**DEBATE:** Infrapopliteal DVT Should Not Be Treated Aggressively
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The need for treatment of calf-level DVT remains controversial. There currently is clinical equipoise, with some recommending anticoagulant treatment and others serial observation.\(^1,2\) Outpatient studies report that the proportion of all DVTs that are “distal” is as high as 60% to 70%, demonstrating the magnitude of the problem.\(^2,3\) Calf DVT is more commonly associated with transient risk factors, and has lower mortality than proximal DVT (4.4% vs. 8.0%, \(p<0.01\)).\(^4\) The important clinical consequences of calf vein thrombosis include proximal extension, VTE recurrence, PE, and post-thrombotic syndrome (PTS). The limited available evidence for the natural history of calf level DVT suggests that complications, including PE and PTS, are significantly decreased with distal versus proximal DVT, although these rates still remain high.\(^5\) The studies are highly heterogeneous, and rates vary widely between older and more modern cohorts.

Extension to proximal segments subjects patients to the known risks of proximal DVT. In a review of the literature, the rate of proximal extension was highly variable, ranging from 0% to 23% in patients without anticoagulants to 0% to 44% in patients with anticoagulants.\(^6\) The studies were too heterogeneous to allow comparisons between the untreated and treated patients, or a pooled analysis. In contrast, in studies following patients with serial proximal ultrasound, the rate of proximal extension on the repeat ultrasound in untreated patients ranges from 0.9% to 5.7%.\(^6\) The recent CALTHRO study assessed the clinical consequence of untreated calf DVT in 431 symptomatic outpatients with initial negative ultrasound for proximal vein DVT and an abnormal D-dimer suggestive of distal clot. Calf DVT was identified in 15.3% of subjects, who enjoyed a largely benign clinical course. At 3 month follow-up, excluding 2 patients with proximal clot identified on serial 7 day ultrasound examination, adverse outcomes occurred in 3 patients including: proximal vein extension (1), PE (1), and worsening symptoms (1) \(3/64, 4.7%\) versus patients without calf vein DVT \(0.8\%\), \(p=0.049\).\(^7\) In contrast, in limited randomized studies, recurrent thrombotic events have been noted in up to 29% of patients with inadequately treated calf vein thrombosis.\(^8\) In prospective cohorts of patients with isolated calf-level DVT largely treated with anticoagulants, VTE recurrence rates at 3 months are 2% to 2.2%, including 0.7% to 1.1% rates of PE.\(^4,9\)

Meissner et. al. followed a prospective cohort of patients with acute DVT and noted that at 12 months, PTS symptoms occurred in 23% of limbs with calf DVT \(3/13\), versus 54% with proximal DVT \(51/95\). Mean thrombus load decreased by 50% at 30 days, 75% at 90 days and 100% at 1 year with recanalization. However, valvular incompetence progressed to 24% at one year, likely contributing to the symptoms of PTS.\(^10\) Massuda et al. also studied a cohort of patients with distal DVT and found complete lysis of clot in 14/16 patients \(88\%\) at 90 days. At 3 year follow-up, 9% \(2/23\) had valvular reflux and 5% had severe PTS. Similar findings have been seen in other cohorts. Of note, in all of these small studies, the proportion of patients treated with anticoagulation varied (from 51% to 72%), as well as the length of time of anticoagulation.

Widely accepted management studies suggest that it is safe to withhold anticoagulation in outpatients with suspected DVT if serial compression ultrasound is negative for proximal DVT.
at baseline and 1 week.\textsuperscript{11-16} The pooled estimate of the 3 month thromboembolic risk in untreated patients in studies using only serial proximal vein ultrasound was 0.6\% (95\% CI 0.4\% to 0.9\%).\textsuperscript{1} This strategy is clearly based on the premise that calf level DVT do not need to be treated. Randomized studies assessing the usefulness of anticoagulation in distal DVT are limited. Lagerstedt followed 51 patients with symptomatic distal DVT and found an increased recurrence rate in non-anticoagulated as opposed to anticoagulated patients (29\% vs. 0\%, \( p<0.01 \)). However, this study has been criticized because follow up diagnosis of DVT occurred via insensitive physical examination and serial isotopic tests.\textsuperscript{8} The Anticoagulation of Calf Thrombosis (ACT) pilot study is planned in the UK.\textsuperscript{17}

There is clearly a need for randomized trials assessing the usefulness of anticoagulant treatment in distal DVT and thus, the conclusion of clinical equipoise in treatment options at the present time. However, clinical equipoise does not imply no treatment, just treatment with either serial observation or anticoagulation. As suggested by Masuda in the most recent review on this issue, given the risks of propagation, PE and recurrence, “The option of doing nothing should be considered unacceptable”. Either anticoagulation or imaging surveillance should be the methods of choice.\textsuperscript{18}

**REFERENCES**


