CHEST

The PERT Concept

A Step-by-Step Approach to Managing Pulmonary Embolism

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Pulmonary embolism (PE) is a major source of morbidity and mortality. The presentation of acute PE varies, ranging from few or no symptoms to sudden death. Patient outcome depends on how well the right ventricle can sustain the increased afterload caused by the embolic burden. Careful risk stratification is critical, and the PE response team (PERT) concept offers a rapid and multidisciplinary approach. Anticoagulation is essential unless contraindicated; thrombolysis, surgical embolectomy, and catheter-directed approaches are also available. Clinical consensus statements have been published that offer a guide to PE management, but areas remain for which the evidence is inadequate. Although the management of low-risk and high-risk patients is more straightforward, optimal management of intermediate-risk patients remains controversial. In this document, we offer a case-based approach to PE management, beginning with diagnosis and risk stratification, followed by therapeutic alternatives, and finishing with follow-up care.

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Pulmonary embolism (PE) is the world's third leading cause of cardiovascular death, and its incidence continues to rise.[1] It is a major cause of hospitalization, morbidity, and mortality, with approximately 100,000 deaths each year in the United States.[2,3]

Acute PE can present variably, ranging from asymptomatic and incidentally identified to sudden death. The outcome is proportional to the ability of the right ventricle (RV) to tolerate the embolic obstruction. The increased pulmonary arterial pressure together with hypoxic vasoconstriction can lead to RV dilation and dysfunction, which may lead to decreased cardiac output and systemic hypotension.[4,5] The presence of abnormal RV function increases mortality, even in normotensive patients.[6]

Anticoagulation is essential, and although additional reperfusion strategies exist, optimal management, particularly of intermediate-risk patients, remains debated. Variations in recommendations by societies, such as the American College of Chest

ABBREVIATIONS: BNP = B-type natriuretic peptide; CDL = catheter-directed thrombolysis; CTA = CT angiography; CTEPH = chronic thromboembolic pulmonary hypertension; DOAC = direct-acting oral anticoagulants; ESC = European Society of Cardiology; HR = heart rate; ICH = intracranial hemorrhage; IVC = inferior vena caval; LMWH = low-molecular-weight heparin; PE = pulmonary embolism; PERT = pulmonary embolism response team; PESI = Pulmonary Embolism Severity Index; RV = right ventricle; SBP = systolic BP; sPESI = simplified Pulmonary Embolism Severity Index; UFH = unfractionated heparin

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Physicians,[7] American Heart Association,[8] and European Society of Cardiology (ESC),[9] make treatment decisions challenging.

In response to increasing therapeutic options, the pulmonary embolism response team (PERT) concept has evolved. This rapid-response approach offers a real-time multidisciplinary discussion, with shared decision-making, expedited recommendations, and plan execution. The PERT Consortium created a consensus practice document outlining PE management.[9,10]

In this document, we provide a step-by-step approach to PE management, starting with diagnosis and risk stratification, followed by treatment, and finishing with follow-up care, all framed within the context of a case.

Clinical Case

A 68-year-old man without any significant medical history presented to the ED with sudden-onset dyspnea beginning 3 hours after deplaning from a 15-hour international flight. He had associated lightheadedness, but denied cough, chest discomfort, hemoptysis, syncope, or leg swelling or pain. The initial respiratory rate was 22 breaths/minute; heart rate (HR), 128 beats/min; BP, 92/52 mm Hg; and room air O_2 saturation, 88%. These improved to 18 breaths/min, 120 beats/minute, 102/66 mm Hg, and 98%, respectively, after 500 mL intravenous normal saline and 6 L/min oxygen by nasal cannula. Physical examination was otherwise unremarkable.

Initial laboratory testing showed a hemoglobin of 14.0 g/dL, WBC 7,200/mm^3, platelets 182,000/mm^3, BUN 22 mg/dL, creatinine 1.2 mg/dL, B-type natriuretic peptide (BNP) 349 pg/mL, and troponin 0.64 ng/mL (upper limits of normal = 100 pg/mL and 0.04 ng/mL, respectively), with serum lactate at 2.4 mmol/L.

Acute PE was suspected, and no significant bleeding risk was evident. Enoxaparin 1 mg/kg subcutaneously was administered.

Step 1: Initial Evaluation—Making the Diagnosis

The presentation of acute PE is heterogeneous, and clinical suspicion is critical, because signs and symptoms are nonspecific. The Wells and Geneva scoring systems combine clinical findings to assess clinical pretest probability for PE.[11,12] The utility of clinical judgment or gestalt should not be underestimated.[13] With low pretest probability, the Pulmonary Embolism Rule-Out Criteria[14] or a negative D-dimer may be used to effectively rule out PE. With high pretest probability, contrast-enhanced chest CT angiography (CTA) should be pursued. With renal insufficiency, $\dot{V}/\dot{Q}$ scintigraphy is recommended; leg ultrasonography and echocardiography also may be useful.

Case Continuation

CTA revealed extensive bilateral acute PE involving main pulmonary arteries, lobar and segmental branches. Echocardiography showed severe RV dilation and dysfunction. Leg ultrasound indicated DVT in the left peroneal, posterior tibial, and popliteal veins, and into the distal femoral vein.

