

PRIORITY UPDATES FROM THE RESEARCH LITERATURE (PURLS)

Reducing Anticoagulation Duration for Children After a Provoked Deep Venous Thrombosis

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In patients younger than 21 years of age with a provoked deep venous thrombosis (DVT), anticoagulation for 6 weeks is noninferior to anticoagulation for 3 months.¹ (J Am Board Fam Med 2025;38:589–591.)

Keywords: Blood Coagulation, Deep Venous Thrombosis, Treatment, Venous Thromboembolism

Strength of Recommendation B:

Based on a single multinational randomized controlled trial.²

Illustrative Case

An 8-year-old sustained a right femur fracture after a collision with a tree while on a family ski trip. Four days later, after surgical correction at a trauma center, he was driven 15 hours to his home. He presents to your office 3 days after their return home with increased pain and new swelling in his leg per mother's report. An ultrasound confirms an occlusive thrombosis distal to the right popliteal vein. In consult with your local pediatric hematologist, the patient was started on 3 months of low weight molecular heparin (LMWH) per current guidelines. After 4 weeks of anticoagulation, the patient and his mother follow up with you and are frustrated with daily injections and ask if they can stop. Does this patient need to complete a full 3 months of anticoagulation?

Clinical Context

Ongoing management and treatment discontinuation for a first provoked venous thrombosis and thromboembolism (VTE) in adults is often managed in the primary care office. However, VTE in pediatric patients is far less common (0.07 to 0.49 per 10,000 children vs 1 per 1,000 annually in adults) and less routinely managed by family physicians.^{3,4} The majority of VTEs in pediatric patients are provoked and often managed in the hospital setting in conjunction with pediatric hematology. However, these patients and their families may choose or need follow-up in the primary care ambulatory setting.

Current guidelines on VTE treatment in children is based on CHEST guidelines from 2012 and the American Society of Hematology from 2018.^{5,6} Despite the introduction of direct oral anticoagulation agents (DOACs) since publication of these guidelines, data for using these medications in pediatric patients is less robust and their use is not definitively reflected in the guidelines.

Though the evidence to support anticoagulation to prevent recurrent VTE is robust, recommendations for treatment duration for provoked DVT stem from a single RCT conducted on adults in the 1990s,⁷ and pediatric recommendations were derived from these results. As early as 2008, the American College of Chest Physicians suggested a duration as short as 6 weeks could be considered for first provoked DVT in pediatric patients; however, this recommendation lacked high-quality evidence.⁸

This trial evaluated the effectiveness of 6 weeks of DVT anticoagulation treatment in patients less than 21 years of age if the patient has improved

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symptoms and evidence of resolution on imaging compared with a full 3 months of anticoagulation.¹

Methods

This article was identified as a potential PURL through the standard systematic methodology.⁹ An additional literature search was conducted by searching PubMed with the terms “VTE incidence children” and “VTE incidence adults” and by searching Up To Date with the terms “VTE management children” and “VTE management adults” to find additional literature to place this research into the context of current clinical practice.

Study Summary

This multinational randomized controlled trial of patients younger than 21 years of age evaluated whether 6 weeks of anticoagulation was noninferior to 3 months of anticoagulation for an acute venous thromboembolism (VTE) verified by imaging and determined to be provoked, such as recent hospitalization, traumatic injury or central venous catheterization within the previous 30 days. Patients with persistent antiphospholipid antibodies, severe anticoagulant deficiencies, active malignancy, pulmonary embolism without deep vein thrombosis, or prior VTE were excluded.

Patients were initiated on IV unfractionated heparin or subcutaneous low-molecular-weight heparin (LMWH) for the acute VTE treatment, followed by anticoagulation with vitamin K antagonists, direct oral anticoagulants (DOAC), fondaparinux or LMWH at the discretion of the physician according to the American College of Chest physicians guidelines. After 6 weeks of anticoagulation, patients had repeat imaging to verify venous flow. If venous flow was evident and there were no persistent antiphospholipid antibodies on repeat testing, patients were randomized to either stop anticoagulation or continue for the complete 3 months. The primary end point was symptomatic recurrent VTE, and the primary safety end point was clinically relevant bleeding event (fatal bleed, decrease of hemoglobin by at least 2g/dL, bleed requiring blood products or surgical intervention, or a bleed for which a patient sought medical attention) within 1 year of the index VTE.

Patients (n = 297, median age = 8.3 years) most often used LMWH in the acute treatment (84.0%) and continued during the subacute treatment period

(86.7%). In per-protocol population analysis, 6 weeks of anticoagulation was found to be noninferior to 3 months of treatment in one-year risk of recurrent VTE (0.66% vs 0.70%; absolute risk difference -0.04%; 95% CI, -3.18 to 3.56). There was also no difference in all randomized patients (n = 417, absolute risk difference -0.57%; 95% CI, -4.1 to 2.9). There was no difference in clinically relevant bleeding events between the 2 groups in per-protocol analysis population (absolute risk difference -0.05%; 95% CI, -3.78 to 3.54). Overall adverse events, including fever, diarrhea, and abdominal pain, between the 6 week treatment group and the 3 month treatment group were similar (26% vs 32%). No Heparin-Induced Thrombocytopenia (HIT) events occurred in either group.

What Is New

In patients younger than 21, it is reasonable to consider VTE imaging at 6 weeks of anticoagulation and if DVT has resolved, stop anticoagulation at that point, instead of continuing LMWH injections for a total of 3 months.

Caveats

The initial study design excluded patients with cancer or pulmonary embolism; therefore, further investigation will be required before extending these findings across all provoked VTEs. Furthermore, all patients received an ultrasound at 6 weeks, which is not routine standard of care and may be prohibitive in some clinical settings for decision-making purposes. Finally, study enrollment began in 2008, before the introduction of DOAC options to treat pediatric VTE. Evolving pediatric literature, similar to the evolution in treatment of VTE in adult populations, would indicate a movement toward treatment with DOACs as they are better tolerated and have higher adherence rate over LMWH injections. DOACs have generally been shown to be noninferior and comparable to LMWH in treatment of VTE in children; however, few patients in this study were treated with a DOAC and no subgroup analysis was provided by these authors.^{10,11}

Challenges to Implementation

Pediatric provoked VTE is a rare clinical event, most often primarily managed by pediatric hematologists. Family physicians may be unaware of current guidelines and are seldom required to manage these

interventions independently. Discontinuation of anticoagulation may also be appropriately deferred to the primarily managing hematologist if applicable. However, family physicians should be aware of these data for families struggling to complete 3 months of LMWH therapy. In addition, these results may spur further investigation in the adult literature regarding anticoagulation treatment duration.

To see this article online, please go to: <http://jabfm.org/content/38/3/589.full>.

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