

CORRESPONDENCE

Risk for Recurrent Venous Thromboembolism in Patients With Subsegmental Pulmonary Embolism Managed Without Anticoagulation

TO THE EDITOR: Le Gal and colleagues' article (1) adds valuable information on the course of patients with symptomatic subsegmental pulmonary embolism (PE) who do not receive initial anticoagulation. In this study, structured follow-up revealed that 1.4% of patients with this condition who were initially managed without anticoagulation had progression of their PE within the first 90 days. Another 1.5% developed a proximal deep venous thrombosis. Because the CIs for venous thromboembolism (VTE) at 90 days crossed 3%, these results will undoubtedly push the needle toward recommending anticoagulation in all patients with symptomatic subsegmental PE. However, whether this study closes the chapter on anticoagulation for this condition remains unclear.

Practice patterns related to the evaluation of PE vary, particularly those between the United States and other countries. Le Gal and colleagues' study was done largely in Canada with participating centers in France, Switzerland, and the Netherlands. In the United States, only a few who have imaging for PE have a PE. This imaging yield for PE (that is, the number of studies with positive findings for PE divided by the number of PE studies) is as low as 2% at some U.S. centers (2). In other geographic settings, the yield is markedly higher (3). Patients who have imaging for PE in low-yield centers may have more false-positive findings or clinically insignificant symptomatic subsegmental PEs. This may be partially due to the interrater reliability of computed tomographic pulmonary angiography, which is lower in isolated and peripheral PEs. Studies assessing interrater reliability indicate that 5% to 25% of PEs identified on computed tomographic pulmonary angiography are deemed false-positive when evaluated by a second radiologist (4).

In addition, the American College of Chest Physicians guideline recommends surveillance over anticoagulation for patients with symptomatic subsegmental PE and no proximal deep venous thrombosis who are not at high risk for recurrent VTE. Factors that place patients at high risk include immobility, active cancer, and no reversible risk factors for VTE (5). Although Le Gal and colleagues excluded those with active cancer, what other VTE risk factors these patients had is unclear. Patients with risk factors for VTE may carry these throughout the 90-day outcome period. These patients may benefit from anticoagulation, but the benefit may be less (or nonexistent) for those with few or no VTE risk factors. Other characteristics, such as age, may play a role. For example, Le Gal and colleagues found that recurrent VTE within 90 days was much lower in patients aged 65 years or younger than in those older than 65 years. Their well-done study paves the way for further investigation.

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IN RESPONSE: We agree with Drs. Westafer and Vinson that our study does not close the chapter on the use of anticoagulation for subsegmental PE without proximal deep venous thrombosis. Confirmation of the diagnosis of subsegmental PE by an experienced thoracic radiologist remains a key component in the management of these patients. False-positive findings due to suboptimal vessel opacification can be caused by respiratory or heart pulsation artifacts, obesity, or mucus plug. Inter-observer agreement between radiologists is low for the diagnosis of subsegmental PE in the emergency department, and many findings are reported as false-positive upon reinterpretation by a more experienced or thoracic radiologist (1, 2). In case of uncertainty, clinicians need to consider additional variables (such as high pretest probability of pulmonary embolism, elevated D-dimer levels, or convincing signs and symptoms) to help confirm the diagnosis and avoid unnecessarily exposing patients to therapeutic-dose anticoagulation (3) and its potential bleeding complications.

The decision to initiate or withhold anticoagulation for patients with confirmed subsegmental PE on the basis of the underlying risk for recurrence is more complicated. Patients with permanent risk factors (such as active cancer) or unprovoked events are at higher risk for recurrent VTE and probably should receive anticoagulation until more data are available (4, 5). Patients with major or minor transient risk factors (such as surgery with general anesthesia for greater than 30 minutes within 3 months or admission to the hospital for less than 3 days with acute illness within 2 months, respectively) have a lower risk for recurrent VTE; however, the underlying risk may fluctuate on the basis of the timing of the subsegmental PE diagnosis. For example, the risk for recurrent VTE may differ between a patient diagnosed with subsegmental PE within a week of total hip arthroplasty and another patient diagnosed 8 weeks after a minor surgery.

The decision to initiate anticoagulation in patients with subsegmental PE without proximal deep venous thrombosis should be individualized. A randomized controlled trial allocating patients with subsegmental PE to rivaroxaban or placebo

LETTERS

(ClinicalTrials.gov: NCT04263038) will provide an estimate for the risk-benefit ratio of anticoagulation in this patient population.

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