsy studies done in three different decades.¹¹⁻¹³ CVT was found to be the source of 5-35% of pulmonary emboli that caused respiratory symptoms in two other studies.^{14,15} Two additional studies done 25 years apart have documented a 33% incidence of silent pulmonary emboli in those with isolated CVT.^{10,16}

Meissner et al¹⁷ also conducted a study to define the early natural history of CVT in relation to persistent lower extremity symptoms, propagation, recanalization, and the development of valvular incompetence. Fifty-eight patients (12%) of a group of 499 patients were found to have isolated CVT, and 29 of these individuals were followed up clinically and with duplex scans at intervals of one day, seven days, one month, every three months for the first year, and yearly for three years. He found that 77% of the extremities were symptomatic at the time of diagnosis. Although the prevalence of clinical signs and symptoms decreased to 29% by one month, 23% of the patients had

persistent pain, edema, or both at 12 months. In contrast, 54% of extremities with proximal DVT remained symptomatic at one year. The recanalization of the calf thrombus load proceeded rapidly, with 50% reduction of the clot load in one month, and total clearing by one year. Reflux, however, was seen in 24 % of the extremities at one year. Although no ulceration was seen in any of the CVT victims at one year, three patients demonstrated skin pigmentation.

Unfortunately, Meissner was unable to follow these patients longer, so one can only speculate as to the eventual incidence of the post-thrombotic syndrome. Among the 24% demonstrating reflux at 12 months, one might assume that most, if not all, of these individuals will develop some form of this long-term disability over time. Propagation of isolated CVT was seen in four patients (13%), and in two more patients with CVT and contralateral proximal DVT despite anticoagulation. Pulmonary emboli were diagnosed in 5/47 patients (11%) at the time of diagnosis of isolated CVT. It is interesting to note that 64/419 patients (15%) with proximal DVT presented with concomitant pulmonary emboli. One CVT patient developed a pulmonary embolus 33 days after CVT diagnosis despite adequate anticoagulation. Overall, 72% of CVT patients were treated with anticoagulants, and this author finds it amazing that despite adequate treatment, these additional problems were seen over time in patients with isolated CVT. This paper certainly does not resolve all of the questions surrounding isolated CVT, but the data presented in this paper should make one think seriously about routine anticoagulation in these individuals.

Langerstedt et al⁶ conducted a randomized prospective trial in 51 patients with isolated CVT diagnosed by contrast venography and comparing three months of Warfarin

to placebo after an initial five day course of heparin treatment. During the first three months eight patients in the placebo group (29%) developed recurrent thrombosis compared to none in the treated group. Three non-fatal pulmonary emboli were seen in the placebo group and two pulmonary emboli developed in the treated group during the first three months. All three pulmonary emboli in the placebo group also had recurrent DVT. After one year, 22 of 23 patients in the Warfarin group were free from any recurrent thrombosis, compared to 19 of 28 patients in the placebo group ($p < 0.02$). Pain scores were similar in both groups, with 56% of patients symptom-free at two weeks, and 93% asymptomatic at three months unless recurrent disease had occurred. Patients with recurrent disease had higher pain scores than those not developing recurrent disease. The author concludes from his study that treatment of all CVT patients with heparin and Warfarin for three months is appropriate.

Another important consideration in CVT is the incidence of markers of thrombophilia. While it is not feasible to test the general population, testing those with CVT may yield important data for the patient and their families. These patients may require longer treatment with anticoagulants depending on the specific defect seen. The presence of these markers may provide critical management strategies on occasion for the patient or family if surgery or other situations arise.

In conclusion, abundant evidence exists that CVT is an important problem. The incidence of recurrent disease, including extension of thrombosis, the post-thrombotic syndrome, and both fatal and non-fatal pulmonary emboli, is significant. Furthermore, the availability of LMWH and other new anticoagulants coming soon allow the safe and effective treatment of these disorders with reduced concern regarding clinically

significant bleeding complications. There will always be exceptions given special patient circumstances, but the authors feel that almost all patients with CVT should receive anticoagulant therapy for an appropriate period of time according to individual clinical circumstances.

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