Step 2: Risk Stratification

Rapid PE risk stratification remains a critical step in guiding management. PE is classified into three main categories: high-risk or massive, intermediate-risk or submassive, and low-risk. Hemodynamic stability must be considered initially. Low-risk patients are normotensive with normal RV function and biomarkers, and they have excellent prognosis once anticoagulation is established.[8] High-risk PE is defined as persistent hypotension (systolic BP [SBP] $<$ 90 mm Hg or a decrease in SBP of $>$40 mm Hg from baseline, for $\geq$15 minutes), obstructive shock, evidence of end-organ hypoperfusion, such as altered mental status, cold/clammy skin, oliguria/anuria, increased serum lactate, or cardiac arrest.[8,9] These patients account for 5% to 10% of cases but have a high mortality (30%-50%), requiring rapid decision-making.[15,16]

In the absence of hypotension, further assessment is necessary to determine the risk of early death. This involves clinical, imaging, and laboratory indicators of PE severity. The Pulmonary Embolism Severity Index (PESI) or simplified PESI (sPESI) scores predict 30-day mortality.[17] Presence of RV dilation and dysfunction,[6,18] or elevated troponin or BNP/N-Terminal pro-BNP are associated with adverse prognosis and increased mortality.[19] Although multiple CTA and echocardiographic parameters have been associated with worse prognosis in acute PE, there is not one uniform definition of RV dysfunction, and often it is defined by a combination of findings. The integration of clinical, imaging, and laboratory parameters has been proposed to be superior, providing enhanced risk stratification.[20,21]

Intermediate-risk PE patients have RV dysfunction without hypotension and account for 30% to 50% of cases.[15,16] This group is further subclassified into intermediate-high risk (both RV dysfunction on imaging and biomarker elevation) or intermediate-low risk (RV dysfunction or biomarker elevation).[9] Those with both RV dysfunction and elevated biomarkers have a higher

in-hospital mortality and risk for decompensation and may benefit from closer observation and consideration of advanced therapies.[9,10]

Case Continuation

The patient was diagnosed with intermediate-high risk PE. The extensive clot burden was causing severe RV dysfunction and elevated troponin. The sPESI score was 2 (based on tachycardia and O_2 saturation $< 90\%$). The PERT was consulted.

Step 3: PERT

PERTs are multidisciplinary teams that specialize in rapid PE assessment with risk stratification and treatment, as well as follow-up, with the goal of improving patient care. The PERT concept builds on the success of the rapid response team or heart team incorporating a process in which immediate multidisciplinary consultation is used to achieve consensus regarding the optimal, individualized care for a complex clinical scenario. PERTs have emerged given the lack of consensus agreement, conflicting guideline recommendations, and increasing advanced therapeutic alternatives.

The PERT concept was initially established in 2012[22] and has been increasingly adopted worldwide. In 2014, the PERT Consortium was established, and it now includes approximately 100 institutional members. The PERT Consortium's primary goal is to guide and influence PE care through a multicenter collaboration in clinical guidelines, research, communication, and education.[23]

PERT structure varies by institution, but it may include emergency medicine, pulmonary/critical care, cardiac surgery, interventional radiology and cardiology, hematology, clinical pharmacy, vascular medicine, and vascular surgery.[24,25] Activation approach also may vary, but it usually involves a single-contact pager or phone, with a PERT member who obtains relevant patient information. In a survey of PERT programs, most programs have the complete multidisciplinary team respond to the initial activation (63%), and less frequently a tiered approach (32%), with a single physician consultation for the initial response and a multidisciplinary team-based discussion for more complex cases.[24] Ideally, the multidisciplinary discussion should involve a clinician (pulmonary/critical care, cardiologist, emergency medicine, or vascular medicine) and an interventionalist (interventional cardiologist or radiologist, vascular or cardiac surgeon). Real-time (face-to-face, telephone, or secure web conference platforms) discussion can take place if needed, followed by consensus agreement and immediate plan execution.

PERTs may be particularly useful in patients with intermediate- or high-risk PE,[10] and PERT care has been associated with improved outcomes, such as 30-day mortality, lower rates of bleeding, and shorter time to therapeutic anticoagulation, at a single institution.[26] Efforts to analyze and report outcomes from the multicenter, national PERT database are ongoing. Despite a paucity of literature and the need for more robust prospective studies, PERTs have been endorsed by the ESC and changed the paradigm of PE care.[23,27]

Step 4: Specific Management Measures

Despite increasing reperfusion therapies available for intermediate- and high-risk PE,[28] therapeutic anticoagulation remains the primary therapy for acute PE. Patients achieving therapeutic anticoagulation within 24 hours of admission have reduced 30-day mortality.[29] However, results from a large academic PERT center demonstrated that fewer than half of the patients treated with unfractionated heparin (UFH) achieved therapeutic levels within the first 24 hours.[30] Thus, low-molecular-weight heparin (LMWH) is favored by many as the initial anticoagulant of choice, based on achieving predictable therapeutic levels within 3 to 4 hours of administration.[31] LMWH may be used even if advanced therapies are being considered; however, UFH may be preferred in those with overt hemodynamic instability and imminent need of reperfusion therapy.[9] Direct acting oral anticoagulants (DOACs) are considered first-line treatment in patients with low-risk PE. Figure 1 summarizes acute PE treatment algorithm.

