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RESEARCH **REVIEW ARTICLE**

Evidence-Based Management of Pulmonary Embolism: A Literature Review

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ABSTRACT

Acute pulmonary embolism (PE) can lead to life-threatening complications, such as shock due to right ventricular failure and death. PE cases can be stratified as low, intermediate, or high-risk. Intermediate-risk and high-risk PE present with right ventricular dysfunction and elevated cardiac troponins, but only high-risk PE is associated with hemodynamic instability. Although low-risk PE management is well-defined, that is not the case with intermediate and high-risk PEs. All PEs are initially managed with anticoagulation; however, systemic thrombolysis is the treatment of choice for high-risk ones. Treatment modalities such as reduced-dose thrombolysis, catheter-directed therapy (catheter-directed thrombolysis and mechanical thrombectomy), and surgical pulmonary embolectomy were explored in various trials. Despite this arsenal of treatments for PE, each modality carries risks and complications that further complicate PE management. Supportive care measures such as fluid management, vasopressors and inotropes, oxygen therapy, mechanical ventilation, and extracorporeal membrane oxygenation can mitigate clinical deterioration and hemodynamic collapse, especially in high-risk PE. This review provides an overview of acute PE presentation, diagnosis, risk stratification, and management while emphasizing the diverse modalities of treatment and the studies exploring each.

KEYWORDS - pulmonary embolism; submassive; massive; high-risk; intermediate-risk; thrombolysis; catheter-directed therapy; supportive care

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INTRODUCTION

Acute pulmonary embolism (PE) occurs when an embolus disrupts pulmonary perfusion, leading to life-threatening complications such as acute right ventricular (RV) failure and shock. It is a major cause of mortality, with an increasing incidence in recent years [1,2]. Its risk factors could be genetic or acquired; genetic factors include hypercoagulable states due to gene mutations (e.g., factor V Leiden), protein deficiencies (e.g., protein C deficiency), and hyperhomocysteinemia. Acquired factors include prolonged immobilization, malignancy, indwelling venous catheters, obesity, pregnancy, smoking, and infections [3–5]. Worldwide, over 10 million venous thromboembolism cases are diagnosed annually. In the United States, PE results in an annual mortality rate ranging from 60,000 to 100,000 cases, equating to approximately one fatality every 6 minutes. Alarmingly, up to one-third of these fatalities occur within one month of diagnosis [5–9]. As PE incidence continues to rise, so do its treatment options. Although having alternatives gives physicians the freedom to select the most appropriate treatment, each option's relative merits can complicate decision-making. This review aims to help mitigate confusion by summarizing the literature regarding diagnostic modalities, risk stratification tools, and management of PE.

SEARCH STRATEGY AND STUDY SELECTION

A literature search was performed using PubMed, ScienceDirect, ClinicalTrials.gov, and Google Scholar by entering the following: "pulmonary embolism," "acute pulmonary embolism," "low-risk pulmonary embolism," "massive pulmonary embolism," "high-risk pulmonary embolism," "submassive pulmonary embolism," "intermediate-risk pulmonary embolism," "catheter-directed thrombolysis AND pulmonary embolism," "mechanical thrombectomy AND pulmonary embolism," "surgical pulmonary embolectomy AND pulmonary embolism." All relevant articles retrieved were reviewed; articles not published in English and whose full text was unavailable were excluded. Guidelines published by the American Heart Association (AHA), American College of Chest Physicians (ACCP), European Society of Cardiology (ESC), and National Institute for Health and Care Expertise (NICE) and references cited in the analyzed articles were also reviewed.

