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Understanding and treating pulmonary embolism in acute settings: Review article for pharmacists and emergency medical services

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***Abstract*---Background:** High-risk pulmonary embolism (PE), encompassing a small but critical subset of cases, is associated with severe hemodynamic instability and high mortality rates. Representing 5–10% of all PE cases, high-risk PE is a leading cause of cardiovascular mortality, contributing to significant patient morbidity and mortality. **Aim:** This review aims to elucidate the management strategies and clinical approaches for high-risk PE, particularly in acute emergency settings. It seeks to provide a comprehensive overview of diagnostic and therapeutic strategies based on current guidelines. This review aimed to gain insights about treatment and management of PE via EMS and pharmacists. **Methods:** A thorough literature search was conducted using PubMed and Google Scholar, focusing on high-risk pulmonary embolism from the inception of these databases until October 1, 2023. The review included 147 articles comprising case reports, clinical trials, and systematic reviews. The search emphasized high-quality studies and guidelines, including those from the European Society of Cardiology (ESC) and the American Heart Association (AHA). **Results:** The review highlights the critical role of systemic thrombolytics (ST) in managing high-risk PE, despite their underutilization. It discusses the ESC and AHA guidelines for classifying PE risk and outlines the pathophysiology of right ventricular failure. Effective management strategies include early recognition, use of advanced imaging, and timely administration of thrombolytics. Multidisciplinary PE Response Teams (PERTs) improve outcomes but are not universally available. **Conclusion:** High-risk PE requires prompt and effective management to improve patient outcomes. Systemic thrombolytics remain a cornerstone of treatment, yet their application is inconsistent. Enhanced clinical protocols and access to specialized teams are crucial for optimizing patient care. Emergency clinicians must be adept at recognizing and managing severe PE manifestations to improve survival rates.

***Keywords*---**High-risk pulmonary embolism, systemic thrombolytics, right ventricular failure, emergency management, ESC guidelines, AHA guidelines.

Introduction

High-risk pulmonary embolism (PE), also known as massive PE, constitutes 5–10% of all PE cases [1, 2, 3, 4]. This condition is associated with a 30–40% mortality rate within 30 days and an in-hospital mortality rate between 22 and 32% [3, 5, 6, 7]. Despite representing a small fraction of overall PE cases, high-

risk PE significantly contributes to the total mortality from PE. In the United States, PE is responsible for up to 300,000 deaths annually and ranks as the third leading cause of mortality among cardiovascular diseases [8, 9, 10].

For the purposes of this review, the European Society of Cardiology (ESC) guidelines are employed to classify PE into high-risk, intermediate-high risk, intermediate-low risk, and low-risk categories, as opposed to the alternative terms of massive and submassive [11]. According to the ESC guidelines, high-risk PE is characterized by hemodynamic instability resulting from one or more of the following conditions: 1) cardiac arrest; 2) obstructive shock, which is defined as a systolic blood pressure (BP) < 90 mmHg or the requirement of vasopressors to maintain a systolic BP ≥ 90 mmHg with evidence of end-organ ischemia (e.g., altered mental status, cool skin, oliguria/anuria, increased serum lactate); 3) persistent hypotension, described as a systolic BP < 90 mmHg or a reduction ≥40 mmHg lasting more than 15 minutes without an alternative explanation (e.g., hypovolemia, sepsis, arrhythmia) [11].

The ESC guidelines for PE classification are summarized as follows:
High-risk PE: Defined by hemodynamic instability with any of the following criteria:

1. Cardiac arrest
2. Obstructive shock, indicated by a systolic BP < 90 mmHg or the use of vasopressors to maintain BP ≥ 90 mmHg despite adequate filling status, and evidence of end-organ ischemia
3. Persistent hypotension, characterized by a systolic BP < 90 mmHg or a drop ≥40 mmHg for over 15 minutes without an alternative cause [11].

Intermediate-high risk PE: Hemodynamically stable with:

1. Elevated cardiac troponin levels and imaging evidence of right ventricular (RV) strain (CTPA or TTE)
2. PESI Class III-V or sPESI ≥ 1 [11].

Intermediate-low risk PE: Hemodynamically stable with:

1. Elevated cardiac troponin levels or imaging evidence of RV strain (CTPA or TTE)
2. PESI Class III-V or sPESI ≥ 1 [11].