Intermediate-Risk PE

Systemic anticoagulation is recommended over systemic or catheter-directed thrombolysis (CDL) by the American College of Chest Physicians, American Heart Association, and ESC consensus statements for most patients with intermediate-risk PE.[7-9] Intermediate-risk PE patients deemed at increased risk of impending clinical deterioration (based on vital signs, severity of RV dysfunction, tissue perfusion, or gas exchange) who have not yet developed hypotension may be considered for additional interventions, such as systemic thrombolysis, CDL, or catheter embolectomy.[7-9] Important considerations include risk of bleeding, local expertise, and available resources.

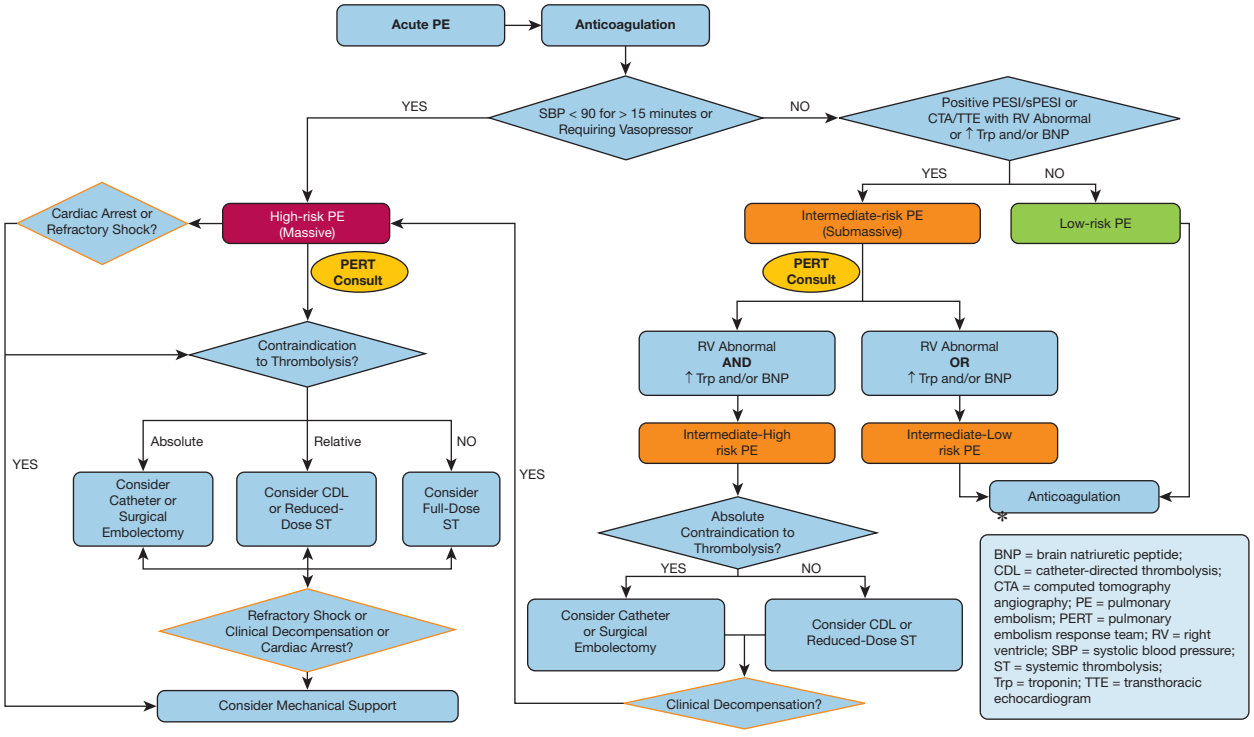

Figure 1 – *Acute pulmonary embolism treatment algorithm. Adapted from "Diagnosis, Treatment, and Follow-Up of Acute Pulmonary Embolism: Consensus Practice from the PERT Consortium," by Rivera-Lebron BN.* Clin and Appl Thrombosis Hemost. *2019;25:1-16. Copyright 2019 by SAGE. Reprinted with permission.*

Full-dose systemic thrombolysis is not recommended as a first-line therapy in patients with intermediate-risk PE. This was particularly influenced by the large double-blind randomized placebo-controlled Pulmonary Embolism Thrombolysis trial,[32] which showed a decrease in hemodynamic deterioration without a difference in 7- or 30-day mortality, offset by increased major bleeding (6.3%) and intracranial hemorrhage (ICH) (2%) in the thrombolysis group. Notably, major bleeding risk was highest among patients older than 75 years, and every ICH patient was 65 years of age or older. These findings may suggest age cutoffs to consider with systemic thrombolysis. Additionally, no long-term mortality benefit or difference in the incidence of chronic thromboembolic pulmonary hypertension (CTEPH) was seen.[33] Meta-analytic data has suggested mortality benefit with thrombolysis in intermediate-risk PE with increased risk of major bleeding (9.24%) and ICH (1.46%).[34] However, these data would be more helpful if there were more specific information about the severity of the intermediate-risk patients, as this is a heterogeneous group. Half-dose thrombolysis represents an alternative in selected intermediate-high risk patients with signs of impending clinical deterioration; in such patients, a catheter-directed approach, if available, could offer an alternative approach and may have a lower bleeding risk.[35]

