Practice Guidelines

Venous Thromboembolism: Management Guidelines from the American Society of Hematology

Key Points for Practice

- In-hospital and home treatment of PE provide similar outcomes, although home treatment of DVT produces better outcomes.
- After primary DOAC treatment for three to six months, decisions for indefinite anticoagulation depend on risk factors associated with initial VTE.
- When VTE is unprovoked or associated with chronic factors, indefinite anticoagulation reduces recurrent VTE with a slightly increased risk of major bleeding.
- Aspirin is less effective than anticoagulants at reducing VTE risk but has similar major bleeding risk.

From the *AFP* Editors

Every year, up to two in every 1,000 people in the United States experience venous thromboembolism (VTE). The American Society of Hematology has updated recommendations for management of VTE, which includes deep venous thrombosis (DVT) and pulmonary embolism (PE).

Initial Management of VTE

TREATMENT SETTING

Treating VTE at home often produces better outcomes than treating in the hospital. In patients with uncomplicated DVT, treating at home reduces the likelihood of PE development. The risk of a subsequent DVT is also less (number needed to treat [NNT] = 29; 95% CI, 24 to 143). Mortality and bleeding rates with DVT are similar between treatment settings. For patients with clinically stable PE, home treatment produces outcomes similar to those with hospital treatment.

THROMBOLYSIS

In the absence of threat to the limb or high risk of severe postthrombotic syndrome, thrombolytic therapy is not recommended for DVT. Up to one-half of patients with proximal DVT develop postthrombotic syndrome, although only 10% will experience severe symptoms. Thrombolysis reduces postthrombotic syndrome (NNT = 6; 95% CI, 5 to 11) but increases major bleeding (number needed to harm [NNH] = 33; 95% CI, 20 to 63), with similar mortality and subsequent VTE risks. Systemic, regional, and catheter-directed thrombolysis have similarly elevated bleeding risks. With extensive DVT, the benefits of catheter-directed thrombolysis to prevent PE are uncertain.

In patients with PE and hemodynamic compromise demonstrated by systolic blood pressure reduction of at least 40 mm Hg from baseline or systolic blood pressure measurement below 90 mm Hg, the guideline strongly recommends thrombolytic therapy to reduce mortality despite a significant risk of major bleeding that includes intracranial bleeding. In PE with right ventricular dysfunction but no hemodynamic compromise, also called submassive PE, the decision is complicated by poor evidence quality. Mortality may slightly improve after thrombolysis, and catheter-directed thrombolysis may be better than systemic thrombolysis, but evidence is insufficient to recommend these treatments and anticoagulation alone is suggested.

MEDICATION

Although direct oral anticoagulant (DOAC) treatment has similar effects on mortality and subsequent VTE risk as vitamin K antagonists, the risk of major bleeding is lower using DOACs (NNT = 167; 95% CI, 112 to 334). DOAC treatment appears to reduce cost by eliminating

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This series is coordinated by Michael J. Arnold, MD, contributing editor.

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monitoring requirements. Patients who have antiphospholipid antibody syndrome or morbid obesity, or who have had bariatric surgery, are poor candidates for DOAC treatment. No particular DOAC is recommended.

INFERIOR VENA CAVA FILTERS

Inferior vena cava filters are not recommended with anticoagulation because they do not reduce PE or mortality and commonly cause adverse effects.

Primary VTE Treatment

Treatment of initial VTE is most effective for three to six months. Although longer treatment reduces the likelihood of recurrence, this benefit may be offset by increases in bleeding and mortality. After primary treatment, secondary VTE prevention is recommended for patients with a chronic persistent risk factor *(Table 1)* without a high risk of bleeding complications. There are separate recommendations for patients with cancer.

Patients with unprovoked VTE do not need follow-up studies such as D-dimer testing or ultrasonography to detect residual thrombosis to consider extending treatment. Limited study suggests that using these methods results in increased major bleeding with only slight reductions in future VTE.

Secondary Prevention

Secondary prevention is deciding whether to continue antithrombotic therapy indefinitely after VTE. In secondary prevention, the presence of provoking factors for the initial VTE is most important for this decision *(Table 1)*. Clinical prognostic scores have been proposed to determine the risk of recurrence, but patient-oriented evidence is lacking.