Low-risk PE: Hemodynamically stable with:

1. No evidence of RV strain on imaging and normal cardiac troponin levels (if measured)
2. PESI Class I-II or sPESI score 0 [11].

In contrast, the American Heart Association (AHA) guidelines classify PE as follows:

Massive PE: Defined by hemodynamic instability with:

1. Sustained hypotension, indicated by a systolic BP < 90 mmHg for at least 15 minutes or requiring inotropic support not attributed to an alternative cause
2. A drop in systolic BP > 40 mmHg for at least 15 minutes
3. Pulselessness [12].

Submassive PE: Hemodynamically stable with:

1. RV dysfunction or myocardial necrosis [12].

Low-risk PE: Not meeting criteria for submassive PE [12].

Definitions according to the AHA guidelines include:

- **RV dysfunction:** Characterized by RV dilation or systolic dysfunction on echocardiography, RV dilation on CT, elevated brain natriuretic peptide (BNP) > 90 pg/mL, elevated N-terminal pro-BNP > 500 pg/mL, electrocardiographic changes including new complete or incomplete right bundle-branch block, anteroseptal ST elevation or depression, or anteroseptal T-wave inversion.
- **Myocardial necrosis:** Defined as troponin I > 0.4 ng/mL or troponin T > 0.1 ng/mL [12].

The Pulmonary Embolism Severity Index (PESI) is a clinical tool used to assess the severity of pulmonary embolism (PE) and predict the risk of mortality. It helps guide management decisions and stratify patients based on their risk of adverse outcomes. The PESI scoring system is based on a set of clinical variables that are associated with mortality and complications in patients with PE.

PESI Scoring System

1. Variables and Scoring:
The PESI score is derived from the presence or absence of specific clinical parameters, each assigned a point value. These variables include:

- **Age**: Points are added based on the patient's age. For instance, age ≥ 80 years might contribute more points than age 40-49 years.
- **Cancer**: The presence of active cancer or cancer within the past year adds points.
- **Chronic Heart Failure**: A history of chronic heart failure contributes points.
- **Chronic Lung Disease**: Chronic lung disease, such as chronic obstructive pulmonary disease (COPD), adds to the score.
- **Vital Signs**: Abnormalities in vital signs, such as systolic blood pressure, heart rate, and oxygen saturation, contribute to the score. For example, a systolic blood pressure < 100 mmHg might add points.
- **Mental Status**: Altered mental status, including confusion or disorientation, adds to the score.
- **Temperature**: Fever (> 38°C or 100.4°F) is another factor.
- **Respiratory Rate**: A high respiratory rate can also contribute points.

2. Risk Classes:
Based on the total score from these variables, patients are classified into different risk categories:

- **Class I**: Low risk. These patients have a lower probability of short-term mortality and complications.
- **Class II**: Intermediate risk. Patients in this category have a moderate risk of mortality and adverse outcomes.

- **Class III**: High risk. These patients are at high risk for mortality and are more likely to experience adverse outcomes.

3. Simplified PESI (sPESI):

The Simplified PESI (sPESI) is a modified version that uses fewer variables for quicker risk assessment:

- **Age ≥ 80 years**
- **Cancer**
- **Chronic Heart Failure**
- **Chronic Lung Disease**
- **Systolic BP < 100 mmHg**
- **Heart Rate ≥ 110 bpm**
- **Oxygen Saturation < 90%**
- **Altered Mental Status**

The sPESI categorizes patients into:

- **Low Risk**: sPESI score of 0.
- **High Risk**: sPESI score of 1 or more.

4. Clinical Use:

The PESI score and sPESI are used to guide treatment decisions, such as whether to manage the patient on an outpatient basis or consider more intensive treatments and monitoring. They also help predict the likelihood of adverse outcomes and can aid in determining the need for thrombolysis or other interventions.

Importance

Despite the severe and potentially fatal nature of high-risk pulmonary embolism (PE), the application of optimal treatment practices remains insufficiently widespread. A significant number of patients who would benefit from primary reperfusion therapy with systemic thrombolytics (ST) do not receive it, even though established consensus guidelines advocate for its use [10, 11, 15]. Multidisciplinary PE Response Teams (PERTs) have been shown to improve the administration of reperfusion therapy to suitable patients; however, the availability of these teams is limited, leaving many emergency clinicians to manage high-risk PE cases independently [16]. This narrative review aims to address the critical aspects of managing high-risk PE with a focus on the emergency clinician's role. The review covers clinical assessment, the pathophysiology of right ventricular failure, management strategies for hemodynamic instability, airway management, and the application of reperfusion therapies. The emphasis is placed on systemic thrombolytics (ST) as the cornerstone of treatment for high-risk PE. Emergency clinicians must be adept at recognizing and managing the severe clinical manifestations of high-risk PE while pursuing primary reperfusion therapy.

