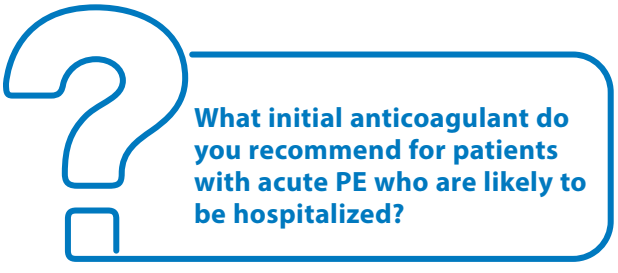
Approach to Acute Intermediate-Risk Pulmonary Embolism

Moderator: Geoffrey D. Barnes, MD, MSc
Panelists: Michael McDaniel, MD, FACC, FSCAI, and Frances Mae West, MD, MS, FACP

CASE PRESENTATION

A male patient in his early 70s with a history of congestive heart failure, type 2 diabetes mellitus, and obesity presented to the emergency department (ED) with 3 hours of sudden-onset shortness of breath and chest discomfort. He was newly hypoxic, tachycardic, and dyspneic. He could converse in full sentences but became winded ambulating around his house. His vital signs were notable for mild tachycardia (heart rate, 106 bpm), stable blood pressure (126/82 mm Hg), mild tachypnea at rest (22 breaths/min), and hypoxia (Spo_2, 88% on room air, 96% via 3-L nasal cannula). His electrocardiogram was notable for sinus tachycardia but no signs of coronary ischemia or right ventricular (RV) strain. His D-dimer was elevated (3 times the upper limit of normal), and his high-sensitivity troponin T was elevated at 22 pg/mL (normal, < 19 pg/mL).

He underwent CT pulmonary angiography, which demonstrated an acute pulmonary embolism (PE) in his right upper and mid lobar arteries. His RV/left ventricular (LV) ratio on CT scan was 1.2. The echocardiogram confirmed mild RV enlargement and baseline LV dysfunction (40%), without new LV wall motion abnormality. The ED physician classified him as having an intermediate-high–risk PE with a Pulmonary Embolism Severity Index (PESI) score of 112 (class IV). A PE response team (PERT) call was activated.



Dr. McDaniel: In this case, I would start low-molecular-weight heparin (LMWH) and then transition to a direct oral anticoagulant. Although both LMWH and unfractionated heparin (UFH) are good initial options for intermediate-risk acute PE, LMWH is probably preferred in this case due to the rapid mechanism of action, reliable bioavailability, and excellent safety.[1] In addition, from a nursing perspective, LMWH is easier to use than UFH because it does not require titration. If the patient were at higher risk for early mortality, then UFH may be preferred when considering systemic thrombolysis, surgery, or catheter-based interventions because it allows for management flexibility. When full-dose systemic thrombolysis is administered, anticoagulation is often omitted during the alteplase infusion. When catheter-directed thrombolysis (CDT) is performed, the UFH is often adjusted to the lower-intensity protocols or low-dose, fixed doses (500-1,000 units/hour). Finally, when catheter embolectomy is performed, UFH is often used in case of bleeding complications from the larger-French sheaths and devices. Although bleeding is rare, it can be life threatening, and rapid anticoagulation reversal is required, which is easier with UFH than LMWH.

Dr. West: This is a great question and one that is very relevant for clinicians at the forefront of acute PE management. For this patient with intermediate-risk PE, the concern is whether reperfusion therapy is required due to clinical decompensation or if the PERT should recommend catheter-based therapy. Historically, the recommendation has been to start with a weight-based bolus of UFH followed by an infusion, which is interrupted or dose-reduced periprocedurally. Even with pharmacy-managed and nursing-driven protocols, UFH has unpredictable pharmacokinetics that require careful monitoring and frequent laboratory checks. Pooled data suggest that LMWH is superior to UFH for the initial management of PE in important clinical outcomes, including recurrent venous thromboembolism, major bleeding, and mortality. Similarly, data are emerging from single centers and registries regarding the safety of performing catheter-based therapies with LMWH therapy.

For initial management in this patient, I would recommend LMWH therapy. This recommendation represents predefined consensus with our institutional PERT, including vascular medicine and interventional radiology groups. Having an institutional protocolized approach is important for treatment consistency and to disseminate to consulting physicians who often initiate anticoagulation prior to or simultaneously with a PERT consultation.

What is the evidence supporting any catheter-based therapy beyond anticoagulation alone in this clinical situation?

Dr. West: Clinical trials have shown that CDT is effective for improving RV dilation and pulmonary hypertension postprocedure and is safe, with low rates of major bleeding in patients with intermediate-risk PE. However, when ultrasound-assisted CDT plus UFH was evaluated against UFH alone, there was no difference in RV/LV ratio between the two groups at 90 days.[2] Similarly, two different percutaneous thrombectomy devices have shown efficacy in improving RV dilation and lowering pulmonary artery (PA) pressure postprocedure in this population. Safety profiles are also acceptable and have the benefit of performing the procedure without or with small doses of fibrinolytic. However, catheter-directed therapies have been insufficiently studied to assess long-term clinical (including functional) outcomes. The efficacy and safety trials of these devices have proven clinical equipoise for therapeutic options in patients with intermediate-risk PE, including the patient presented in this case. Currently enrolling randomized controlled trials are underway to assess long-term outcomes of ultrasound-assisted CDT plus anticoagulation versus anticoagulation alone, and another trial comparing CDT to percutaneous thrombectomy is also in progress.

