

Challenges in Managing Isolated Subsegmental Pulmonary Embolism

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ABSTRACT

This commentary explores the clinical conundrums arising when caring for patients with acute pulmonary embolism isolated to the subsegmental pulmonary arteries. We discuss ways to confirm the radiologic diagnosis, how to distinguish patients for whom anticoagulation is indicated from those who are eligible for structured surveillance without anticoagulation, what surveillance entails, and why ensuring continuity of care matters. We report a case from our own experience that illustrates these decision-making crossroads and highlights the importance of cross-disciplinary collaboration. Because the evidence in the literature is currently weak and indirect, we draw on expert opinion in US and European guidelines, a recent statement from a multidisciplinary consensus panel, and several ongoing well-designed clinical trials. This discussion will help clinicians better manage the spectrum of patients who present with isolated subsegmental embolism.

INTRODUCTION

The management of pulmonary embolism (PE) isolated to the subsegmental pulmonary arteries presents several challenging clinical questions: Are the radiologic findings truly positive? Is anticoagulation necessary? Is outpatient management appropriate? Is the patient agreeable with the treatment and follow-up plans? The most controversial of these is withholding anticoagulation from select patients with subsegmental PE.¹⁻⁶ The research supporting outpatient structured surveillance is limited and the current evidence indirect.⁷⁻⁹ No randomized trials have been published to guide treatment decisions. Society guidelines and expert panels, however, offer sensible direction on patient selection, while we await the results of several ongoing trials (eg, [clinicaltrials.gov: NCT01455818](https://clinicaltrials.gov/ct2/show/study/NCT01455818), [NCT04263038](https://clinicaltrials.gov/ct2/show/study/NCT04263038), and [NCT04727437](https://clinicaltrials.gov/ct2/show/study/NCT04727437)).

For the generalist, consultants are another valuable source of informed advice. Does the radiologist or pulmonologist feel confident that this is a genuine PE? Does the thrombosis expert, eg, hematologist or pulmonologist, suspect the venous thromboembolism (VTE) recurrence risk to be sufficiently low to safely forgo anticoagulation? And if the treating decision maker is not the patient's primary care clinician, eg, an emergency- or hospital-based clinician, can the primary care clinician be informed of the treatment plan? They, after all, will be seeing the patient for follow-up and will be overseeing long-term management. Establishing consensus

around a unified treatment plan and a smooth transfer of care requires effective communication.¹⁰⁻¹²

We present an illustrative case that demonstrates outpatient management of a low-risk ambulatory emergency department (ED) patient with subsegmental PE. The case addresses the questions we raised above and introduces the commentary that follows, in which we offer clinically useful lessons for emergency clinicians, hospitalists, and primary care clinicians (Table 1).

ILLUSTRATIVE CASE

A healthy 47-year-old woman presented to her primary care physician with mild exertional dyspnea for 2 months. One week prior to presentation, she had sustained minor knee contusions and ecchymoses from a ground-level fall. She had no other risk factors for VTE, including malignancy, prior VTE, recent travel or immobilization, or estrogen use. She denied fever, chills, persistent leg pain or swelling, wheezing, hemoptysis, orthopnea, and cough. Her medical history included iron-deficiency anemia and hypertension treated with intravenous iron infusions and hydrochlorothiazide, respectively. She had no family history of VTE.

Her vital signs were within normal limits: blood pressure 117/86 mmHg, pulse 87 beats per minute, and oxygen saturation 100% on room air. Her body mass index was 33 kg/m². She did not exhibit any respiratory distress, and her physical examination was unremarkable, including normal breath sounds and no lower extremity tenderness or swelling.

Her primary care physician ordered a D-dimer level, which was elevated at 632 ng/mL (normal < 500 ng/mL). This

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Abbreviations: CTPA = computed tomography pulmonary angiogram; DVT = deep vein thrombosis; ED = emergency department; PE = pulmonary embolism; VTE = venous thromboembolism

Table 1. Components of care integral to structured surveillance without anticoagulation of select ambulatory patients with acute subsegmental pulmonary embolism

