

FPIN's Clinical Inquiries

Treatment of Calf Deep Venous Thrombosis

Clinical Inquiries provide answers to questions submitted by practicing family physicians to the Family Practice Inquiries Network (FPIN). Members of the network select questions based on their relevance to family medicine. Answers are drawn from an approved set of evidence-based resources and undergo peer review. The strength of recommendations and the level of evidence for individual studies are rated using criteria developed by the Evidence-Based Medicine Working Group (http://www.cebm.net/levels_of_evidence.asp).

This series of Clinical Inquiries is coordinated for American Family Physician by John Epling, M.D., State University of New York Upstate Medical University, Syracuse, N.Y. The complete database of evidence-based questions and answers is copyrighted by FPIN. If you are interested in submitting questions to be answered or writing answers for this series, go to <http://www.fpin.org> or contact CI2Editor@fpin.org.

Clinical Question

What is the most appropriate therapy for a patient with a calf deep venous thrombosis (DVT)?

Evidence-Based Answer

Patients with a first episode of calf DVT with a transient risk factor should receive heparin therapy followed by oral anticoagulation for six to 12 weeks. [Strength of recommendation: A, based on systematic review of randomized controlled trials (RCTs)] If anticoagulation is contraindicated, physicians should monitor for proximal thrombus extension with duplex ultrasound twice weekly for two weeks. [Strength of recommendation: C, based on consensus guideline] The use of low-molecular-weight heparin (LMWH), outpatient therapy, compression stockings, elevation of the extremity, and early mobilization may be beneficial based on extrapolation from studies of proximal DVT.

Evidence Summary

A systematic review¹ of the treatment of DVT conducted by the Agency for Healthcare Research and Quality (AHRQ) concluded that anticoagulation is beneficial for symptomatic calf DVT, based primarily on two studies of isolated calf thromboses. One RCT² of 51 adults with calf DVT demonstrated that three months of warfarin treatment (International Normalized Ratio [INR] 2.5 to 4.2) significantly reduced the likelihood of recurrence, extension, and pulmonary embolism at three months (29 versus zero percent, number needed to treat [NNT]: 4) and one year (32 versus 4 percent, NNT: 4) compared to initial heparin followed by compression

stockings alone. Another RCT³ compared six weeks of oral anticoagulation to 12 weeks of oral anticoagulation (INR 2 to 3) in 197 adults with a first episode of calf DVT. They found no statistically significant difference in recurrence rates (2 to 3 percent, respectively) or bleeding (13 to 22 percent, respectively) during 15 months of follow-up. All patients also received compression stockings and initial unfractionated heparin or LMWH therapy.

Further recommendations for treating calf DVT come from studies of proximal DVT. Based on 14 systematic reviews comparing LMWH to unfractionated heparin for initial treatment of any DVT (some with pulmonary emboli), the AHRQ review¹ concluded that LMWH reduced the rate of thrombus extension, DVT recurrence, major bleeding, and death. However, reviews since 1998 report smaller magnitudes of benefit than older reviews.¹ A Cochrane systematic review⁴ was updated in August, 2004, and came to similar conclusions.

A 2001 Cochrane systematic review⁵ found limited evidence (three RCTs that excluded many patients and had other methodological flaws) that outpatient management of proximal DVT with unfractionated heparin or LMWH in selected patients did not increase complications. They noted that LMWH is likely to become common practice because of patient preference and cost savings.⁵

Another Cochrane systematic review⁶ of proximal DVT found that graduated elastic compression stockings (20 to 40 mm Hg at the ankle) significantly reduced the likelihood of post-thrombotic syndrome two years later (NNT: 4; 95 percent confidence interval, 3 to 6).⁶ This syndrome of chronic leg discomfort, edema, and skin changes affects one third of patients with DVT within five years.⁶

Recommendations from Others

In the Seventh Conference on Antithrombotic and Thrombolytic Therapy, the American College of Chest Physicians (ACCP) recommends treating symptomatic isolated calf DVT with anticoagulation for three months (INR 2 to 3).⁷ They explicitly place higher value on "preventing recurrent thromboembolic events...[than] on bleeding and cost."⁷

