there is a greater than low clinical suspicion for a PE and if not otherwise contraindicated, we support treatment with anticoagulation in patients diagnosed with isolated subsegmental PE. Furthermore, the use of DOACs has been shown to be safer than the previous vitamin K antagonist regimen historically used for acute management of PE.[10] We believe there is insufficient evidence to argue against treatment of isolated subsegmental PE. Ultimately, we advocate for initiating anticoagulation due to logistical barriers associated with obtaining confirmatory studies and evaluation for thrombophilia risk factors; the legal implications a practitioner may face when choosing not to treat a diagnosis; the ethical dilemma of performing a study involving withholding treatment when potential harm exists; and the safety and efficacy profile of current recommended outpatient anticoagulation regimens.

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ANTICOAGULATION SHOULD NOT BE ROUTINELY USED FOR ISOLATED SUBSEGMENTAL PULMONARY EMBOLISM

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Pulmonary embolism (PE) is a common consideration in patients presenting to the emergency department (ED), accounting for 0.2% of ED visits and up to 200,000 deaths annually.[1] Computed tomography pulmonary angiography (CTPA) remains a common modality for assessment, and the increasing use of CTPA has resulted in a rise in PE diagnoses.[2,3] However, with improved CT technology, there has been a rise in the diagnosis of subsegmental pulmonary embolism, defined as PE confined to the subsegmental pulmonary arteries.[2,3] These arteries are 6 to 7 mm in diameter after the initial branch and less than 1.5 mm in the periphery, with subsegmental PE typically considered to be 1 mm or less diameter within 1 artery.[4] Despite the increase in diagnosis, there are little data demonstrating improved patient outcomes with treating these smaller PEs, suggesting that a component of overdetection may be occurring.[5] Although the management of segmental and larger PEs involves anticoagulation, there is controversy whether anticoagulation is necessary in patients with isolated subsegmental pulmonary embolism. Here, we argue that anticoagulation is not necessary in patients with

isolated subsegmental PE who can undergo clinical surveillance due to several factors including the risk of false positives, limited clinical benefits, and the harms associated with anticoagulation.

CTPA is typically considered the diagnostic modality of choice for PE, which appears as an intraluminal filling defect; however, imaging interpretation becomes less reliable the more peripheral the filling defect with poor interrater reliability (kappa 0.21 to 0.38 for subsegmental PE).[6-8] The number of false-positive PE diagnoses based on CTPA is also significant, with studies reporting between 5% and 59%.[6-8] Moreover, studies have found 11% to 59% of initial subsegmental PE diagnoses on CTPA were later determined to be an artifact when imaging was reinterpreted by a chest radiologist.[7-9] Although these data come from studies prior to 2018, many subsegmental PE may be false positives, exposing the patient to the risks of unnecessary anticoagulation without any benefits.

Even if a subsegmental PE is present, they are by definition small and unlikely to be associated with poor outcomes. Studies suggest that subsegmental PE is not associated with increased mortality or recurrent venous thromboembolism (VTE) rates. A 2021 prospective cohort study included patients with isolated subsegmental PE in the absence of a proximal deep venous thrombosis (DVT) who did not receive anticoagulation and evaluated recurrent VTE at 90 days.[10] Patients underwent clinical surveillance with bilateral lower extremity ultrasound between days 5 and 7, and 3.1% of patients experienced recurrent VTE at 90 days. Among this cohort, the rate of recurrent VTE was only significantly different in patients aged more than 65 years and in those with multiple subsegmental PE.[10] However, this study excluded patients with active cancer, those with a history of VTE, those who had a requirement for oxygen, those who were pregnant, who had received anticoagulation prior to enrollment, those who were hospitalized at time of the subsegmental PE diagnosis, and those with other indications for long-term anticoagulation.[10] Notably, this study was also stopped early by the data and safety monitoring boards. More recently, a 2024 meta-analysis of subsegmental PE found no difference in rates of recurrent VTE or mortality in patients undergoing anticoagulation compared with those who did not.[5] This suggests that there appears to be minimal harm in foregoing anticoagulation in patients with subsegmental PE.

Importantly, anticoagulation also carries a risk of complications. The most common complication is bleeding, which can include life-threatening hemorrhage (eg, bleeding requiring transfusion 2 or more units or admission, bleeding affecting a critical organ, or death). This risk of bleeding is based on the agent used (eg, warfarin versus direct oral anticoagulants) and patient factors (older age, renal or liver disease, alcohol use, or prior bleeding history). Literature suggests the rate of major bleeding for anticoagulation for PE is 1% to 5% and 4% to 11% for minor bleeding.[11,12] In a retrospective study of patients with PE, 87% of patients with subsegmental PE were anticoagulated, and 34% of these patients had clinically meaningful bleeding (2 g/dL or more decrease in hemoglobin or requiring a blood transfusion).[13] Given the risk of bleeding and low likelihood of benefit with anticoagulation for subsegmental PE, the evidence suggests the harms outweigh any benefits.

Although we do not advocate for routine anticoagulation, several important caveats should be considered in the patient with subsegmental PE. First, the patient should have an isolated subsegmental PE in the absence of DVT (which would warrant anticoagulation). Patients should also not be in the higher risk cohort (ie, those with age 65 years or older, who are pregnant, who have a poor cardiopulmonary reserve, those with active cancer, who are hospitalized or have reduced mobility, who have no reversible risk factor, or who have multiple subsegmental PEs). Third, clinicians need to ensure the patient has reasonable follow-up and can undergo clinical surveillance. This is consistent with guidelines from the American College of Chest Physicians, which recommend clinical surveillance over anticoagulation in patients with subsegmental PE and no proximal DVT who are not at high risk of recurrent VTE.[3] The American College of Emergency Physicians provides a level C recommendation that anticoagulation should be guided by the individual patient risk profile and not routinely prescribed in the setting of isolated subsegmental PE and no DVT.[14] Finally, shared decision making with the patient is imperative, with the physician considering the patient's wishes concerning therapy and any likely barriers present at the patient, family, system, and quality review levels concerning treatment versus surveillance. Based on the current evidence, we believe that anticoagulation is not necessary for the majority of patients with isolated subsegmental PE who are not at high risk of recurrent VTE, as data suggest many subsegmental PEs may be false positives or clinically insignificant, and there is no significant difference in rates of recurrent VTE or mortality.

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