Component	Description
Diagnostic confirmation	Generalists should consult a radiologist or pulmonologist to confirm that imaging findings support a genuine diagnosis of subsegmental pulmonary embolism.
Patient eligibility	Select patients with subsegmental pulmonary embolism may be candidates for structured surveillance without anticoagulation if they are not pregnant and have neither active cancer, high-risk features for venous thromboembolism recurrence, nor concurrent deep vein thrombosis (Table 2; Figure A1 in the appendix for P-CARD acronym). The results of ongoing studies will strengthen the low-certainty evidence currently available to guide management decisions.
Multispecialty communication	Consult pulmonologist to discuss criteria for and against anticoagulation. Hospitalists and emergency physicians should communicate the treatment plan and its rationale to the follow-up clinician to facilitate seamless continuity of care.
Structured surveillance	Structured surveillance entails repeat bilateral compression ultrasonography in 5-7 days to evaluate for proximal lower-extremity deep vein thrombosis with close outpatient follow-up to monitor for emerging signs and symptoms of venous thromboembolism.

prompted a next-day multi-row detector computed tomography pulmonary angiogram (CTPA), which showed several small defects in the left lower lobe subsegmental pulmonary arteries. As the imaging study was reported after-hours when the primary care physician was unavailable, the radiologist called the patient and referred her to the ED. The emergency physician documented intermittent dyspnea for 2 days. She underwent a complete blood count, basic metabolic panel, electrocardiogram, and bilateral lower-extremity compression ultrasonography, which were all unremarkable. She remained clinically stable throughout her ED stay.

One dose of 150 mg enoxaparin was administered subcutaneously, and a hospitalist was consulted. After a thorough evaluation of the patient and review of imaging and laboratory studies, the hospitalist felt that hospitalization and anticoagulation were not indicated. This treatment plan included a suggestion to repeat the CTPA “in a couple weeks.” The plan was discussed with the patient and her husband, who both agreed. The patient was discharged home with recommendations to see her primary care physician the following week. The rationale for withholding anticoagulation was not documented in the electronic health record and had not been communicated to the primary care physician, whom the patient saw 5 days later. The patient’s physician believed that anticoagulation was indicated and consulted a pulmonologist, who concurred. The patient was started on 150 mg of enoxaparin subcutaneously daily for 5 days, followed by 150 mg dabigatran orally twice daily for 3 months.

The pharmacy-led, telephone-based anticoagulation management service contacted the patient the next day for anticoagulant education. She completed the course of dabigatran uneventfully.

COMMENTARY

This case illustrates some of the key considerations in the management of patients with subsegmental PE. The first

asks if the CTPA findings of subsegmental PE are truly positive. Filling defects only at the level of the subsegmental arteries are prone to overdiagnoses, with high false positive rates.^{3,4,13-15} A recent multispecialty expert panel agreed to the following diagnostic criteria of subsegmental PE: “A contrast defect in a subsegmental artery, ie, the first arterial branch division of any segmental artery independent of artery diameter, visible in at least two subsequent axial slices, using a CT scanner with a desired maximum collimator width of ≤ 1 mm”.¹ The American College of Chest Physicians (CHEST) guideline and expert panel also report CTPA characteristics that favor a diagnosis of subsegmental PE (Table A1 in the appendix).^{3,4} Most generalists will depend on their local radiologists or pulmonologists to help interpret the reliability of radiologic findings.^{7,16} Equivocal findings may be an indication for close outpatient observation and consideration for subsequent imaging. Our patient’s radiologic findings supported a diagnosis of subsegmental PE.

When subsegmental PE has been diagnosed, the question of the necessity of anticoagulation needs to be addressed. The clinical significance of isolated subsegmental PE is not clear; most clinicians believe that it may have less consequence in select low-risk patients than more proximal PE.^{1,2,17-19} Thus, the utility of *routine* anticoagulation has been called into question.^{1,2,17} The primary literature is not as helpful as we would like, as it includes relatively few patients who were managed without anticoagulation, and these were not randomly assigned.²⁰⁻²⁶ In fact, the indications for withholding anticoagulation and content of the subsequent management (eg, structured surveillance or not) are often unreported or unclear, with the exception of an observational study from New Zealand of a treatment algorithm for select patients with single subsegmental PE.²⁴ Treatment of subsegmental PE has been shown to vary across countries and physicians.² Agreement appears widespread that patients with subsegmental PE and active cancer, concurrent deep vein thrombosis (DVT), or pregnancy

should receive anticoagulation, barring contraindications.^{1,3,4,7} This determination requires bilateral proximal lower-extremity compression ultrasonography, even if the patient lacks signs and symptoms of DVT. Patients with central venous catheters and those with symptoms of upper-extremity DVT should also be investigated with imaging, and, if DVT is present, anticoagulation begun. Other high-risk factors for recurrence besides active cancer also favor anticoagulation.^{1,3,4,19} Though current evidence is limited and indirect, stable outpatients with neither pregnancy, active cancer, nor DVT who are low risk for recurrent VTE may not require anticoagulation (Table 2; Figure A1 in the appendix for the P-CARD acronym). Patients at high risk for bleeding complications also might be better served with surveillance over anticoagulation.^{3,4,6} Structured surveillance entails repeat imaging for proximal lower-extremity DVT in 5–7 days with close outpatient follow-up to monitor for new or worsening VTE signs and symptoms.