The Institute for Clinical Systems Improvement (ICSI) notes: "Increasing evidence suggests that patients with symptomatic calf DVT benefit from treatment similar to that for proximal DVT," but does not recommend specific durations of anticoagulation for calf DVT.⁸ If a patient with calf DVT has contraindications to anticoagulation, they state that: "serial ultrasound (e.g., at 3 and 7 days) may be useful to evaluate for propagation of thromboses," which typically occurs in the first week or two after diagnosis.⁸

Clinical Commentary

Without long-term anticoagulation (six to 12 weeks), patients with uncomplicated calf DVT have a 20 percent risk of clot propagation into proximal DVT,⁸ a 30 percent risk of recurrence,^{1,8} and a 20 percent or greater risk of developing post-thrombotic syndrome.^{1,7} Oral anticoagulation for DVT carries a steady 2 percent annual risk of major hemorrhage plus risk of minor hemorrhage.¹ It is appropriate to consider longer durations of anticoagulation for recurrent DVT,

prothrombotic genotype or permanent risk factors, cancer, and idiopathic calf DVT. For these patients, clinicians must extrapolate from the AHRQ, ICSI, and ACCP recommendations for risk stratification and treatment duration, which are based on proximal DVT studies.

The authors indicate that they do not have any conflicts of interest. Sources of funding: none reported.

Address correspondence by e-mail to Eric M. Rotert, M.D., eric.rotert@fammed.wisc.edu. Reprints are not available from the authors.

ERIC M. ROTERT, M.D.

JOHN R. BASARICH, M.D.

Department of Family Medicine, University of Wisconsin
Madison, Wisconsin

JOAN NASHELSKY, M.L.S.

Managing Editor and Librarian Coordinator
Family Practice Inquiries Network
Iowa City, Iowa

REFERENCES

1. Diagnosis and treatment of deep venous thrombosis and pulmonary embolism. Evidence Report/Technology Assessment No. 68. AHRQ Publication No. 03-E012. Rockville, Md.: Agency for Healthcare Research and Quality, January 2003. Accessed online March 25, 2005, at: <http://www.ahrq.gov/clinic/epcsums/dvtsum.htm>.
2. Lagerstedt CI, Olsson CG, Fagher BO, Oqvist BW, Albrechtsson U. Need for long-term anticoagulant treatment in symptomatic calf-vein thrombosis. *Lancet* 1985;2:515-8.
3. Pinede L, Ninet J, Duhaut P, Chabaud S, Demolombe-Rague S, Durieu I, et al. Investigators of the "Duree Optimale du Traitement AntiVitamines K" (DOTAVK) study. Comparison of 3 and 6 months of oral anticoagulant therapy after a first episode of proximal deep vein thrombosis or pulmonary embolism and comparison of 6 and 12 weeks of therapy after isolated calf deep vein thrombosis. *Circulation* 2001;103:2453-60.
4. van Dongen CJ, van den Belt AG, Prins MH, Lensing AW. Fixed dose subcutaneous low molecular weight heparins versus adjusted dose unfractionated heparin for venous thromboembolism. *Cochrane Database Syst Rev* 2004;(4):CD001100.
5. Schraibman IG, Milne AA, Royle EM. Home versus in-patient treatment for deep vein thrombosis. *Cochrane Database Syst Rev* 2001;(2):CD003076.

6. Kolbach DN, Sandbrink MW, Hamulyak K, Neumann HA, Prins MH. Non-pharmaceutical measures for prevention of post-thrombotic syndrome. *Cochrane Database Syst Rev* 2003;(3):CD004174.

7. Buller HR, Agnelli G, Hull RD, Hyers TM, Prins MH, Raskob GE. Antithrombotic therapy for venous thromboembolic disease: the Seventh ACCP Conference on Antithrombotic and Thrombolytic Therapy [published correction appears in *Chest* 2005;127:416]. *Chest* 2004;126(3 suppl):S401-28.

8. Institute for Clinical Systems Improvement. Health care guideline: thromboembolism. 5th ed. Bloomington, Minn.: 2004. Accessed online March 25, 2005, at: <http://www.icsi.org/knowledge/detail.asp?catID=29&itemID=202>.

Copyright Family Practice Inquiries Network. Used with permission.