Methods

The authors conducted a comprehensive search of PubMed and Google Scholar using keywords such as “high-risk,” “massive,” “pulmonary embolism,” “PE,” and “pulmonary embolus.” The search spanned from the inception of these databases up to October 1, 2023. PubMed provided over 800 articles, and the first 200

articles from Google Scholar were also reviewed. The selection process included evaluating case reports, series, retrospective and prospective studies, systematic reviews, meta-analyses, and other narrative reviews. Only English-language studies within the fields of emergency medicine and critical care were considered. The inclusion of studies was determined by consensus among the authors. Systematic reviews and meta-analyses were prioritized, followed by randomized controlled trials (RCTs), prospective studies, retrospective studies, case reports, and other narrative reviews when applicable. Ultimately, 147 articles were selected for inclusion in this narrative review.

Clinical Assessment

High-risk pulmonary embolism (PE) is diagnosed based on clinical evaluation, reflecting the dynamic and varied nature of PE presentation and pathophysiology. The severity of PE ranges widely, with presentations spanning from hypotension to severe shock and cardiac arrest. Although some literature refers to PE causing refractory shock or cardiac arrest as "catastrophic PE," this terminology is neither widely accepted nor extensively studied [17]. Emergency clinicians must be well-versed in the risk stratification of PE to identify and manage high-risk cases effectively.

When high-risk PE is suspected, it is advisable to bypass D-dimer testing and proceed directly to computed tomography pulmonary angiography (CTPA). If the patient's condition is too unstable for CTPA, the clinician should consider other potential causes of shock and conduct point-of-care ultrasound (POCUS), with a particular focus on echocardiography [18]. Although laboratory tests play a minimal role in the diagnosis of high-risk PE due to its clinical nature, it is beneficial to obtain additional diagnostic studies alongside emergent CTPA. Although there are no established thresholds, various diagnostic tests have been associated with the risk of deterioration or mortality in PE patients. These include electrocardiogram (EKG), troponin levels, B-type natriuretic peptide (BNP), N-terminal pro B-type natriuretic peptide (NT-proBNP), and echocardiography (**Table 1**).

Table 1. Clinical assessment of patients with high-risk PE [13, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29]

Assessment	**Finding**	**Risk for Decompensation or Mortality**
Syncope	Presence of syncope [a]	OR 2.00, 95% CI 1.11–3.60 (30-day PE-related decompensation)
EKG	Atrial fibrillation	OR 1.75, 95% CI 1.15–2.66 [b] (30-day decompensation)
Complete RBBB	OR 2.67, 95% CI 1.81–4.95	
S1Q3T3	OR 2.06, 95% CI 1.23–3.45	
Sinus tachycardia	OR 4.46, 95% CI 1.68–	

Assessment	Finding	Risk for Decompensation or Mortality
	11.84	
ST elevation in lead aVR	OR 5.24, 95% CI 3.98–6.91	
T-wave inversions in Lead V1	OR 2.63, 95% CI 1.47–4.73	
T-wave inversions in Lead V2	OR 6.94, 95% CI 2.41–19.96	
T-wave inversions in Lead V3	OR 7.07, 95% CI 1.13–44.22	
Lab Values	Elevated troponin [c, d]	OR 5.24, 95% CI 3.28–8.38 (in-hospital or 30-day mortality)
Elevated BNP, NT-proBNP	OR 3.71, 95% CI 0.81–17.02 (in-hospital or 30-day mortality)	
CTPA	RV/LV ratio > 1.0	OR 5.0; 95% CI 2.7–9.2 (PE-related mortality with median follow-up at 30 days)
Echocardiography	TAPSE <17 mm	HR 4.4; 95% CI 1.3–15.3

BNP, brain-type natriuretic peptide; CI, confidence interval; CTPA, computed tomography pulmonary angiography; EKG, electrocardiogram; HR, hazard ratio; LV, left ventricle; mm, millimeters; NT-proBNP, N-terminal pro B-type natriuretic peptide; OR, odds ratio; PE, pulmonary embolism; RBBB, right bundle branch block; RV, right ventricle; TAPSE, tricuspid annular plane systolic excursion.