The case report associated with this commentary describes a patient who lacked major anticoagulation indications—no active cancer, concurrent DVT, no marked PE symptoms. This supported a surveillance approach. She did, however, have multiple subsegmental pulmonary emboli, for which one set of guidelines and one treatment pathway²⁴ recommend anticoagulation (Table 2). Her risk for recurrent VTE, on the other hand, was harder to gauge, given the disparate reports of dyspnea duration: if 2 months, PE may not have had a reversible cause (and hence was more likely to recur), but if 2 days, the minor leg trauma may have incited the PE (which was then less likely to recur).²⁷ This complexity of risk assessment contributed to different treatment plans, each of which was justifiable: surveillance, launched by the hospitalist, versus anticoagulation, undertaken by the primary care physician and pulmonologist.

This case also underscores the importance of communication between clinicians (Table 1). When embarking on a

Table 2. Characteristics that favor structured surveillance without anticoagulation in clinically stable outpatient adults with acute pulmonary embolism isolated to the subsegmental pulmonary arteries^a

Characteristics	Sources					
	CHEST guideline and expert panel reports (2016/2021) ^{3,4}	European Society of Cardiology guidelines (2019) ⁷	Multispecialty panel of experts in Delphi consensus study (2020) ¹	Multicenter prospective cohort management study ^b	Multicenter randomized placebo-controlled trial (SAFE-SSPE) ^b	Stopping Anticoagulation for Isolated or Incidental Subsegmental Pulmonary Embolism trial (STOPAPE) ^b
No active cancer ^c	✓	✓	✓	✓	✓	✓
No major risk factors for VTE recurrence (examples follow):	✓		✓	✓	✓	✓
Prior VTE (qualification)			✓	✓	✓ (unprovoked)	✓ (unprovoked)
Antiphospholipid syndrome			✓			✓
Reduced mobility or currently hospitalized	✓					
Reversible VTE risk factor to explain current PE (eg, recent surgery)	✓					
No current DVT (proximal) ^d	✓	✓	✓	✓	✓	✓
Other factors						
No pregnancy ^e			✓	✓	✓	✓
No marked PE-related symptoms	✓					
Normal cardiopulmonary reserve	✓					
Only single subsegmental PE (not multiple) ^f		✓				

^aConsideration of VTE surveillance without anticoagulation assumes clinical stability (eg, normal vital signs), no other indication for anticoagulation (eg, high-risk atrial fibrillation), and reliable follow-up. Examples of *outpatients* include those diagnosed with PE in the clinic, ambulatory care, emergency department, or short-term observation settings. This table excludes patients with hospital-acquired PE. The CHEST guideline is clear that structured surveillance without anticoagulation for select patients is currently a “weak recommendation” based on “low-certainty evidence.”^{3,4}

^bWe include in the table select study criteria most relevant to deliberation on withholding anticoagulation. Complete lists are available at clinicaltrials.gov: NCT01455818 (for the prospective cohort management study), NCT04263038 (for the SAFE-SSPE randomized trial), and NCT04727437 (for the STOPAPE study).

^cDefinitions vary, eg, the multicenter prospective cohort management study (NCT01455818) defines this as follows: “other than basal-cell or squamous cell carcinoma of the skin; cancer within the past 6 months; any treatment for cancer in the past 6 months; or recurrent or metastatic cancer.” The European Society of Cardiology guidelines recommend anticoagulation for most patients with active cancer and subsegmental PE.⁷

^dSymptomatic or asymptomatic DVT. Includes DVT in other locations, eg, upper extremity, abdomen.

^ePregnant patients may have been excluded from the three ongoing trials also because of medication contraindications.

^fThe European Society of Cardiology guidelines recommend anticoagulation for *multiple* subsegmental PE, even without active cancer or concurrent proximal DVT. Surveillance, however, is recommended for *single* subsegmental PE without active cancer or concurrent proximal DVT.