PATHOPHYSIOLOGY OF PE

Rudolf Virchow, one of the first physicians to study PE, stated that emboli arose from distant thrombi [10]. He attributed peripheral clotting to three factors (Virchow's triad): endothelial injury, blood stasis, and hypercoagulability. A thrombus can detach from peripheral veins, traveling to the right heart and the pulmonary vasculature [11]. The disruption of lung perfusion releases vasospastic mediators like serotonin that further decrease perfusion, even in unaffected areas of the lung [12]. The ventilation-perfusion (V/Q) mismatch from the embolus leads to hypoxic pulmonary vasoconstriction that, along with the clot's mechanical obstruction, increases pulmonary vascular resistance (PVR) [13]. As RV afterload increases, ventricular emptying becomes impaired, and left ventricle (LV) preload decreases. Increased RV end-diastolic pressure pushes the interventricular septum into the LV, impairing its filling (ventricular interdependence) [14]. This eventually lowers the cardiac output (CO) and blood pressure. Hypotension and increased RV end-diastolic pressure reduce cardiac blood supply, causing RV ischemic necrosis [15,16]. Clinically, the rise in PVR increases the mean pulmonary arterial pressure, sometimes to a value double that of the baseline (in previously healthy patients) or four times the baseline, if there was a history of pulmonary hypertension. RV distention increases natriuretic peptide levels, myocardial ischemia increases troponin levels, and the drop in CO leads to organ ischemia and acidosis due to lactate build-up [17,18]. PE patients may be asymptomatic or may deteriorate rapidly if hemodynamic collapse ensues. Acute circulatory failure is the leading cause of death in PE patients and is primarily due to RV outflow obstruction, as explained above [19].

CLINICAL PRESENTATION AND RISK STRATIFICATION

Dyspnea is the most common PE symptom, but other presentations include cough, hemoptysis, leg swelling, and syncope. Retrosternal or pleuritic chest pain may occur from pulmonary infarction, pleural irritation, and myocardial ischemia [20–22]. Clinical assessment raises suspicion of PE but is insufficient to diagnose the condition, and investigations are often needed. Computed tomographic pulmonary angiography (CTPA) is the gold standard for diagnosis, but investigations like D-dimer and V/Q scans also help [23]. D-dimer is a sensitive, non-specific test; a negative D-dimer test with a low clinical suspicion of PE yields a negative predictive value of

about 99% [24–27]. A V/Q scan is an alternative to CTPA in those with contraindications (e.g., contrast allergy and renal failure). Clinicians can rule out PE if a V/Q scan is normal, and no further investigations are needed if it reveals a high PE probability [23]. The electrocardiogram typically reveals sinus tachycardia, but other non-specific findings may be present (e.g., S1Q3T3 pattern) [28–30]. Electrocardiograms showing atrial arrhythmias, Q-waves, ST segment changes, or complete right bundle branch block carry worse prognoses [31–33].

Another test of value when aiming to diagnose PE is the point-of-care ultrasound (POCUS). POCUS has no contraindications and can be used in pregnant patients, renal insufficiency, and those with contrast allergies. POCUS has garnered traction in emergency departments and intensive care units due to its instantaneous results, unlike the CTPA and V/Q scans. Several studies evaluated the accuracy of POCUS by using a triple ultrasound approach, which involved examining the heart, lungs, and lower extremity veins [34–36]. Two of the studies found that CTPA can be safely avoided in around 50% of cases because alternative diagnoses, or DVT, were identified [34,35]. In the study conducted by Nazerian et al., none of the patients with negative d-dimer and triple ultrasound tests had PE. Although none of the existing guidelines discussed the utilization of triple ultrasound in the preliminary diagnosis of PE, Nazerian et al. suggested an algorithm that limits the usage of CTPA to patients with a Wells' score of ≥ 4, a positive d-dimer test, and suspicious triple ultrasound findings [34]. Sonographically, a two-dimensional (2-D) transthoracic echocardiogram (TTE) in parasternal long and short-axis views may show an enlarged, dilated RV and a flattened, D-shaped LV, respectively. A 2D-TTE apical four-chamber view shows an RV:LV > 1 [37]. Also, a tricuspid annular plane systolic excursion (TAPSE) of <18 mmHg is an independent risk factor for intraoperative resuscitation and death in patients undergoing pulmonary embolectomy. Importantly, these signs may help with risk stratification in patients but lack specificity for pulmonary embolism as they can be seen in patients with non-thrombotic pulmonary vascular diseases such as pulmonary arterial hypertension (PAH) [38]. Another PE finding is the 60/60 sign, which refers to the coexistence of a pulmonary acceleration time of < 60 milliseconds and a tricuspid regurgitation jet gradient of < 60 mmHg. This sign, unlike the TAPSE, is more specific but less sensitive. The presence of the 60/60 sign combined with RV hypokinesia with preserved apical contraction (McConnell sign) can establish the diagnosis of acute PE with 94% specificity [39]. Therefore, despite being operator-dependent, POCUS has shown promising results when used in emergency settings as its results are instantaneous and can reveal various sensitive and/or specific signs that aid in PE diagnosis.