[a] Syncope may indicate high-risk PE in the appropriate context. In the absence of syncope, evaluation for presyncopal symptoms is necessary, as presyncope may independently predict the need for intensive care unit admission in PE patients.
[b] Various EKG abnormalities are linked to increased risk of hemodynamic instability in PE patients. Given that up to 25% of PE patients may have a normal EKG, repeat EKGs are recommended if there is a change in hemodynamic status or symptoms.
[c] Data refer to studies before the introduction of high-sensitivity troponins. Typically, elevated troponins were identified as exceeding the 99th percentile of healthy individuals, with higher levels associated with increased mortality.
[d] There are no established guidelines for BNP or NT-proBNP thresholds.
[e] CTPA is not effective in detecting RV strain, with transthoracic echocardiography being the standard method for assessing RV function.
[f] Quantitative and qualitative methods are used to evaluate RV strain on transthoracic echocardiography (TTE). TAPSE, measured via m-mode over the lateral tricuspid annulus, quantifies RV systolic function. A TAPSE value <17 mm indicates decreased RV systolic function. Qualitatively, the RV should be smaller than two-thirds the size of the LV in both parasternal long and apical 4-chamber views. McConnell's sign, characterized by akinesis of the RV free wall and

preserved motion of the apex, is not exclusively indicative of PE. RV dysfunction observed on echocardiography may also reflect chronic conditions such as chronic obstructive pulmonary disease, pulmonary hypertension, and interstitial lung disease.

Currently, no specific risk scores exist for predicting clinical outcomes in patients with high-risk PE. The PE Severity Index (PESI) and Simplified PESI (sPESI) scores are used to predict 30-day mortality in all PE patients [13, 14]. Although these scores may estimate the risk of deterioration, their specific application to high-risk PE patients has not been extensively researched. Other scores such as Bova, SHIeLD, and TELOS are being investigated for their potential to predict worsening in normotensive PE [30, 31, 32, 33]. However, like PESI and sPESI, none of these scores are designed specifically for high-risk PE patients.

Pathophysiology of Right Ventricular Failure

The anatomical and functional characteristics of the right ventricle (RV) differ markedly from those of the left ventricle (LV). The RV's thinner myocardial wall renders it more susceptible to increases in afterload. Under normal conditions, the RV is not capable of generating a systolic pressure exceeding 40 mmHg [34, 35]. In cases of high-risk pulmonary embolism (PE), hemodynamic instability arises as the elevation in pulmonary artery pressure (PAP) induced by the embolus surpasses the RV's adaptive capacity, leading to a reduction in RV cardiac output (CO) [35, 36]. As the RV fails to manage the heightened PAP, it undergoes dilation, which results in myocardial stretching and diminished contractility [36, 37, 38]. This stretching also affects the tricuspid annulus, causing tricuspid regurgitation and further compromising RV CO [37]. Additionally, RV distention displaces the interventricular septum towards the LV, thereby reducing LV volume—a phenomenon known as ventricular interdependence [39]. The resultant decrease in LV preload due to RV failure and ventricular interdependence ultimately leads to a reduction in LV CO. Systemic hypotension further exacerbates the ischemia of the RV wall. Unlike the LV, which receives optimal coronary artery perfusion during diastole, the RV's perfusion is maximized during systole when the pressure gradient is highest [35, 37].

Management of Hemodynamic Instability

The management of RV failure must align with its underlying pathophysiology. Since RV over-distention is the primary driver of decompensation in high-risk PE, excessive volume resuscitation can exacerbate cardiovascular compromise rather than enhance hemodynamics [37, 38]. Nevertheless, some degree of volume resuscitation may be warranted to improve preload in the presence of hypotension. Clinicians should employ various assessment tools, including pulse variability, stroke volume variation, and the straight leg raise maneuver to evaluate volume status [40]. The straight leg raise maneuver involves positioning the patient flat and elevating the legs to 45 degrees; an increase in stroke volume or CO may indicate that fluid administration could benefit the patient's hemodynamics [41]. If fluid resuscitation is deemed necessary, a cautious bolus of 250–500 mL is recommended, with repeated assessments to guide further

management. Evidence from one randomized trial involving intermediate-high risk PE patients suggests that diuresis with furosemide could reduce RV wall stress and prevent RV dysfunction [42]. However, the use of diuretics in high-risk PE patients, who are inherently hemodynamically unstable, has not been extensively studied and may risk further end-organ perfusion compromise.