DVT = deep vein thrombosis; PE = pulmonary embolism; VTE = venous thromboembolism.

mode of management uncommon in many practice settings (like withholding anticoagulation in acute PE), communication between participating clinicians is essential. Consulting a pulmonologist or hematologist may provide a generalist with valuable input. If both treating clinician and consultant agree that surveillance is prudent, the management plan may better withstand scrutiny. If, as in our case, the treatment decision-maker is someone other than the primary care clinician, then efforts should be made to inform the primary clinician of the management plan and secure close follow-up. Such collaboration and communication would facilitate continuity of care and reduce the odds of an abrupt change of follow-up plans.²⁸ Sometimes patients are discharged home from the ED or inpatient ward during off-hours, or the discharging clinician is simply unable to reach the patient's primary care clinician. In these cases, communication of the treatment plan and its rationale by voicemail or secure messaging is critical to streamline continuity of care. The availability of shared inpatient-outpatient electronic health records in many settings facilitates the seamless exchange of time-sensitive health information.²⁹ More novel features such as group chat (or "chart chat") embedded in the electronic health record can help clinicians leverage technology to bring all members of the medical team on the same page to solidify cross-site communication and build a robust coalition using a shared decision-making approach.

As our case illustrates, not all patients with acute PE require hospitalization. The evidence for the safe management of normotensive low-risk patients with acute PE is growing, even for those with emboli more proximal than subsegmental.³⁰⁻³² Several prognostic tools have been studied to help with patient selection.^{33,34} Among the most commonly used validated triage tools are the Hestia clinical decision rule, a list of 11 contraindications to outpatient care,³⁵ and the PE Severity Indices (the original index³⁶ and its simplified counterpart),³⁷ which estimate 30-day all-cause mortality. The simplified PE Severity Index and the Hestia clinical decision rule appear to perform similarly when compared head-to-head, identifying over one-third of ED patients with acute PE for safe outpatient management.^{32,38} More recently, attention has turned to the management of patients diagnosed with acute PE in primary care.³⁹⁻⁴³ Our patient was low risk on the PE Severity Index (score 47 points, Class I), lacked all the Hestia criteria that might warrant inpatient management, and met the CHEST criteria for outpatient management.^{3,4} By these several indicators, she was eligible for outpatient care, even if she had been discharged with anticoagulation.

We have discussed the importance of inter-specialty collaboration in confirming the radiologic diagnoses and selecting the best treatment plan. But specialists are not the only ones we should engage in shared decision-making: patients

and their families should also be included in the conversation about treatment options. Patient involvement rises to a different level if the clinician is at a crossroads regarding a treatment decision, eg, anticoagulation versus surveillance or inpatient observation versus discharge to home. Shared decision-making moves to center stage in situations of clinical equipoise, where patient and family input are most valuable.⁴⁴ When asked about her perspective on the care she received during her ED and outpatient PE management, our patient emphasized the caring engagement of her physicians: "I appreciated the time the doctors spent explaining to us the treatment options. My husband and I valued being included in the decision-making by all the doctors at every stage."

The hospitalist was exemplary in engaging the patient and her husband in the treatment plan. But other elements of his care plan could have been improved (Table 1). It would have been valuable 1) to have consulted a thrombosis specialist and documented the discussion in the electronic health record, 2) to have arranged bilateral proximal lower-extremity compression ultrasonography for 5-7 days after discharge, and 3) to have communicated the surveillance plan and its rationale to the primary care physician. Because it was near midnight when the patient was discharged home, the hospitalist could have supplemented his electronic health record documentation with a voicemail or secure email to the primary care physician.

CONCLUSION

In summary, select patients with subsegmental PE may be candidates for structured surveillance without anticoagulation. Patients eligible for this approach are non-gravid adults without active cancer, high-risk features for VTE recurrence, or DVT. Generalists should obtain specialty consultation to confirm the radiologic diagnosis of subsegmental PE and discuss criteria for and against anticoagulation. Hospitalists and emergency clinicians should communicate the management plan and its rationale to the follow-up clinician to facilitate seamless continuity of care. Structured surveillance entails repeat imaging for proximal lower-extremity DVT in 5-7 days with close outpatient follow-up to monitor for emerging signs and symptoms of VTE. Results of several ongoing trials will sharpen these recommendations when published in the coming years. ♦

Supplemental Material

Supplemental Material is available at www.thepermanentejournal.org/files/2021/21.077supp.pdf

Disclosure Statement

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Authors' Contributions

David R Vinson, MD, and Etsehiwot Taye, MD, identified the case. All authors acquired and analyzed data. David R Vinson, MD, drafted the initial report and all authors contributed to its critical revision. All authors approved the final version. David R Vinson, MD, is accountable for the work.

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