New VTE Guidelines Issued for Primary Care

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New venous thromboembolism guidelines aimed at primary care providers emphasize the need for swift diagnosis and initial treatment with low-molecular-weight heparin over the unfractionated formulation.

Issued jointly by the American College of Physicians and the American Academy of Family Physicians, the guidelines represent an acknowledgement that diagnosis of venous thromboembolism (VTE) is first and foremost a primary care challenge.

Risk factors for the condition, such as recent hospitalization, surgery, trauma, and immobilization, are well known, but early diagnosis—which is critical to a successful outcome—is difficult because thromboembolic events are often "clinically silent," said Dr. B. Gail Macik, of the division of hematology and oncology at the University of Virginia, Charlottesville.

Advances in therapy are poised to reduce VTE-associated mortality, but they can only do so if they are well disseminated through the primary care ranks, which, historically, they have not been, Dr. Macik added.

In fact, most management guidelines to date have been geared toward patients with difficult or complicated disease in inpatient health care settings, such as intensive care units. In contrast, the new guidelines offer "clinically relevant screening and treatment recommendations specifically for primary care physicians who are the most likely to have front-line contact with [undiagnosed] VTE," she said. "As with most guidelines, these leave wiggle room for individual application, but the concise review and recommendation for care is very welcome," said Dr. Macik, who was not involved in writing the recommendations.

The diagnostic and management guidelines, published separately, are based on findings of a comprehensive systematic literature review published in 2003 and recently updated by Dr. Jodi B. Segal and colleagues at the Johns Hopkins University Evidence-Based Practice Center in Baltimore (Ann. Intern. Med. 2007;146:211-22).

Diagnosis

The importance of early diagnosis of VTE "cannot be overstressed," wrote guideline coauthor Dr. Amir Qaseem, senior medical associate in the Clinical Programs and Quality of Care Division at the ACP.

To that end, diagnostic guidelines encourage using validated clinical prediction tools, such as the Wells prediction rule, to determine the probability of deep-vein thrombosis (DVT) and pulmonary embolism before performing more definitive testing (Ann. Fam. Med. 2007;5:57-62).

Because the Wells prediction rule performs better in younger patients without comorbidities or VTE history, "physicians should use their clinical judgment in cases where a patient is older or presents with comorbidities," according to the guidelines.

Obtaining a high-sensitivity D-dimer assay is a reasonable option in appropriately selected patients with low pretest probability of DVT or pulmonary embolism, including younger patients without associated comorbidity or history of VTE and with short duration of symptoms. "In older patients, those with associated comorbidity, and long duration of symptoms, a D-dimer alone may not be sufficient to rule out VTE," according to the authors.

Obtain an ultrasound in patients with intermediate to high pretest probability of DVT in the lower extremities. "Ultrasound is less sensitive in patients who have DVT limited to the calf, therefore a negative ultrasound does not rule out DVT in these patients," the authors stressed. Additionally, "repeat ultrasound or venography may be required for patients who have suspected calf-vein DVT and a negative ultrasound," as well as for those patients with suspected proximal DVT and an inadequate ultrasound.

Imaging is essential for patients with intermediate or high pretest probability of pulmonary embolism. Ventilation-perfusion, multidetector helical computed axial tomography, and pulmonary angiography are among the potential imaging options.

Treatment and Prevention

Compared with unfractionated heparin, low-molecular-weight heparin (LMWH) is associated with a reduced risk of major bleeding and mortality in the treatment of DVT, and as such "should be used whenever possible for the initial inpatient treat-

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ment" of these patients, according to the treatment guidelines (Ann. Intern. Med. 2007;146:204-10).

Other recommendations regarding management include:

► **Home-based therapy.** Patients who have adequate support at home can receive LMWH treatment on an outpatient basis. Data on the risks among inpatients versus outpatients demonstrate only slight differences in the rates of recurrent VTE, major bleeding, and death. However, most studies relevant to this question "excluded patients with previous VTE, thrombophilic conditions, or significant comorbidity, pregnant patients, and patients unlikely to adhere to outpatient therapy," the authors wrote. Also, several of the studies allowed for brief inpatient admissions for stabilization prior to randomization to outpatient treatment.