Vasopressors should be employed temporarily in patients with high-risk PE to support them until primary reperfusion therapy can be administered (Fig. 1) [35, 37]. Norepinephrine, a commonly used first-line vasopressor, is generally effective in this context as it induces both venoconstriction and vasoconstriction, thereby maintaining blood pressure without significantly increasing pulmonary vascular resistance (PVR). However, high doses of norepinephrine may elevate PVR and exacerbate RV dysfunction [43]. If hypotension persists despite norepinephrine administration, vasopressin may be used to stabilize blood pressure and potentially lower PVR [44]. Phenylephrine, which only increases systemic afterload, should be avoided; studies indicate that norepinephrine is more effective than phenylephrine in patients with chronic pulmonary hypertension and RV dysfunction [45, 46].

Inotropic support should be considered alongside vasopressor therapy. Epinephrine can serve as both a vasopressor and an inotrope but is associated with a risk of tachyarrhythmias; thus, alternative vasopressors might be preferred in patients exhibiting significant tachycardia [47]. Dobutamine, a phosphodiesterase inhibitor, provides positive inotropy to the RV without increasing PVR and reduces filling pressure [48]. However, dobutamine can cause worsening hypotension and should be administered with caution, ideally in conjunction with norepinephrine or vasopressin. Concurrent use of epinephrine and dobutamine is contraindicated due to their combined risk of tachyarrhythmias. Milrinone, another phosphodiesterase inhibitor, can be utilized for inotropic support, particularly in patients on chronic beta-blockers, as its action bypasses beta-1 receptors. Milrinone has a longer half-life compared to dobutamine, making its titration more complex [35]. Comparative studies have shown similar effectiveness between milrinone and dobutamine in congestive heart failure exacerbation [35]. The application of intravenous pulmonary vasodilators in acute PE is explored but remains inconclusive in terms of reliably enhancing RV function in acute settings [49].

Airway Management

The primary objective in managing hypoxia in patients with high-risk PE is to enhance oxygen saturation without escalating intrathoracic pressure. Hypoxia in PE often results from ventilation/perfusion (V/Q) mismatch due to clot burden and right-to-left shunting, with hypercapnia resulting from increased dead space [40]. Treatment should aim to maintain oxygen saturation above 90% [11]. High-flow nasal cannula (HFNC) is effective in improving oxygenation while minimizing increases in intrathoracic pressure in high-risk PE patients [35, 49, 50].

Non-invasive positive pressure ventilation and intubation should be avoided when possible, as they can deteriorate RV hemodynamics and may lead to cardiac arrest. The positive pressure from mechanical ventilation raises intrathoracic

pressure, reduces venous return, and decreases RV CO [35, 37, 38]. The peri-intubation period is particularly hazardous; thus, emergency clinicians should ensure proper intravenous access, including a central line, and consider placing an arterial line for hemodynamic monitoring. A retrospective study revealed that 20% of PE patients experienced immediate hypotension or cardiac arrest following general anesthesia induction for emergent surgical embolectomy [51]. Before rapid sequence intubation in high-risk PE patients, vasopressor infusion should be initiated, with push-dose pressors, preferably epinephrine, readily available. Generally, fluids alone are inadequate in preventing and treating peri-intubation hypotension [52].

Transient apnea between induction and intubation may worsen hypoxia and hypercapnia, further aggravating RV failure and potentially leading to cardiac arrest [53]. When intubation is necessary, the use of hemodynamically neutral agents, such as ketamine, for rapid sequence intubation is recommended. An awake intubation approach may also be considered [53]. Post-intubation, ventilator settings should aim for low positive end-expiratory pressure (PEEP) and tidal volumes (TV) around 6 mL/kg to avoid exacerbating hypoxia and hypercarbia [43]. High PEEP and large TV can worsen RV preload and CO, contributing to shock [54].