CDL involves positioning catheters directly into the clot in one or both pulmonary arteries and infusing low doses of thrombolytic drug. CDL may be performed using a standard 4- to 6-Fr multi-hole catheter or an ultrasound-assisted EkoSonic catheter (Ekos/BTG/Boston Scientific); most CDL trials have been with this device.[36,37] In the only prospective, randomized-controlled trial (ULTIMA), 59 patients were randomized to either UFH alone or ultrasound-assisted CDL plus UFH, and the latter group demonstrated improved RV:left ventricle diameter ratio in the first 24 hours, with a very low risk of bleeding.[38] A single-arm, prospective trial of ultrasound-assisted CDL (SEATTLE II) additionally showed early reduction in pulmonary pressures and obstruction index, with a 10% moderate bleeding rate and no ICH.[39] The advantage of CDL is the use of lower-dose thrombolytic agents, doses ranging from 4 to 12 mg per lung, with infusion durations of 4 to 24 hours.[40] This may translate into a lower risk of bleeding, including an overall risk of ICH of aproximately 0.35%.[37] Given the usual infusion duration of at least several hours, patients needing immediate

restoration of hemodynamics may not be ideal candidates for CDL. Most of the CDL data rely on registries or retrospective reviews, with few available randomized controlled data.[28] The use of LMWH before and after CDL appears safe,[41] as is subsequent transition to a DOAC for continuation of AC.[42]

Another percutaneous interventional option is catheter embolectomy. This technique can be combined with catheter-directed thrombolysis or used alone. The FlowTriever (Inari Medical) is a large-bore (22 Fr) cannula placed into the pulmonary artery to aspirate embolic material with manual suction. The recently published FLARE trial[43] offers safety and efficacy data comparable to the CDL data. The Penumbra Indigo (Penumbra Inc) consists of an 8-Fr catheter that aspirates thrombus via a suction pump. A prospective multicenter trial investigating the safety and efficacy of this catheter was recently completed (NCT03218566).[44] The advantage of catheter embolectomy is that it may be used in patients with high bleeding risk or in those with contraindications to systemic anticoagulation, and it may offer rapid improvement. No randomized-controlled data compared with anticoagulation alone are available.

High-Risk PE

Management of high-risk PE is centered around aggressive reperfusion therapies and hemodynamic support. Systemic thrombolysis (tissue-type plasminogen activator 100 mg over 2 hours) remains the mainstay of therapy[7-9]; 50 mg has been studied and can be considered when the bleed risk is higher but not prohibitive.[35] Patients with relative contraindications to thrombolytic therapy can be considered for CDL; in the setting of absolute contraindications to thrombolysis, catheter or surgical embolectomy can be considered.

In a small subset of SEATTLE II with high-risk PE patients, CDL showed early reduction in pulmonary pressures, RV size, and obstruction index[39]; however, no control arm of anticoagulation alone or systemic thrombolysis was included. When CDL or clot extraction is used in the high-risk PE setting, a protocol guaranteeing rapid evaluation and plan execution by experienced personnel is highly recommended.

Surgical embolectomy is considered in high-risk PE patients with an absolute contraindication to thrombolysis or for whom thrombolytic therapy has failed.[7-9] Mechanical hemodynamic support with veno-arterial extracorporeal membrane oxygenation can provide immediate stabilization of high-risk PE, refractory cardiogenic shock, or cardiac arrest patients, and it can serve as a bridge to reperfusion therapies. No randomized trials examining the role of surgical embolectomy or extracorporeal membrane oxygenation in PE are available, but multiple case series have demonstrated favorable outcomes, with survival ranging from 88% to 96%[45,46] and 53% to 78%,[47-49] respectively.

Temporary inferior vena caval (IVC) filters are only indicated in patients with absolute contraindications to anticoagulation or recurrent thrombosis despite adequate anticoagulation.[7,9] This was primarily influenced by the Prevention of Recurrent Pulmonary Embolism by Vena Cava Interruption trial, where there was no difference in recurrent VTE in 399 patients that received anticoagulation with or without an IVC filter.[50] Other patients in whom additional emboli might be catastrophic may be candidates (ie, high-risk PE with a free-floating DVT), although robust data are not available.

Hemodynamic management of high-risk PE includes early vasopressor use (eg, norepinephrine), cautious volume administration, and avoiding preload reduction with diuretics. If a hemodynamically unstable PE patient requires intubation, it is ideally performed by an experienced provider, with early vasopressor therapy use or immediately available, and the understanding that further hemodynamic deterioration could occur. Mechanical ventilation should focus on avoiding hypercapnia and excessive positive end-expiratory pressure.

Management of intermediate- and high-risk can be complex, and the multidisciplinary PERT concept may facilitate management. Table 1 provides additional complex clinical scenarios and potential treatment options.