► **Compression stockings.** On the basis of evidence demonstrating a marked reduction in the incidence of postthrombotic syndrome among patients with DVT who wear compression stockings, the guidelines recommend the routine use of either over-the-counter or custom-fit stockings beginning 1 month after diagnosis of proximal DVT, and continuing for a minimum of 1 year. Of three randomized, controlled trials that studied the use of compression stockings, the two that enrolled patients within 1 month of developing proximal DVT showed a significant reduction in postthrombotic syndrome, while no such benefit was seen in the one trial that enrolled patients 1 year after the DVT event, the authors reported.

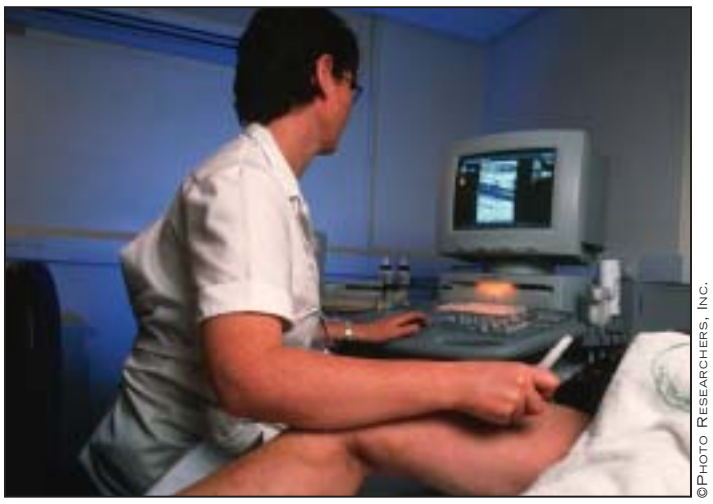
► **Pregnancy.** Anticoagulation management during pregnancy is particularly important, as the risk of VTE in pregnant women is five times greater than in nonpregnant women, the authors stated. However, the available data are insufficient to recommend specific therapies in pregnant women. The guideline recommends avoiding vitamin K antagonists because they can cross the placenta and have been associated with fetal bleeding and embryopathy at 6-12 weeks' gestation. "Neither LMWH nor unfractionated heparin crosses the placenta, and neither is associated with embryopathy or fetal bleeding," they wrote.

► **Secondary and idiopathic VTE.** For VTE secondary to transient risk factors, such as surgery, trauma, or immobilization, the available evidence indicates that patients may be well served with 3-6 months of oral anticoagulation therapy.

With respect to idiopathic VTE, available data suggest that extended-duration anticoagulation therapy is associated with a reduced relative risk of recurrence, although the optimal duration is not known as the length of therapy in the trials varied substantially, and the results reflect follow-up only to 4 years. Consequently, the guideline advises continuing anticoagulant therapy for more than 12 months for recurrent VTE.

► **Long-term treatment.** In comparing long-term treatment with LMWH versus vitamin K antagonists, the former is "safe and efficacious for the long-term treatment of VTE in selected patients, and may be preferable for patients with cancer," as studies have linked LMWH to a survival advantage in this population. Specifically, the data suggest that "LMWH may be a useful treatment for patients in whom INR [international normalized ratio] control is difficult."

► **Pulmonary embolism.** Regarding pulmonary embolism treatment, "LMWH is at least as effective as unfractionated heparin," according to a review of the available evidence; thus, either drug is appropriate for initial treatment, said Dr. Vincenza Snow, director of clinical programs and quality of care for the ACP. The authors did note, however, that additional trials are needed to more rigorously examine the efficacy of LMWH for pulmonary embolism. ■



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Ultrasound should be performed in patients who are at intermediate to high risk of deep-vein thrombosis in the lower extremities.