BRITISH JOURNAL OF HOSPITAL MEDICINE

REVIEW

Investigation and management of pulmonary embolism 1: a probability-based approach

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Abstract

Pulmonary embolism remains a common and potentially deadly disease, despite advances in diagnostic imaging, treatment and prevention. Managing pulmonary embolism requires a multifactorial approach involving risk stratification, determining appropriate diagnostics and selecting individualised therapy. This article reviews the pathophysiology, risk factors, clinical presentation, diagnostic evaluation and therapeutic management and early outpatient management of pulmonary embolism. The second part summarises pulmonary embolism in the setting of pregnancy, COVID-19, recurrent disease and chronic thromboembolic pulmonary hypertension.

Key words: Computed tomography pulmonary angiogram; D-dimer; Pulmonary embolism; Thrombolysis; Ventilation/perfusion scan

Submitted: 8 May 2021; accepted following double-blind peer review: 30 June 2021

Introduction

Pulmonary embolism is a common acute cardiovascular disorder with high mortality rates. The incidence is estimated to be 60 per 100 000 (Oger, 2000) and pulmonary embolism has been found in up to 14.6% of hospitalised patients at post-mortem (Stein and Henry, 1995). It accounted for nearly 28 000 NHS hospital admissions and 250 000 bed days in 2011 (British Lung Foundation, 2019), and is the third most common acute cardiovascular disorder behind myocardial infarction and stroke (Raskob et al, 2014). This article outlines modern probability-based approaches to the investigation of pulmonary embolism and discusses management options, including early outpatient management. The second part (https://doi.org/10.12968/hmed.2021.0286a) summarises pulmonary embolism in the setting of pregnancy, COVID-19, recurrent disease and chronic thromboembolic pulmonary hypertension.

Pathophysiology

Around 70% of pulmonary emboli are generated in the deep venous system of the lower limbs and pelvis. Clots ascend the inferior vena cava to the right heart and obstruct the pulmonary vasculature (Hull et al, 1983). Platelet aggregation around venous valve sinuses, activation of the clotting cascade and the influence of Virchow's triad result in thrombus formation. The haemodynamic effects of a pulmonary embolism depend upon thrombus size, area of obstruction and pre-existing cardiac function. Early studies showed an increase in mean pulmonary artery pressure when angiographic pulmonary vascular obstruction exceeded 30% (McIntyre and Sasahara, 1971). The reduction in pulmonary blood flow causes reduced left ventricular filling and systemic hypotension. Inability of the right heart to maintain adequate cardiac output may lead to circulatory collapse. Arterial hypoxaemia results from reduced cardiac output and ventilation/perfusion mismatching (Huet et al, 1985).

How to cite this article:
Stolberg S, Mudawi D, Dean K, Cheng A, Barraclough R. Investigation and management of pulmonary embolism 1: a probability-based approach. Br J Hosp Med. 2021. https://doi.org/10.12968/hmed.2021.0286a

Clinical presentation

Presenting features of pulmonary embolism include dyspnoea, pleuritic chest pain, cough, substernal chest pain, dizziness, fever, haemoptysis and syncope. Haemodynamic instability leading to cardiac arrest may occur with extensive pulmonary artery occlusion from massive pulmonary embolism (Pollack et al, 2011). Stein et al (2007) identified the most common clinical signs in patients with a confirmed pulmonary embolism: tachypnoea (57%), signs

of deep vein thrombosis (47%), tachycardia (26%) and, less frequently, crackles (21%), reduced breath sounds (21%), prominent P2 component of second heart sound (15%) and raised jugular venous pressure (13%).

Risk factors

The common risk factors for pulmonary embolism are shown in Table 1.

Thrombophilia risk

Inherited thrombophilia (eg antithrombin III deficiency, a prothrombin gene defect, protein C or protein S deficiency) frequently interacts with additional acquired risk factors to cause venous thromboembolism.

Thrombophilia testing is not recommended in those with a provoked venous thromboembolism or those who are continuing anticoagulation treatment. Hereditary thrombophilia testing should be considered for those with unprovoked venous

Table 1. Risk factors for pulmonary embolism

Strong risk factors (odds ratio >10)	■ Fracture of lower limb ■ Hospitalisation for heart failure or atrial fibrillation or flutter (≤3 months) ■ Hip or knee replacement ■ Major trauma ■ Myocardial infarction (≤3 months) ■ Previous venous thromboembolism ■ Spinal cord injury
Moderate risk factors (odds ratio 2–9)	■ Arthroscopic knee surgery ■ Autoimmune diseases ■ Blood transfusion ■ Central venous lines ■ Intravenous catheters and leads ■ Chemotherapy ■ Congestive heart failure or respiratory failure ■ Erythropoiesis-stimulating agents ■ Hormone replacement therapy ■ In vitro fertilisation ■ Oral contraceptive therapy ■ Postpartum period ■ Infection ■ Inflammatory bowel disease ■ Cancer ■ Paralytic stroke ■ Superficial vein thrombosis ■ Thrombophilia
Weak risk factors (odds ratio <2)	■ Arterial hypertension ■ Bed rest >3 days ■ Diabetes mellitus ■ Immobility caused by sitting ■ Increasing age ■ Laparoscopic surgery ■ Obesity ■ Pregnancy ■ Varicose veins