Case Continuation

Conservative management with enoxaparin was initiated, followed by ICU admission for close monitoring. Three hours after the initial presentation, on patient reevaluation, he noted persistent dyspnea with minimal movement in bed. His HR remained between 120 and 128 beats/min and SBP 98 to 108 mm Hg. His appearance, sPESI, HR, O_2 requirement of 6L/min, biomarkers, echocardiographic parameters, and clot burden suggested a potential for a poor outcome. However, he was neither hypotensive nor deteriorating, so the most aggressive reperfusion therapy

TABLE 1] Complex Clinical Scenarios and How Do I Do It

Clinical Scenario	Bleeding Risk	How Do I Do It?[a]
Young patient with intermediate-high risk PE	Low	Anticoagulate. Consider CDL if clinical worsening,[b] lack of improvement, or on severe end of spectrum but not meeting criteria for high-risk.[c] Consider systemic thrombolysis if clinical worsening,[b] particularly if other procedural resources not available.
Young patient with intermediate-high risk PE	High[d]	Anticoagulate. Consider catheter embolectomy (without thrombolytic) if clinical worsening,[b] lack of improvement, or if on severe end of spectrum but not meeting criteria for high risk[c]
Young patient with intermediate-high risk PE and clot-in-transit	Low	Anticoagulate (consider anticoagulation alone, if clot-in-transit small). Consider systemic thrombolysis, suction,[e] or surgical embolectomy—particularly if PFO.
Elderly patient with intermediate to high risk PE	High[d]	Anticoagulate. Consider catheter embolectomy if clinical worsening,[b] lack of improvement, or on severe end of spectrum but not meeting criteria for high risk[c]
Elderly patient with intermediate to high risk PE and clot-in-transit	Low	Anticoagulate (consider anticoagulation alone, if clot-in-transit small). Consider suction embolectomy.[e] Consider systemic thrombolysis if clinical worsening,[b] particularly if other procedural resources not available. If PFO, consider surgical embolectomy.
Young patient with high-risk PE	Low	Systemic thrombolysis. Can consider CDL or catheter extraction if stable for transfer and if procedure can be rapidly accomplished[f]
Young patient with high-risk PE	High[d]	CDL, catheter or surgical embolectomy. If severely hypotensive and no other resources available, consider systemic thrombolysis, unless bleeding risk involves a critical site (eg, ICH)
Elderly patient with high-risk PE	Low	CDL, catheter or surgical embolectomy. If severely hypotensive, rapidly deteriorating, and no other resources available, consider systemic thrombolysis[f]
Elderly patient with high-risk PE	High[d]	Catheter or surgical embolectomy. Consider anticoagulation alone, if hypotension mild or pressor requirement low
PE and cardiac arrest	Low	Mechanical support and systemic thrombolysis
PE and cardiac arrest	High[d]	Mechanical support and catheter or surgical embolectomy

CDL = catheter-directed thrombolysis; ICH = intracranial hemorrhage; PE = pulmonary embolism; PFO = patent foramen ovale.
[a]Treatment recommendation should be individualized by PE severity, bleeding risk, urgency for intervention, and availability of local expertise. There are no head-to-head trials strongly supporting these different approaches in the specific settings described; no grade IA recommendations can be made.
[b]Clinical worsening is defined by deterioration of one or more of the following: clinical appearance, systolic BP, heart rate, respiratory rate, or oxygen requirement.
[c]For example, heart rate > 120 beats/min, severe tachypnea, or hypoxemia.
[d]For example, GI bleed or recent surgery. Inferior vena cava filter should be placed if, in fact, anticoagulation is contraindicated.
[e]AngioVac if clot is deemed accessible.
[f]As with other risk categories, high-risk PE is heterogeneous. For example, a mildly hypotensive high-risk patient may be considered for CDL or clot extraction, whereas a patient on high-dose pressors who is deteriorating should receive systemic thrombolysis unless contraindicated. Half-dose thrombolysis can be considered in patients deemed acceptable thrombolysis candidates, but who have relative contraindications.

(ie, systemic thrombolysis), was not emergently indicated. Similarly, surgical embolectomy was not indicated. Not only did the patient meet intermediate-high risk PE but parameters were severely abnormal and not improving after 5 hours of therapeutic anticoagulation. Therefore, PERT recommended CDL. An infusion catheter was placed in each lung and administered 6 mg of tissue-type plasminogen activator per lung over 6 hours. Based on the therapeutic enoxaparin dose 5 hours prior, no additional anticoagulation was given during the procedure.

Step 5: Assessment of Treatment and Follow-up

All patients should have outpatient follow-up after acute PE. Timing for post-discharge follow-up (2 weeks to 3 months) and type of clinic (primary care, subspecialty, or post-PE clinic) may vary depending on resources and PE severity. PERTs facilitate follow-up care by referring patients into a post-PE clinic, where available. Table 2 lists action items that can be addressed on the first follow-up visit. After acute PE, most patients recover completely and do not require routine testing. However, close to one third continue to experience exertional