RISK STRATIFICATION

Not all PEs carry the same prognosis, and thus, cases are usually risk-stratified. The AHA, ACCP, and ESC have established different stratification systems. Table 1 presents an example of such a stratification system and was reproduced from the data in the 2019 ESC guidelines. A massive or high-risk PE presents with hemodynamic instability. It carries the worst prognosis, with an in-hospital mortality rate of 25 – 65% [40]. The pulmonary embolism severity index (PESI) and the simplified pulmonary embolism severity index (sPESI) further divide submassive, or intermediate-risk, PE into intermediate-high and intermediate-low risk; intermediate-high risk has both RV dysfunction and elevated markers of myocardial injury (i.e., troponins and BNP). Intermediate-low risk may or may not present with RV dysfunction or elevated troponins but will not present with both [23].

Table 1. European Society of Cardiology 2019 pulmonary embolism stratification.

		Hemodynamic Status	RVD on imaging	Elevated Troponins	PESI Class ≥ III or sPESI ≥ 1
Low-Risk		Stable	Absent	Absent	No
Intermediate	**Intermediate-Low**	Stable	Only one (or none) present		Yes
	Intermediate-High	Stable	Present	Present	Yes
High-Risk		Unstable	Present	Present	Yes

RVD: Right ventricular dysfunction; PESI: pulmonary embolism severity index; sPESI: simplified pulmonary embolism severity index; colors: for risk stratification.

MANAGEMENT

LOW-RISK PE

Low-risk PE has no hemodynamic instability or cardiac injury. The cornerstone of its management is anticoagulant therapy with low molecular weight heparin (LMWH), vitamin K antagonist (VKA), or direct oral anticoagulants (DOACs). Guidelines encourage outpatient management in compliant, clinically stable patients with no discharge contraindications (e.g., severe thrombocytopenia, severe hepatorenal diseases, recent bleeding) [41–44]. Rivaroxaban or apixaban are recommended, when appropriate, for at least 3 months. If not suitable, LMWH can be initiated for 5 days, followed by either a VKA or dabigatran. Unlike dabigatran, VKA must be bridged with LMWH (for at least 5 days or until INR is 2). Patients suitable for outpatient care may be discharged on DOACs, which are recommended over VKA [45–49]. The ESC, ACCP, and NICE guidelines suggest long-term anticoagulation for a minimum of 3 months in all cancer patients, with LMWH recommended over VKA therapy [23,50,51].

Up to 5% of PE patients can develop chronic thromboembolic pulmonary hypertension (CTEPH), which occurs when the pulmonary vasculature undergoes remodeling that chronically narrows vessels [52]. The AHA recommends evaluating patients at 6 weeks post-PE for CTEPH [53]. The ESC, on the other hand, suggests examining patients 3-6 months after a PE episode to assess for recurrence, physical activity impairment, treatment complications, CTEPH, and cancer; patients with persistent dyspnea and poor physical activity undergo further testing that includes an echocardiogram, various labs, and V/Q scans [23].

INTERMEDIATE-RISK PE

Intermediate-risk PE management, specifically fibrinolysis, has long been a controversial matter. Although fibrinolytics alleviate RV pressure overload (preventing RV failure), they increase fatal bleeding risk. The AHA recommends anticoagulation with fondaparinux or LMWH over unfractionated heparin (UFH) in those with minor myocardial necrosis or RV dysfunction, especially if there is no clinical worsening [53]. Although there is no difference in overall mortality with either drug, LMWH has a lower risk of recurrent thrombosis, heparin-induced thrombocytopenia, and hemorrhage [54–57]. For orally administered medications, DOACs are preferred over VKAs [23]. Guidelines recommend inferior vena cava (IVC) filters to those with absolute contraindications to anticoagulation and active bleeding or as primary prophylaxis in patients with high thromboembolism risk [23,50,58,59]. Frequent filter use, however, is disadvantageous due to its thrombogenic nature and minimal effect on survival [60–62]. In massive and submassive PE patients, duplex ultrasound may have a major therapeutic implication. Given the poor cardiopulmonary reserve, these patients may benefit from the identification of DVT and placement of IVC filter, as there may be a survival benefit in this population [63]. In general, the preventive role of IVC filters in patients with contraindications to anticoagulation is evident. However, using anticoagulants and IVC filters simultaneously in patients without contraindications to either intervention is controversial. The PREPIC trial was the first to study this concept and revealed that IVC filters decrease PE recurrence but increase DVT risk [61]. Overall, the use of IVC filters with anticoagulation is still under study.