In cases of refractory hypoxia, inhaled pulmonary vasodilators, such as inhaled nitric oxide (iNO) and epoprostenol, may be considered to reduce PVR, enhance oxygenation, and ameliorate V/Q mismatch [53]. While evidence on iNO's effectiveness is limited, it may offer benefits in hypoxia and hemodynamics [55]. A multicenter randomized controlled trial of iNO in intermediate-risk PE patients found no significant improvement in complete RV recovery, although RV hypokinesis showed some improvement [56]. In scenarios where iNO is unavailable, there are case reports of alternative methods, such as using sublingual or intravenous nitroglycerin to mimic iNO effects, though these are not standard practice [57].

Primary Reperfusion Therapies

In managing patients with high-risk pulmonary embolism (PE), the initiation of primary reperfusion therapies, which may include systemic thrombolysis (ST), surgical embolectomy (SE), or catheter-directed interventions (CDI) ([Fig. 2]), is crucial. Anticoagulation is generally recommended unless contraindicated. For patients with a high likelihood of unstable PE, presumptive anticoagulation is advisable ([58], [59], [60], [61]). Unfractionated heparin is preferred for unstable patients due to its short half-life and adjustability, making it compatible with various reperfusion strategies ([11]). Nonetheless, some studies indicate that patients with severe PE may not achieve adequate anticoagulation with unfractionated heparin alone, necessitating vigilant monitoring ([62]). Direct-oral anticoagulants are not recommended for high-risk PE due to insufficient evidence of their efficacy in this context.

Systemic Thrombolytics

International guidelines widely endorse standard-dose systemic thrombolysis as the first-line treatment for high-risk PE ([11], [63]). Unlike anticoagulants, which passively reduce thromboembolism, thrombolytic agents such as tissue plasminogen activator (tPA) and tenecteplase (TNK) actively dissolve thrombi by hydrolyzing fibrin molecules ([64]). These agents can rapidly resolve clots, lower pulmonary artery pressure (PAP), enhance hemodynamics, and reduce mortality ([65], [66]). However, evidence shows that only about one-third of eligible high-risk PE patients actually receive ST ([67], [68]). Furthermore, patients requiring specialized care may not receive timely thrombolytics in rural settings and might benefit from transfer to high-volume centers offering comprehensive reperfusion options ([69], [70]). In cases where transfer is necessary, administering ST should be considered if contraindications are absent, aligning with current guidelines and literature.

Early trials assessing ST for high-risk PE demonstrated notable benefits. The 1970 urokinase PE trial (UPET) randomized patients with PE to receive either a urokinase bolus with a 12-hour heparin infusion or heparin alone ([67]). Among participants, approximately 9% had massive PE. Although the urokinase group did not show a mortality benefit, those with poor cardiac indices displayed improved cardiac function after ST, suggesting potential benefits for the highest-risk patients ([67]). A subsequent randomized controlled trial (RCT) compared streptokinase with heparin to heparin alone in patients with massive PE, finding that the group receiving streptokinase and heparin had improved survival rates, leading to the trial's early termination ([71]).

No RCTs have directly compared ST to anticoagulation alone for high-risk PE, but multiple systematic reviews and meta-analyses have investigated this issue. These analyses are constrained by limited recent trials, resulting in meta-analysis cohorts with fewer high-risk PE patients than ideal. Nevertheless, the available data suggest that ST is advantageous. A 2015 meta-analysis of over 2000 patients, including only 4 of 15 studies focused on high-risk PE, found that ST reduced early mortality and hemodynamic instability significantly compared to anticoagulation alone (odds ratio [OR] 0.34, 95% confidence interval [CI] 0.22–0.52), as well as all-cause mortality (OR 0.59, 95% CI 0.36–0.96), PE-related mortality (OR 0.29, 95% CI 0.14–0.60), and recurrent PE (OR 0.50, 95% CI 0.27–0.94) ([72]). However, this benefit was diminished when high-risk PE studies were excluded, indicating that improved outcomes in high-risk PE are a significant factor in the observed mortality reduction. An earlier 2004 meta-analysis, including 11 randomized trials across various PE-risk levels, found a composite reduction in recurrent PE or death among hemodynamically unstable PE patients treated with ST compared to heparin alone (OR 0.45, 95% CI 0.22–0.92) and indicated a number needed to treat (NNT) of 10 ([73]). A smaller meta-analysis involving 1500 high-risk PE patients showed that ST was associated with lower short-term mortality (OR 0.69, 95% CI 0.49–0.95) and PE-related mortality (OR 0.66, 95% CI 0.45–0.97) ([74]). Additionally, a 10-year retrospective study revealed a lower in-hospital mortality rate in patients with PE and hemodynamic instability who received ST, controlling for age, sex, and comorbidities (OR 0.42, 95% CI 0.37–0.48) ([7]). Moreover, several studies indicate that ST improves