Adapted from Anderson and Spencer (2003), Rogers et al (2012), Konstantinides et al (2020)

thromboembolism who have a family history of venous thromboembolism in a first degree relative (National Institute for Health and Care Excellence, 2020). Antiphospholipid syndrome carries a high lifetime risk of recurrent venous thromboembolism and arterial thrombosis. Persistently elevated levels of antiphospholipid antibodies with a first venous thromboembolism is an acceptable indication for indefinite anticoagulation (Garcia et al, 2013).

Diagnosis

Diagnosis of pulmonary embolism can be challenging. Initial evaluation should include comprehensive history and examination coupled with pre-test probability assessment. Standardised probability scores, including the Wells score (Wells et al, 2000) (Table 2) and the revised Geneva score (Klok et al, 2008) (Table 3), permit the classification of patients into distinct categories. Haemodynamically stable patients with high clinical probability for pulmonary embolism should directly undergo diagnostic imaging. The pulmonary embolism rule-out criteria were devised by Kline et al (2004) to prevent unnecessary overinvestigation

Table 2. Wells score

Clinical feature	Points
Clinical signs and symptoms of deep vein thrombosis (minimum of leg swelling and pain with palpation of the deep veins)	3
An alternative diagnosis is less likely than pulmonary embolism	3
Heart rate >100 beats per minute	1.5
Immobilisation for more than 3 days or surgery in the previous 4 weeks	1.5
Previous deep vein thrombosis or pulmonary embolism	1.5
Haemoptysis	1
Malignancy (on treatment, treated in last 6 months, or palliative)	1
Clinical probability simplified scores	
Pulmonary embolism likely	>4
Pulmonary embolism unlikely	≤4

From Wells et al (2000)

Table 3. Revised Geneva score

Variable	Score
Age 65 years or over	1
Previous deep vein thrombosis or pulmonary embolism	3
Surgery or fracture within 1 month	2
Acute malignant condition	2
Unilateral lower limb pain	3
Haemoptysis	2
Heart rate 75–94 beats per minute	3
Heart rate 95 or more beats per minute	5
Pain on deep palpation of lower limb and unilateral oedema	5
0–3 points indicates low probability of pulmonary embolism (8%), 4–10 points indicates intermediate probability of pulmonary embolism (29%), 11 points or more indicates high probability of pulmonary embolism (74%)	

From Klok et al (2008)

Table 4. Pulmonary embolism rule-out criteria	
Variable	**Outcome**
Age ≥50 years	Yes / No
Heart rate ≥100 beats per minute	Yes / No
Oxygen saturations on room air <95%	Yes / No
Unilateral leg swelling	Yes / No
Haemoptysis	Yes / No
Trauma or surgery (requiring general anaesthetic) ≤4 weeks	Yes / No
Previous deep vein thrombosis or pulmonary embolism	Yes / No
Hormone use	Yes / No

In patients with a clinically assessed pre-test probability of <15%, if all eight specified criteria are negative, then the risk of pulmonary embolism is <2% and no further investigations are required (Kline et al, 2004; Freund et al, 2018)

for pulmonary embolism in low- or very low-risk populations, supporting cessation of further testing. D-dimer testing is recommended for those with low or intermediate pre-test probability as a further rule-out (Table 4).

Figure 1 shows an algorithm for the investigation and management of pulmonary embolism.

D-dimer

D-dimer is a degradation product of fibrinolysis and its level is increased in patients with acute venous thromboembolism. D-dimer is important in diagnosing and excluding pulmonary embolism but should only be used in conjunction with pre-test clinical probability assessment and clinical evaluation. D-dimer levels are sensitive for pulmonary embolism diagnosis and have a high negative predictive value, but low specificity, being elevated in conditions such as malignancy, sepsis and pregnancy.