After VTE that is unprovoked or provoked by a chronic factor, indefinite anticoagulation should be considered. For unprovoked VTE, indefinite anticoagulation with a DOAC reduces recurrent PE (NNT = 44; 95% CI, 16 to 72) and DVT (NNT = 29; 95% CI, 27 to 31), although with an increase in major bleeding (NNH = 167; 95% CI, 83 to 500). For VTE with a chronic provoking factor, benefits are similar for reducing risk of PE (NNT = 33; 95% CI, 27 to 50) and DVT (NNT = 23; 95% CI, 21 to 25) offset by the same slight risk of major bleeding. After VTE associated with a transient provoking factor, indefinite treatment is not recommended.

TABLE 1

Provoking Factors for Venous Thromboembolism

Chronic factors
Active cancer
Autoimmune disorders
Chronic infections
Inflammatory bowel disease
Transient factors
Within 3 months
Admitted to hospital with acute illness for 3 days or more
Cesarean delivery
Surgery with general anesthesia for 30 minutes or more
Within 2 months
Admitted to hospital with acute illness for less than 3 days
Confined to bed out of hospital for 3 days or more
Estrogen therapy
Leg injury with decreased mobility for 3 days or more
Pregnancy and postpartum
Surgery with general anesthesia for less than 30 minutes

Adapted with permission from Ortel TL, Neumann I, Ageno W, et al. American Society of Hematology 2020 guidelines for management of venous thromboembolism: treatment of deep vein thrombosis and pulmonary embolism. Blood Adv. *2020;4(19):4710.*

After a second VTE, indefinite anticoagulation reduces future PE (NNT = 48; 95% CI, 40 to 77) and future DVT (NNT = 20; 95% CI, 18 to 24) with the same slight risk of major bleeding. Evidence is lacking on whether indefinite anticoagulation is beneficial if both VTE events were associated with transient provoking factors.

Although aspirin reduces long-term VTE risk, anticoagulation is more effective. Aspirin does not definitively reduce bleeding risk compared with anticoagulants but does increase the risk of recurrent PE and recurrent DVT. Limited study suggests that indefinite treatment with lower doses of DOACs does not reduce bleeding and recurrent VTE compared with standard dosing.

Other VTE Management

The risks of combining anticoagulant treatment for VTE with aspirin for secondary cardiac

prevention are uncertain. Because major bleeding rates may be higher with combined therapy, the guideline recommends discontinuing aspirin.

Compression stockings are not recommended in patients with DVT to reduce the risk of postthrombotic syndrome because no benefit has been seen in well-done studies. Compression stockings also do not affect DVT recurrence or mortality risks.

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Editor's Note: The NNTs and NNHs were calculated by the author using data provided in the guideline.

There are two major guideline sources for VTE treatment, the American Society of Hematology and the American College of Chest Physicians (ACCP). The ACCP guidelines are discussed in a recent *AFP* article covering outpatient management of anticoagulation (https://www.aafp.org/afp/2019/1001/p426.html).

Recommendations from these groups differ somewhat. The ACCP recommends three months of primary treatment for VTE, whereas the American Society of Hematology recommends between three and six months.[1] Although both recommend considering indefinite anticoagulation for VTE not associated with a transient risk factor, the ACCP excludes patients with high bleeding risk and the American Society of Hematology discusses excluding only patients at high risk of bleeding complications. The ACCP estimates bleeding risk by counting risk factors, which has not been prospectively validated.[1] ACCP guidelines support aspirin for unprovoked VTE if anticoagulation is stopped because they found bleeding risk with aspirin was similar to no treatment, whereas the American Society of Hematology recommends against aspirin because they found bleeding risk with aspirin was similar to that with anticoagulants.[1] Although the ACCP guidelines are four years older, this difference is likely based on different interpretations of uncertain evidence.

Understanding these conflicts can be helpful for challenging situations, such as when secondary cardiac prevention overlaps with secondary VTE prevention.—Michael J. Arnold, MD, Contributing Editor

Reference

1. Kearon C, Akl EA, Ornelas J, et al. Antithrombotic therapy for VTE disease: CHEST guideline and expert panel report [published correction appears in *Chest*. 2016;150(4):988]. *Chest*. 2016;149(2):315-352.

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