Initiating Treatment for Subsegmental Pulmonary Embolism in the Emergency Department

Opposing authors provide succinct, authoritative discussions of controversial issues in emergency medicine. Authors are provided the opportunity to review and comment on opposing presentations. Each topic is accompanied by an Editor's Note that summarizes important concepts. Participation as an authoritative discussant is by invitation only, but suggestions for topics and potential authors can be submitted to the section editors.

Editor's Note: *The decision to initiate or withhold anticoagulation for patients with subsegmental pulmonary embolisms is challenging for emergency clinicians and requires an assessment of potentially serious consequences that can result from either choice. In this edition of Clinical Controversies, opposing authors present their perspectives on the risks and benefits of initiating treatment in the emergency department.*

PATIENTS WITH ISOLATED SUBSEGMENTAL PULMONARY EMBOLISM SHOULD BE TREATED WITH ANTICOAGULATION

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Pulmonary embolism (PE) represents a potentially catastrophic form of venous thromboembolism (VTE) which, in extreme cases, can cause cardiac arrest and even death. Recent data suggest a 1-year mortality rate of 13%.[1] Prompt treatment upon discovery of a PE is critical to preventing recurrent VTE and potential debilitating outcomes. Although standard management for the majority of PEs is largely agreed upon, there is a lack of consensus on the acute management of isolated subsegmental PE among clinicians, specifically initiating treatment with anticoagulation. Given the inherent risk of withholding treatment, current expert panel guidance, and the safety profile of newer anticoagulants, we argue for initiating anticoagulation in the emergency department (ED) for all patients with diagnosed isolated subsegmental PE, so long as the patient is not deemed high risk for major bleeding.

The dissent may argue improved diagnostic testing has led to increased false-positive results, especially when the initial result was for a subsegmental PE or single PE.[2] In a retrospective review, 26% of initial positive results were independently reviewed by 3 chest radiologists and interpreted as negative for a PE, attributing the initial result to breathing-motion and beam-hardening artifacts.[3] However, we would challenge their definition of a false-positive, for it is not as though our technology has worsened. Although pulmonary angiography is generally considered gold standard for diagnosis, in emergency medicine, we use the clinical standard of computed tomography (CT) scanning to aid in diagnosis and guide treatment. Therefore, when an isolated subsegmental PE is identified based on imaging ordered for an acute complaint, it is hard to argue against treatment if there is potential for harm, especially when we often lack the luxury of having multiple chest radiologists to review and possibly reinterpret the initial imaging. The clinical significance of an isolated subsegmental PE is not fully understood, given a lack of randomized controlled studies pertaining to anticoagulation versus withholding treatment. Yet there is prospective research that suggests increased risk of clot recurrence when treatment is withheld in patients with subsegmental PE.[4] This poses a risk for potential recurrent ED visits and increased patient cost. Furthermore, withholding treatment opens the door for significant medical malpractice litigation in the event of an adverse outcome. Given the lack of strong evidence to support withholding anticoagulation, this practice would be difficult to defend.

The American College of Chest Physicians 2021 guideline suggests anticoagulation over surveillance for isolated subsegmental PE for high-risk patients, which include hospitalization or reduced mobility, active cancer, without reversible risk factor like recent surgery, or pregnancy. Conversely, they also offer a weak recommendation for surveillance over anticoagulation of isolated subsegmental PE if there is no proximal deep vein thrombosis (DVT) and low risk for recurrence.[2] We believe in many EDs, this presents an incredible challenge. To obtain bilateral lower extremity duplex ultrasonography for each of these patients would incur increased cost to both the patients and our health care system at large. Many rural EDs do not have readily available sonographers. The sonographer may be on call and must travel to perform the study. They may only operate during certain hours. Or the ED may simply have no sonographer available. These situations would pose an inherent delay in management and disposition of the patient. Similarly, the ability to obtain follow-up surveillance is not always feasible, as many patients are uninsured, thus creating another barrier to overcome.

In emergency medicine, we have clinical decision support tools to help us determine if advanced imaging is indicated. It has been our experience that many physicians will forego these tools and turn to advanced imaging so long as clinical suspicion is more than low. Thus, it would seem inconsistent to withhold treatment after a positive diagnostic test when one had clinical suspicion. More interestingly perhaps would be to question the inconsistent use of validated tools. One study found one-third of all CT orders for PE were not using these clinical decision tools.[5] Even with mandating pretest probability rules before being able to order the CT, Geeting et al[6] found this changed neither the PE positive rate nor CT utilization, suspecting physicians' gradually inflating the scores. Nevertheless, we recommend treatment with anticoagulation in most alternate cases where a workup was performed due to high clinical suspicion or patient risk for PE.

Clinical guidelines and expert panels largely favor the use of anticoagulation, if not contraindicated, in the treatment of patients with subsegmental PE who are deemed to be at high risk for clot recurrence.[2,7,8] Although there is consensus agreement upon treatment in patients with high-risk factors such as active cancer, concurrent DVT, and pregnancy, there is nuance among various other factors such as antiphospholipid syndrome, normal cardiopulmonary reserve, and the presence of isolated versus multiple subsegmental PE.[8] Current 2018 American College of Emergency Physicians (ACEP) clinical policy regarding VTE management offers a class C recommendation for withholding anticoagulation for subsegmental PE based on 2 studies.[9] The first study referenced suggests patients with subsegmental PE had similar risk of recurrent VTE compared to patients with larger PE, but they do note not all patients were confirmed to have an isolated subsegmental PE. The second suggested it may be safe to withhold anticoagulation in patients with confirmed isolated subsegmental PE (ie, negative bilateral lower extremity duplex ultrasonography) as their 22 patients (though only 20 had confirmatory studies) had no recurrent VTE at 3-month follow-up.

Risk of bleeding is the primary consideration when it comes to the decision to initiate anticoagulation in the management of isolated subsegmental PE. Direct-acting oral anticoagulants (DOACs) have become the recommended first-line option in the initial treatment of VTE.[10,11] DOACs have fixed dosing and do not require routine laboratory monitoring. In comparison to vitamin K antagonists, they have a better safety profile and a lower risk of major bleeding.[12,13] Regardless of the medication class, the initiation of anticoagulation requires thoughtful consideration of a patient's risk for major bleeding. Several risk stratification tools exist to help estimate a risk of major bleeding, allowing for safer disposition when making anticoagulant treatment decisions in the acute setting.[9] In general, major risk predictors for bleeding include the following: history of bleeding, renal failure, thrombocytopenia, liver disease, cancer, coadministration of an antiplatelet drug, poor international normalized ratio (INR) control, or inappropriate dosing of DOAC.[12] In emergency medicine, the primary goal in initiating anticoagulation is to safeguard against imminent complications from isolated subsegmental PE. Ongoing or prolonged anticoagulation warrants close follow-up and further consideration in the outpatient setting.

Future multicenter generalizable randomized controlled trials may help guide the use of anticoagulation. The current paucity of data available at this time may stem from the ethical and logistical challenges conducting randomized controlled trials. It would be difficult to obtain institutional review board approval for studies that involve no treatment, particularly when potential harm exists. The decision to withhold treatment may also be dependent upon the individual physician's risk tolerance, as the recommendations available at this time are made by consensus and not on robust clinical trials.

To confirm a subsegmental PE as truly isolated with bilateral duplex ultrasonography can itself pose a large logistical and financial barrier for many EDs. In an emergency medicine setting, CT scanning is often used to answer a clinical question and guide initial treatment. If

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