TABLE 2] Pulmonary Embolism Follow-up Visit

• Inquire about persistent or recurrent symptoms (dyspnea, fatigue, chest pain, lightheadedness, edema)
• Review anticoagulation regimen, access to medications, and emphasize compliance. Guarantee appropriate monitoring in patients on vitamin K antagonists.
• Review adverse effects of anticoagulation with specific focus on occult bleeding. Order complete blood count in any patients with concerns regarding anemia, thrombocytopenia.
• Patient education focused on disease understanding and expected recovery
• Determine whether there are persisting risk factors, and thus, duration of anticoagulation as well as whether dose can be reduced
• Determine whether thrombophilia evaluation is indicated
• Order age-appropriate cancer screening
• If PE symptoms persist or worsen, particularly after 3 months, consider lung imaging, echocardiography, brain natriuretic peptide, O_2 saturation check (eg, 6-minute walk or cardiopulmonary exercise testing)
• If IVC filter was placed, coordinate filter removal timeline

IVC = inferior vena cava. See Table 1 legend for expansion of other abbreviation.

dyspnea and reduced exercise capacity,[33] in addition to psychological stress and lower quality of life.[51,52]

If persistent post-PE dyspnea or functional limitation is present after 3 months of anticoagulation, further evaluation including imaging is essential. Those with a persistently abnormal echocardiogram or $\dot{V}/\dot{Q}$ scan should be considered for referral to an expert CTEPH center.[9] The $\dot{V}/\dot{Q}$ scan is highly sensitive for chronic PE, although a chest CTA read by an experienced clinician or radiologist is also acceptable. CTEPH is rare (incidence of 0.5%-4%), but progression to right-heart failure and death may occur if untreated.[53]

Post-PE syndrome refers to persisting dyspnea after acute PE, and chronic thromboembolic disease refers to persistent pulmonary vascular obstruction without pulmonary hypertension.[51] Post-PE dyspnea may be multifactorial, representing deconditioning, or potentially related to a comorbidity or the chronic PE spectrum; a detailed evaluation should be undertaken.

Case Continuation

The patient noted improved dyspnea within a few hours after completing the CDL, as well as a reduction in HR to 90 beats/minute. His BP stabilized at approximately 130/78 mm Hg, and O_2 saturation was 98% on room air the following morning. Enoxaparin was continued every 12 hours. Twenty-four hours after admission, his dyspnea had substantially improved, and his vital signs remained stable. He was transitioned to a DOAC and discharged 48 hours after his presentation.

The patient was seen 2 weeks later in the dedicated outpatient PE clinic. At 3 months, the echocardiogram was completely normal, and he denied dyspnea with exertion. No additional imaging was performed.

Conclusion

As the number of treatment options, available technology, and scientific knowledge increases, the need for interdisciplinary communication and teamwork has to grow proportionally. PERTs offer clinical consensus, especially in areas where guidelines are vague and evidence is inadequate. As the PERT concept continues to evolve, data gaps will close with the emergence of robust evidence in both acute PE care and long-term outcomes. The PERT Consortium framework will serve as platform for future research that will help shape PE care.

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References

1. Konstantinides SV, Barco S, Lankeit M, Meyer G. Management of pulmonary embolism: an update. *J Am Coll Cardiol*. 2016;67(8):976-990.
2. Wendelboe AM, Raskob GE. Global burden of thrombosis: epidemiologic aspects. *Circ Res*. 2016;118(9):1340-1347.
3. Rogers MA, Levine DA, Blumberg N, Flanders SA, Chopra V, Langa KM. Triggers of hospitalization for venous thromboembolism. *Circulation*. 2012;125(17):2092-2099.
4. Smulders YM. Pathophysiology and treatment of haemodynamic instability in acute pulmonary embolism: the pivotal role of pulmonary vasoconstriction. *Cardiovasc Res*. 2000;48(1):23-33.
5. McIntyre KM, Sasahara AA. The hemodynamic response to pulmonary embolism in patients without prior cardiopulmonary disease. *Am J Cardiol*. 1971;28(3):288-294.
6. Kucher N, Rossi E, De Rosa M, Goldhaber SZ. Prognostic role of echocardiography among patients with acute pulmonary embolism and a systolic arterial pressure of 90 mm Hg or higher. *Arch Intern Med*. 2005;165(15):1777-1781.
7. Kearon C, Akl EA, Ornelas J, et al. Antithrombotic therapy for VTE disease: CHEST guideline and expert panel report. *Chest*. 2016;149(2):315-352.