Patients with impending or active cardiopulmonary compromise and those with moderate to severe RV dysfunction may benefit from systemic fibrinolysis. The ACCP recommends reserving it until hypotension develops or clinical deterioration occurs in normotensive patients (e.g., drop in blood pressure, rapid rise in heart rate, increase in cardiac biomarkers) [50]. Likewise, the ESC recommends using anticoagulants upon PE suspicion and delaying thrombolysis when clinical deterioration is imminent [23]. The NICE guidelines are against thrombolytic use in stable patients, regardless of RV function and cardiac biomarker levels [51].

The PEITHO trial revealed that thrombolytics increase bleeding risk, and hence, instead of the standard 100 mg dose, a half-dose of 50 mg or an ultra-low dose of 25 mg may be safer [64]. A study comparing half-dose thrombolytics with LMWH found a significant decrease in clinical decompensation at 7- and 30-days post-thrombolysis but no significant difference between either treatment in the occurrence of bleeding events [65]. Surgit et al. compared slow infusion of half-dose fibrinolytics with UFH and concluded that the former is safer and equally effective as the standard dose [66]. A meta-analysis of 13 studies examined low-dose thrombolytics versus standard-dose and anticoagulation; the total bleeding risk for low-dose thrombolytics was lower than the standard-dose but higher than anticoagulants [67]. There is no consensus regarding low-dose thrombolysis in intermediate PE. An ongoing randomized clinical trial, the PEITHO-3, will explore the dose's efficacy, safety, and overall clinical benefit [68].

Catheter-directed therapy, which includes mechanical thrombectomy (MT) and catheter-directed thrombolysis (CDT), recently gained popularity in intermediate PE management. Catheter-directed therapy is typically reserved for PE patients with hemodynamic instability (or clinical deterioration despite anticoagulation alone) who either fail systemic thrombolysis or have a contraindication to systemic thrombolytics. Patient selection for catheter-directed therapies is individualized based on several factors such as CT findings (usually large proximal clots), patient factors (i.e., absence of contraindications to pulmonary artery catheterization such as tricuspid or pulmonary valve prosthesis or vegetation, etc), and institutional experience. The potential benefits of catheter-directed therapies, such as reducing clot burden and improving right ventricular function, should be weighed against the risks associated with the procedure [23,50,69]. Trials like ULTIMA, SEATTLE II, PERFECT, and OPTALYSE revealed an efficacious reduction in clot burden and RV dysfunction with CDT [70–73]. Ultrasound-assisted CDT (UA-CDT) may theoretically be more effective than conventional CDT since ultrasound alters fibrin structure, allowing for better thrombolytic penetration and clot binding [74,75]. However, the PERFECT and the SUNSET sPE trials compared UA-CDT with conventional CDT and found that UA-CDT was not superior to the latter [72,76]. A meta-analysis showed no difference in all-cause mortality and bleeding incidence in either group, but conventional CDT improved RV function faster and had a shorter hospital stay [77]. Although larger studies are needed, such findings indicate that conventional CDT may be more cost-effective and efficacious than UA-CDT. CDT may increase bleeding risk (e.g., intracranial hemorrhage) and embolization, but a meta-analysis pooling patients from 12 studies revealed that CDT had similar bleeding rates and lower mortality rates than anticoagulation [70–73]. MT involves percutaneous clot removal via suction (aspiration thrombectomy), fragmentation, or a combination of both (rheolytic thrombectomy) [78–80]. Its minimal bleeding risk and effectiveness in decreasing RV:LV ratio was demonstrated in the single-arm FLARE study [81]. In a retrospective cohort study, those who underwent MT had a shorter ICU stay than CDT, but there was no difference in mortality, bleeding events, and overall complications from either procedure [82].

Surgical pulmonary embolectomy (SPE) involves incising the main pulmonary arteries to remove the embolus. SPE can rapidly reduce RV strain, interrupting progression to hemodynamic instability [83–85]. For more central clots (i.e., at the pulmonary trunk bifurcation or in proximal pulmonary arteries), SPE may be beneficial, but for clots in the distal pulmonary arteries, CDT may be a more reasonable option [86].