pulmonary blood flow by 30–35% within the first 24 hours compared to heparin alone ([75], [76], [77]). However, the benefit of ST becomes less pronounced when considering all types of PE ([78]). Therefore, it is crucial for emergency clinicians to differentiate outcomes for high-risk PE from those for non-high-risk patients in the literature. Despite limitations and the need for further trials, ST remains the primary reperfusion therapy for high-risk PE.

Unlike myocardial infarction and ischemic stroke, which have defined time windows for reperfusion therapy, there is no established timeframe for administering ST in high-risk PE. Although no RCTs have specifically explored the timing of ST for high-risk PE ([15]), existing literature suggests that earlier administration improves outcomes ([79]). Early ST is associated with a decreased need for inotropic and respiratory support, and administration beyond 24 hours from symptom onset correlates with higher mortality (OR 5.67, 95% CI 2.64–10.67) ([80]). An observational study found that administering ST 8.5 hours or later after symptom onset increased the risk of 30-day cardiovascular death (hazards ratio 7.81, 95% CI 1.84–33.5) and bleeding events compared to ST administered within 8.5 hours ([81]). Another cohort study reported a 94% survival rate at 24 hours for high-risk PE patients receiving ST within one hour of emergency department arrival ([82]). Despite these findings, retrospective studies may be subject to bias and confounding variables. Nevertheless, current evidence supports that early administration of ST improves outcomes in high-risk PE.

The most significant adverse effect of thrombolytics is major bleeding. Prior to administering ST, emergency clinicians should evaluate absolute and relative contraindications ([11], [65], [83], [84], [85]). Estimates of major bleeding events following ST vary across studies. In the PEITHO trial, which compared TNK plus heparin to heparin alone in intermediate-risk PE patients, the 7-day incidence of hemorrhagic stroke was 2.4% in the TNK group versus 0.2% in the heparin-only group, and extracranial bleeding occurred in 6.3% of the TNK group compared to 1.2% of the heparin-only group ([86]). Notably, the risk of bleeding was lower in patients under 75 years of age, with only one of twelve patients experiencing a stroke after TNK being under 65. A large meta-analysis found a higher frequency of major hemorrhage (OR 2.91, 95% CI 1.95–4.36) and fatal or intracranial bleeding (OR 3.18, 95% CI 1.25–8.11) associated with ST ([72]). Conversely, the MAPPET-3 trial, involving 256 patients with intermediate-risk PE, found no cases of hemorrhagic stroke or fatal bleeding with tPA plus heparin ([87]). Similarly, the TOPCOAT trial of 83 intermediate-risk PE patients receiving TNK plus low-molecular-weight heparin reported no increase in bleeding events, though this study was not designed to evaluate bleeding rates comprehensively ([88]). A systematic review and Bayesian network meta-analysis of mortality and bleeding risks in intermediate-risk PE showed no significant difference in major bleeding between ST and anticoagulation alone (relative risk [RR] 0.95, 95% credible interval [CrI] 0.31–2.42), though a slight increase in minor bleeding was observed (RR 1.95, 95% CrI 1.03–3.63) ([89]).

Conclusion

High-risk pulmonary embolism (PE) is a critical condition characterized by severe hemodynamic instability and high mortality rates. Representing a small fraction