8. Jaff MR, McMurtry MS, Archer SL, et al. Management of massive and submassive pulmonary embolism, iliofemoral deep vein thrombosis, and chronic thromboembolic pulmonary hypertension: a scientific statement from the American Heart Association. *Circulation*. 2011;123(16):1788-1830.
9. Konstantinides SV, Meyer G. The 2019 ESC guidelines on the diagnosis and management of acute pulmonary embolism. *Eur Heart J*. 2019;40(42):3453-3455.
10. Rivera-Lebron B, McDaniel M, Ahrar K, et al. Diagnosis, treatment and follow up of acute pulmonary embolism: consensus practice from the PERT consortium. *Clin Appl Thromb Hemost*. 2019;25:1076029619853037.
11. Wells PS, Anderson DR, Rodger M, et al. Derivation of a simple clinical model to categorize patients probability of pulmonary embolism: increasing the models utility with the SimpliRED D-dimer. *Thromb Haemost*. 2000;83(3):416-420.
12. Le Gal G, Righini M, Roy PM, et al. Prediction of pulmonary embolism in the emergency department: the revised Geneva score. *Ann Intern Med*. 2006;144(3):165-171.
13. Penaloza A, Verschuren F, Meyer G, et al. Comparison of the unstructured clinician gestalt, the wells score, and the revised Geneva score to estimate pretest probability for suspected pulmonary embolism. *Ann Emerg Med*. 2013;62(2):117-124.
14. Kline JA, Courtney DM, Kabrhel C, et al. Prospective multicenter evaluation of the pulmonary embolism rule-out criteria. *J Thromb Haemost*. 2008;6(5):772-780.
15. Kasper W, Konstantinides S, Geibel A, et al. Management strategies and determinants of outcome in acute major pulmonary embolism: results of a multicenter registry. *J Am Coll Cardiol*. 1997;30(5):1165-1171.
16. Goldhaber SZ, Visani L, De Rosa M. Acute pulmonary embolism: clinical outcomes in the International Cooperative Pulmonary Embolism Registry (ICOPER). *Lancet*. 1999;353(9162):1386-1389.
17. Jimenez D, Aujesky D, Moores L, et al. Simplification of the pulmonary embolism severity index for prognostication in patients with acute symptomatic pulmonary embolism. *Arch Intern Med*. 2010;170(15):1383-1389.
18. Ribeiro A, Lindmarker P, Juhlin-Dannfelt A, Johnsson H, Jorfeldt L. Echocardiography Doppler in pulmonary embolism: right ventricular dysfunction as a predictor of mortality rate. *Am Heart J*. 1997;134(3):479-487.
19. Jimenez D, Uresandi F, Otero R, et al. Troponin-based risk stratification of patients with acute nonmassive pulmonary embolism: systematic review and metaanalysis. *Chest*. 2009;136(4):974-982.
20. Sanchez O, Trinquart L, Planquette B, et al. Echocardiography and pulmonary embolism severity index have independent prognostic roles in pulmonary embolism. *Eur Respir J*. 2013;42(3):681-688.
21. Jimenez D, Kopecna D, Tapson V, et al. Derivation and validation of multimarker prognostication for normotensive patients with acute symptomatic pulmonary embolism. *Am J Respir Crit Care Med*. 2014;189(6):718-726.
22. Provias T, Dudzinski DM, Jaff MR, et al. The Massachusetts General Hospital Pulmonary Embolism Response Team (MGH PERT): creation of a multidisciplinary program to improve care of patients with massive and submassive pulmonary embolism. *Hosp Pract (1995)*. 2014;42(1):31-37.
23. Rosovsky R, Zhao K, Sista A, Rivera-Lebron B, Kabrhel C. Pulmonary embolism response teams: purpose, evidence for efficacy, and future research directions. *Res Pract Thromb Haemost*. 2019;3(3):315-330.
24. Barnes GD, Kabrhel C, Courtney DM, et al. Diversity in the pulmonary embolism response team model: an organizational survey of the National PERT Consortium members. *Chest*. 2016;150(6):1414-1417.
25. Barnes G, Giri J, Courtney DM, et al. Nuts and bolts of running a pulmonary embolism response team: results from an organizational survey of the National PERT Consortium members. *Hosp Pract (1995)*. 2017;45(3):76-80.
26. Chaudhury P, Gadre SK, Schneider E, et al. Impact of multidisciplinary pulmonary embolism response team availability on management and outcomes. *Am J Cardiol*. 2019;124(9):1465-1469.
27. Porres-Aguilar M, Anaya-Ayala JE, Heresi GA, Rivera-Lebron BN. Pulmonary embolism response teams: a novel approach for the care of complex patients with pulmonary embolism. *Clin Appl Thromb Hemost*. 2018;24(9 Suppl):48S-55S.
28. Giri J, Sista AK, Weinberg I, et al. Interventional therapies for acute pulmonary embolism: current status and principles for the development of novel evidence: a scientific statement from the American Heart Association. *Circulation*. 2019;140(20):e774-e801.
29. Smith SB, Geske JB, Maguire JM, Zane NA, Carter RE, Morgenthaler TI. Early anticoagulation is associated with reduced mortality for acute pulmonary embolism. *Chest*. 2010;137(6):1382-1390.
30. Prucnal CK, Jansson PS, Deadmon E, Rosovsky RP, Zheng H, Kabrhel C. Analysis of partial thromboplastin times in patients with pulmonary embolism during the first 48 hours of anticoagulation with unfractionated heparin. *Acad Emerg Med*. 2020;27(2):117-127.
31. Quinlan DJ, McQuillan A, Eikelboom JW. Low-molecular-weight heparin compared with intravenous unfractionated heparin for treatment of pulmonary embolism: a meta-analysis of randomized, controlled trials. *Ann Intern Med*. 2004;140(3):175-183.
32. Meyer G, Vicaut E, Danays T, et al. Fibrinolysis for patients with intermediate-risk pulmonary embolism. *N Engl J Med*. 2014;370(15):1402-1411.
33. Konstantinides SV, Vicaut E, Danays T, et al. Impact of thrombolytic therapy on the long-term outcome of intermediate-risk pulmonary embolism. *J Am Coll Cardiol*. 2017;69(12):1536-1544.
34. Chatterjee S, Chakraborty A, Weinberg I, et al. Thrombolysis for pulmonary embolism and risk of all-cause mortality, major bleeding, and intracranial hemorrhage: a meta-analysis. *JAMA*. 2014;311(23):2414-2421.
35. Sharifi M, Awdisho A, Schroeder B, Jimenez J, Iyer P, Bay C. Retrospective comparison of ultrasound facilitated catheter-directed thrombolysis and systemically administered half-dose thrombolysis in treatment of pulmonary embolism. *Vasc Med*. 2019;24(2):103-109.
36. Garcia MJ. Endovascular management of acute pulmonary embolism using the ultrasound-enhanced EkoSonic system. *Semin Intervent Radiol*. 2015;32(4):384-387.
37. 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(4):754-760.
38. Kucher N, Boekstegers P, Muller OJ, et al. Randomized, controlled trial of ultrasound-assisted catheter-directed thrombolysis for acute intermediate-risk pulmonary embolism. *Circulation*. 2014;129(4):479-486.
39. Piazza G, Hohlfelder B, Jaff MR, et al. A prospective, single-arm, multicenter trial of ultrasound-facilitated, catheter-directed, low-dose fibrinolysis for acute massive and submassive pulmonary embolism: the SEATTLE II study. *JACC Cardiovasc Interv*. 2015;8(10):1382-1392.
40. Tapson VF, Sterling K, Jones N, et al. A randomized trial of the optimum duration of acoustic pulse thrombolysis procedure in acute intermediate-risk pulmonary embolism: the OPTALYSE PE trial. *JACC Cardiovasc Interv*. 2018;11(14):1401-1410.
41. Graif A, Kimbiris G, Grilli CJ, Agriantonis DJ, Putnam SG, Leung DA. Safety of therapeutic anticoagulation with low-molecular-weight heparin or unfractionated heparin infusion during catheter-directed thrombolysis for acute pulmonary embolism. *J Vasc Interv Radiol*. 2020;31(4):537-543.
42. Groetzinger LM, Miller TJ, Rivosecchi RM, Smith RE, Gladwin MT, Rivera-Lebron BN. Apixaban or rivaroxaban versus warfarin for treatment of submassive pulmonary embolism after catheter-directed thrombolysis. *Clin Appl Thromb Hemost*. 2018;24(6):908-913.
43. Tu T, Toma C, Tapson VF, et al. A prospective, single-arm, multicenter trial of catheter-directed mechanical thrombectomy for intermediate-risk acute pulmonary embolism: the FLARE study. *JACC Cardiovasc Interv*. 2019;12(9):859-869.