HIGH-RISK PE

A PE with hemodynamic collapse is considered a massive one. Like lower-risk cases, anticoagulants should be empirically administered upon suspicion of massive PE and before confirming the diagnosis if there is a high PE likelihood [51,87,88]. UFH is preferred in massive PE because of its rapid onset and short duration of action when administered intravenously [51]. Providers should initiate continuous UFH while anticipating starting thrombolytics, which are the treatment of choice [23,50,59]. The ACCP recommends thrombolysis be administered via peripheral catheters to those with a low bleeding risk [50]. The agents often used are alteplase and tenecteplase, but trials comparing them with each other are lacking.

Because systemic thrombolysis carries a bleeding risk, catheter-directed therapies and SPE may be used in those with contraindications to thrombolysis or in whom therapy has failed [50]. Catheter-directed therapy can improve RV function and lower pulmonary arterial pressure [59,73,89,90]. Patel et al., using the U.S. Nationwide Inpatient Sample, compared systemic thrombolysis with CDT and revealed a lower intracerebral hemorrhage risk and in-hospital mortality when the latter is used [91]. As for SPE, several studies concluded it is a safe procedure at high-volume centers and can be used more frequently in massive PE [83–85]. Indications for SPE include patent foramen ovale, cardiogenic shock, thrombolysis contraindications or failure, and clot-in-transit [59,92–94].

The modalities above are essential in massive PE, but one cannot undermine the value of supportive care. The high mortality in massive PE is driven by acute RV failure, with most deaths occurring within one hour of symptom onset [23,95]. Therefore, prompt initiation of supportive treatment via judicious fluid management, vasopressors, inotropes, oxygen therapy, as well as mechanical support can prevent deterioration. Although patients are hypotensive, administering fluids has paradoxical effects on the effective circulating volume; excess volume can worsen the ventricular interdependence, thus reducing CO [23,96,97]. As a result, the ESC recommends that patients with low central venous pressure (CVP) be given a trial of fluid (≤ 500 mL ringer's lactate or saline over 15-30 minutes) along with CVP monitoring (fluid administration should stop if CVP increases) [23].

Vasopressors and inotropes are valuable, especially when combined with reperfusion therapy. Norepinephrine is frequently the first-line vasopressor in cases of cardiogenic shock due to RV failure, as it increases systemic vascular resistance and improves RV contractility. Vasopressin can also be used to treat hypotension in cases of RV failure because of its favorable effect on PVR [23,98]. If blood pressure normalizes but the cardiac index is low, inotropic agents like dobutamine or milrinone can be added. Such agents, however, may worsen hypotension when used alone and must be paired with a vasopressor [23,99,100].

There has been a recent interest in employing inhaled vasodilators for PE management. Because these drugs act locally on the pulmonary vasculature, they can have minimal systemic side effects. A systematic review assessed studies that examined a variety of inhaled vasodilators (e.g., prostaglandins, nitric oxide, PDE-5 inhibitors, etc.) and found that all types of inhaled vasodilators, regardless of their mechanism of action, reduced PVR [101,102]. In patients with submassive PE, inhaled nitric oxide (iNO) increased the proportion of patients with a normal RV after 24 hours [103]. Similarly, the use of supplemental oxygen for 48 hours (even in the absence of hypoxemia) in submassive PE may result in improved RV size and function [104]. Though studies assessing its safety and efficacy in clinical practice are minimal, iNO may selectively decrease PVR without worsening hypotension [23,105].

Oxygen therapy can manage the hypoxemia from the V/Q mismatch and is indicated when arterial oxygen saturation < 90% [23]. Lyhne et al. found oxygen therapy effective at alleviating RV afterload in porcine models [106]. A study compared conventional nasal cannulas to high-flow nasal cannulas (HFNC) in a cohort of high and intermediate-risk PE. HFNC was superior to conventional cannulas in improving arterial blood gas and vital signs. The authors concluded that HFNC can be the initial intervention for hypoxic respiratory failure [107]. However, the ESC recommends beginning with conventional oxygen therapy and then escalating to HFNC or mechanical ventilation (MV) only when needed. Positive-pressure ventilation (invasive or not) is not recommended as first-line therapy because it increases intrathoracic pressure, which reduces venous return and worsens hypotension. Invasive MV requires anesthetic agents that aggravate hypotension in already unstable patients. Excessive positive end-expiratory pressure (PEEP) should be avoided when using MV [23].