Dr. McDaniel: I would not recommend catheter-directed therapy for this patient. Although the PESI score suggests elevated risk, the elevation in risk is primarily related to the patient's age and not due to other clinical variables. Another risk-stratification system from the European Society of Cardiology stratifies risk based on RV dysfunction and elevation in cardiac biomarkers. Patients with both elevated biomarkers and RV dysfunction are classified as intermediate-high risk, while patients with one but not both are classified as intermediate-low risk. The rationale for this classification system is that the combination of RV dysfunction and abnormal cardiac biomarkers is associated with a higher risk for early mortality than either alone. However, this was noted in the previous era of before high-sensitivity troponin testing. Although this patient's high-sensitivity troponin level is elevated, this degree of elevation would have probably been normal with assays prior to the high-sensitivity era. As such, this patient would be intermediate-low risk and traditionally excluded from studies investigating advanced therapies such as systemic thrombolysis, CDT, and catheter embolectomy. Furthermore, the patient has LV dysfunction, which also can contribute to elevations in troponin and make the interpretation of risk more difficult. Anticoagulation alone is probably the preferred strategy for this patient.

How would you explain to the patient and his family the potential benefits and risks of a catheter-based intervention versus anticoagulation alone for acute management?

Dr. McDaniel: I would not recommend catheter-based interventions for this patient. As discussed previously, the patient is at lower risk for early mortality despite the elevated PESI score. The right ventricle is only mildly enlarged, and the high-sensitivity troponin is in a range that has not traditionally been considered "elevated." In addition, the heart rate and respiratory rate are not very abnormal. Most studies investigating advanced therapies such as systemic thrombolysis and catheter-based therapies have primarily focused on younger patients at higher risk than the current patient. Despite the lack of data and consensus, there are other reasons to avoid catheter-based therapies in this patient.

Based on the CTA, the clot location is more distal (right upper and mid lobar arteries), making catheter embolectomy more challenging. The right upper PA is a difficult location for clot extraction with larger devices given the degree of angulation off the right main PA. In addition, thrombus located in the lobar arteries is more distal and more challenging for clot extraction compared to proximal thrombus in the main PAs. Although the use of smaller-French embolectomy devices is possible, there is less published experience with these devices.

Although CDT is another option for this patient, it is not clear that the benefits outweigh the risks. One of the most important risks of CDT is intracranial hemorrhage and one of the most important risks for this complication is advanced age. In our series, patients aged > 75 years

who underwent CDT were the only group who experienced intracranial hemorrhage.[3] Given the unclear benefit and increased risk for bleeding complications, anticoagulation alone would be preferred in this patient.

Dr. West: Recommendations for therapy must be individualized to the patient. The current PE classification and risk assessments are imperfect. I have adopted a shared decision-making model with my patients in which I discuss the efficacy and safety as well as the risks and benefits of the various catheter-based interventions in conjunction with anticoagulation or continuing anticoagulation alone. I explain that although these catheter-based therapies have become standard of care at many institutions with short-term benefits, there are no long-term data to show that there is benefit over anticoagulation alone. If the patient has very high-risk features (eg, a heart rate > 140 bpm, a very high RV/LV ratio, an elevated lactate, a large proximal deep vein thrombosis, a low cardiac index as estimated by RV outflow tract or LV outflow tract echocardiographic measurements), then I am more inclined to recommend a procedure. For a patient without such features and with a low functional baseline, I am more inclined to recommend anticoagulation with close monitoring for hemodynamic decompensation. For the case patient, I would assess his values and preferences. Is he more conservative, or is he willing to undergo a procedure to feel better faster? I would assess the patient's current New York Heart Association classification and address expectations for returning to his functional baseline. Ultimately, we would come to a decision in conjunction with my institution's multidisciplinary PERT using a shared decision-making model.

APPROACH OF THE MODERATOR

This patient with intermediate-high–risk PE is an ideal candidate for enrollment in a clinical trial. That is because there is not yet a clear consensus on how best to manage him. He was initially managed with LMWH and placed in a step-down unit for close monitoring. However, over the next 4 hours, his heart rate and oxygen requirements both increased. As such, the PERT recommended proceeding to a catheter-based thrombolytic approach to help avoid hemodynamic decompensation. This was selected given that his overall bleeding risk was not substantially elevated, so the interventional team felt that he was a good candidate for thrombolytic therapy. However, the team elected to give thrombolytics via a catheter to direct them to the areas of the lung vasculature where the thrombus was known to reside and to reduce the overall dose administered. The patient did well, improving his oxygenation and tachycardia over the next 12 hours. He was eventually discharged from the hospital on oral anticoagulation 3 days later and was seen in the PERT follow-up clinic shortly thereafter. ■

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3. Bloomer TL, El-Hayek GE, McDaniel MC, et al. Safety of catheter-directed thrombolysis for massive and submassive pulmonary embolism: Results of a multicenter registry and meta-analysis. Catheter Cardiovasc Interv. 2017;89:754-760. doi: 10.1002/ccd.26900.

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