44. National Institutes of Health Clinical Center. *Evaluating the safety and efficacy of the Indigo® aspiration system in acute pulmonary embolism (EXTRACT-PE). NCT03218566. ClinicalTrials.gov*. Bethesda, MD: National Institutes of Health; 2017. http://clinicaltrials.gov/ct2/show/NCT03218566. Updated August 3, 2020.

45. Leacche M, Unic D, Goldhaber SZ, et al. Modern surgical treatment of massive pulmonary embolism: results in 47 consecutive patients after rapid diagnosis and aggressive surgical approach. *J Thorac Cardiovasc Surg*. 2005;129(5):1018-1023.

46. Keeling WB, Sundt T, Leacche M, et al. Outcomes after surgical pulmonary embolectomy for acute pulmonary embolus: a multi-institutional study. *Ann Thorac Surg*. 2016;102(5):1498-1502.

47. George B, Parazino M, Omar HR, et al. A retrospective comparison of survivors and non-survivors of massive pulmonary embolism receiving veno-arterial extracorporeal membrane oxygenation support. *Resuscitation*. 2018;122:1-5.

48. Meneveau N, Guillon B, Planquette B, et al. Outcomes after extracorporeal membrane oxygenation for the treatment of high-risk pulmonary embolism: a multicentre series of 52 cases. *Eur Heart J*. 2018;39(47):4196-4204.

49. O'Malley TJ, Choi JH, Maynes EJ, et al. Outcomes of extracorporeal life support for the treatment of acute massive pulmonary embolism: a systematic review. *Resuscitation*. 2020;146:132-137.

50. Mismetti P, Laporte S, Pellerin O, et al. Effect of a retrievable inferior vena cava filter plus anticoagulation vs anticoagulation alone on risk of recurrent pulmonary embolism: a randomized clinical trial. *JAMA*. 2015;313(16):1627-1635.

51. Sista AK, Klok FA. Late outcomes of pulmonary embolism: the post-PE syndrome. *Thromb Res*. 2018;164:157-162.

52. Klok FA, van der Hulle T, den Exter PL, Lankeit M, Huisman MV, Konstantinides S. The post-PE syndrome: a new concept for chronic complications of pulmonary embolism. *Blood Rev*. 2014;28(6):221-226.

53. Pengo V, Lensing AW, Prins MH, et al. Incidence of chronic thromboembolic pulmonary hypertension after pulmonary embolism. *N Engl J Med*. 2004;350(22):2257-2264.