Extracorporeal membrane oxygenation (ECMO) is a device that oxygenates venous blood before returning it to an artery or vein (VA- or VV-ECMO). It is a life-saving treatment for patients with respiratory or cardiac failure, especially when other life-sustaining therapies have failed. It can be used in those receiving cardiopulmonary resuscitation, as an initial therapy when systemic thrombolysis is contraindicated, or temporarily before definitive treatment (e.g., catheter-based therapy or SPE) [108–110]. ECMO success is dependent on the treating team's expertise and carries many complications, one of which is the bleeding risk when establishing vascular access in those receiving thrombolytics [23]. In summary, the body of literature concerning supportive care for pulmonary embolism is still developing. Nevertheless, certain treatments have displayed encouraging outcomes in mitigating hemodynamic deterioration.

PERT

The therapeutic modalities discussed in this article are summarized in Table 2. The complexity of some PE cases, however, warrants the assembly of an interdisciplinary team known as the pulmonary embolism response team (PERT), a consulting service established in some institutions to manage incoming PE cases. Specialists in PERT vary between health institutions, but experts in critical care, interventional cardiology, vascular surgery, interventional radiology, and cardiothoracic surgery are usually part of the team. Despite the variations in the make-up of the team and the activation protocol of PERT, the first point of contact is an on-call physician whose role is to provide a preliminary assessment of the case presented. When the cases are complex, and their management is unclear, the physician can initiate a PERT meeting with clinicians who can help diagnose, treat, and follow-up the cases [111]. PERT implementation in Jordan has its challenges; establishing systematic documentation, protocols, efficient communication between team members, and regular PERT meetings must occur before PERT becomes the norm of PE management in Jordan. Despite its recency and challenges, PERT has a promising future and assembling a team with expertise from various specialties is a crucial step moving forward given the ever-growing literature and management modalities of PE.

CONCLUSION

Despite extensive research, PE remains a challenging disease to treat. Low-risk cases are rel-

atively more manageable than higher-risk and unstable PEs, but many elements regarding the clinical approach of PE remain problematic. Although anticoagulants and fibrinolysis are the gold standard for low-risk and high-risk PE, respectively, management of intermediate-risk PE is not as clear-cut. Treatment modalities such as catheter-directed therapy, surgical embolectomy, and various supportive therapies enhanced the handling of challenging cases, but they also complicated decision-making for clinicians. Also, the epidemiological data regarding PE and the extent of PERT implementation in Jordan are all future areas of study that require exploration. Although a lot is known about PE, so much needs to be unraveled before stable and unstable cases can have similar outcomes.

Table 2. Summary of acute pulmonary embolism management.

	Treatment Modality	Notes
Low-Risk	**Anticoagulation** LMWH VKA DOACs: apixaban, rivaroxaban, dabigatran	Early discharge and outpatient management are recommended as soon as possible. DOACs are preferred over VKA upon discharge.
Intermediate-Risk (Submassive)	**Anticoagulation** IV: LMWH preferred Oral: DOACs > VKA **Systemic thrombolysis** Full dose (100 mg) Half dose (50 mg) Ultra-low dose (25 mg) **Catheter directed therapy** Mechanical thrombectomy Conventional CDT Ultrasound-assisted CDT **SPE**	Systemic thrombolysis is reserved for patients deteriorating clinically. If thrombolysis fails or there are contraindications, catheter directed therapy or SPE are the alternatives. SPE is for proximal clots, CDT is for distal ones.
High-Risk (Massive)	**Anticoagulation** UFH preferred **Systemic thrombolysis** Alteplase or Tenecteplase **Catheter directed therapy** Mechanical thrombectomy Conventional CDT Ultrasound-assisted CDT **SPE** **Supportive care** Fluid management Inotropes and vasopressors Oxygen therapy Mechanical support	Systemic thrombolysis is the first line. Indications for catheter directed therapy and SPE are similar to submassive PE.

LMWH: low-molecular weight heparin; VKA: vitamin K antagonist; DOACs: direct oral anticoagulants; CDT: catheter-directed thrombolysis; SPE: surgical pulmonary embolectomy; UFH: unfractionated heparin; PE: pulmonary embolism. .

AUTHOR CONTRIBUTIONS

S.AA.: conceptualization, writing— draft preparation, review and editing. T.E.A.: conceptualization, writing—draft preparation, review and editing. H.E.A.: conceptualization, writing—draft preparation, review and editing. S.I.A: writing—review and editing. M.O.A.: conceptualization, writing—review and editing. All authors approved the submitted manuscript.

DISCLAIMER

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