of all PE cases, high-risk PE significantly contributes to the overall burden of cardiovascular mortality. The European Society of Cardiology (ESC) and American Heart Association (AHA) provide essential guidelines for classifying PE risk and guiding treatment decisions. The ESC classifies high-risk PE based on criteria such as cardiac arrest, obstructive shock, and persistent hypotension, while the AHA uses terms like massive and submassive PE, focusing on hemodynamic instability and right ventricular (RV) dysfunction. The management of high-risk PE involves timely and accurate diagnosis, primarily through advanced imaging techniques like computed tomography pulmonary angiography (CTPA). Given the acute nature of high-risk PE, the role of systemic thrombolytics (ST) is crucial, though their use remains underutilized. Multidisciplinary PE Response Teams (PERTs) are effective in improving the administration of thrombolytics but are not always available. Therefore, emergency clinicians often face the challenge of managing these complex cases independently. Pathophysiologically, high-risk PE leads to right ventricular (RV) failure due to elevated pulmonary artery pressure (PAP), causing RV dilation and compromised cardiac output. The management of hemodynamic instability in high-risk PE requires careful fluid resuscitation and vasopressor support, with a focus on minimizing further RV strain. Inotropic support and the judicious use of medications like norepinephrine and dobutamine are essential for stabilizing patients. Overall, optimizing treatment protocols and ensuring timely access to advanced care are vital for improving outcomes in high-risk PE. Emergency clinicians must be proficient in recognizing severe PE manifestations and implementing effective management strategies to enhance patient survival. Continued research and refinement of clinical guidelines are necessary to address the challenges in managing this life-threatening condition.

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فهم وعلاج الانسداد الرئوي في الحالات الطارئة - مقالة مراجعة لخدمات الصيدلة وطب الطوارئ الطبية

الملخص:

الخلفية :الانسداد الرئوي عالي المخاطر(PE) ، الذي يشمل مجموعة صغيرة، ولكنها حاسمة من الحالات، يرتبط بعدم استقرار هيموديناميكي شديد ومعدلات وفيات مرتفعة. يمثل الانسداد الرئوي عالي المخاطر 5-10% من جميع حالاتPE ، ويعتبر سببًا رئيسيًا للوفيات القلبية الوعائية، مما يساهم في معدل كبير من الأمراض والوفيات لدى المرضى.

الهدف :تهدف هذه المراجعة إلى توضيح استراتيجيات الإدارة والنهج السريرية للانسداد الرئوي عالي المخاطر، خصوصًا في الحالات الطارئة الحادة. تسعى إلى تقديم نظرة شاملة على استراتيجيات التشخيص والعلاج بناءً على الإرشادات الحالية. هدفت هذه المراجعة إلى تقديم رؤى حول علاج وإدارة الانصمام الرئوي (PE) من خلال أدوار خدمات الطوارئ الطبية (EMS) والصيادلة.

الطرق :تم إجراء بحث شامل في الأدبيات باستخدام قواعد بيانات PubMed وGoogle Scholar، مع التركيز على الانسداد الرئوي عالي المخاطر منذ بدء هذه القواعد حتى 1 أكتوبر 2023. شملت المراجعة 147 مقالًا تتضمن تقارير حالات، تجارب سريرية، ومراجعات منهجية. ركز البحث على الدراسات والإرشادات عالية الجودة، بما في ذلك تلك الصادرة عن الجمعية الأوروبية لأمراض القلب (ESC) والجمعية الأمريكية للقلب.(AHA)

النتائج :تسلط المراجعة الضوء على الدور الحاسم للمواد المضادة للتخثر النظامية (ST) في إدارة الانسداد الرئوي عالي المخاطر، على الرغم من استخدامها المحدود. تناقش الإرشادات الصادرة عن ESC و AHAلتصنيف مخاطر الانسداد الرئوي وتستعرض الفيزيولوجيا المرضية لفشل البطين الأيمن. تشمل استراتيجيات الإدارة الفعالة التعرف المبكر، استخدام التصوير المتقدم، والإعطاء الفوري للمواد المضادة للتخثر. فرق الاستجابة المتعددة التخصصات للانسداد الرئوي (PERTs) تحسن النتائج لكنها ليست متاحة عالميًا.

الاستنتاج :يتطلب الانسداد الرئوي عالي المخاطر إدارة سريعة وفعالة لتحسين نتائج المرضى. تظل المواد المضادة للتخثر النظامية حجر الزاوية للعلاج، إلا أن تطبيقها غير متسق. تعد بروتوكولات سريرية معززة والوصول إلى الفرق المتخصصة أمرًا حيويًا لتحسين رعاية المرضى. يجب على الأطباء الطارئين أن يكونوا بارعين في التعرف على وإدارة مظاهر الانسداد الرئوي الشديدة لتحسين معدلات البقاء على قيد الحياة.

الكلمات المفتاحية :الانسداد الرئوي عالي المخاطر، المواد المضادة للتخثر النظامية، فشل البطين الأيمن، الإدارة الطارئة، إرشاداتESC ، إرشادات.AHA