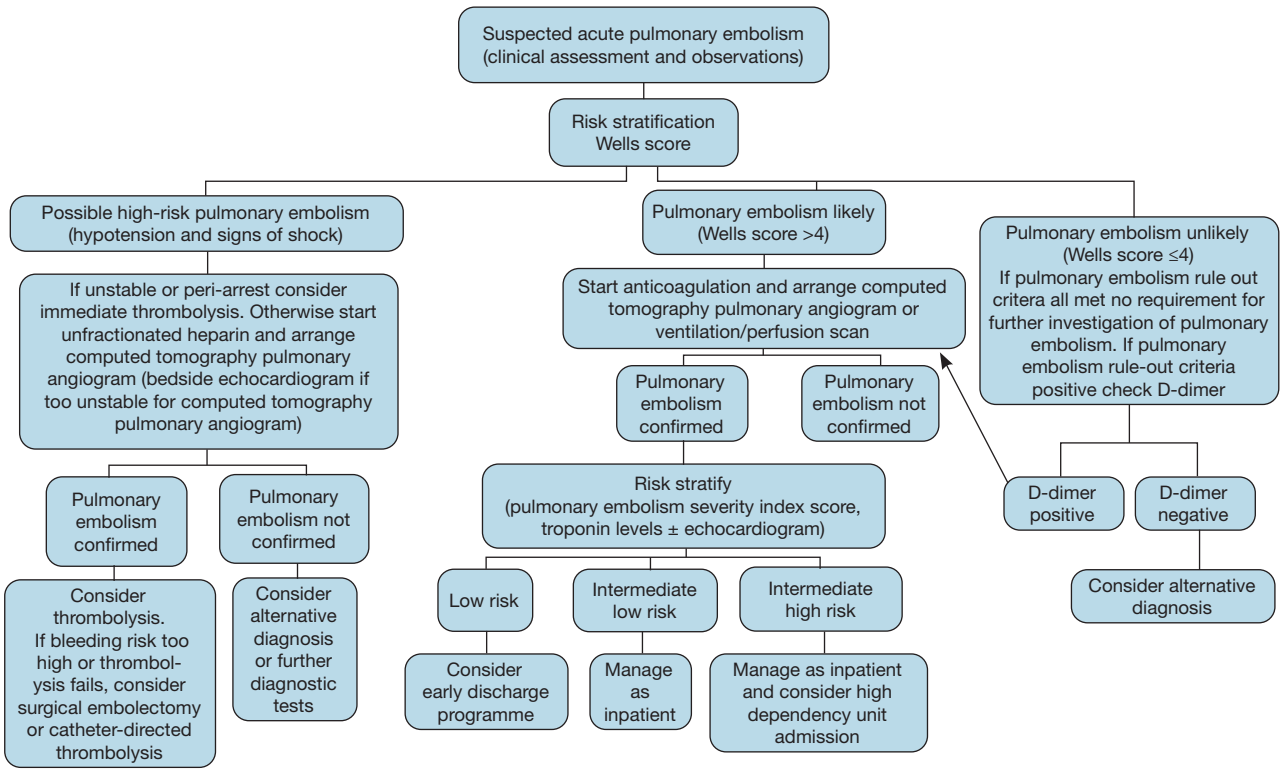

Figure 1. Algorithm for the investigation and management of suspected pulmonary embolism.

Specificity reduces with age to approximately 10% in those aged >80 years (Righini et al, 2000). Righini et al (2014) found that the combination of pre-test clinical probability assessment with age-adjusted D-dimer cut-off (age x 10 µg/litre, for patients >50 years), compared with a fixed D-dimer cut-off of 500 µg/litre, increased the proportion of patients in whom pulmonary embolism could be excluded from 6.4% to 29.7%, without additional false-negatives.

Troponin

Elevated levels of troponin I and T are found in over 30% of patients with acute pulmonary embolism. Meta-analysis has shown that elevated troponin concentrations are associated with an increased risk of mortality (odds ratio 5.2, 95% confidence interval 3.3–8.4) (Becattini et al, 2007).

Lactate

Lactate is a marker of imbalance between tissue oxygen supply and demand, and consequently with pulmonary embolism-associated haemodynamic compromise. Vanni et al (2013) found that patients with pulmonary embolism and lactate level ≥2 mmol/litre had a higher mortality than those with lactate <2 mmol/litre (17.3% vs 1.6% respectively).

Arterial blood gas analysis

Arterial blood gas analysis has limited diagnostic value in pulmonary embolism. Hypoxaemia is frequent, but up to 40% of patients have normal arterial oxygen saturations and 20% have a normal alveolar–arterial oxygen gradient (Rodger et al, 2000).

Electrocardiogram

The most common electrocardiogram abnormality in pulmonary embolism is a sinus tachycardia, present in 40% of patients. Electrocardiogram changes indicative of right ventricular strain include anterior T wave inversion, a QR pattern in V1, a S1Q3T3 pattern, and right bundle–branch block. Atrial arrhythmias, most frequently atrial fibrillation, are also common (Shopp et al, 2015).

Chest X-ray

Chest X-ray in pulmonary embolism is frequently normal and is more helpful in excluding alternative diagnoses. However, three findings are indicative of pulmonary embolism; Westermark sign is an area of oligaemia distal to a vessel that is occluded by a pulmonary embolus (Westermark, 1938), Hampton's hump is a peripheral wedge-shaped pleural-based density caused by lung infarction (Hampton, 1940), and Palla's sign is the presence of an enlarged right descending pulmonary artery (Palla et al, 1983).

Echocardiography

Echocardiographic examination is not mandatory but can be useful in haemodynamically unstable patients. Acute pulmonary embolism may lead to right ventricular pressure overload or dysfunction, associated with increased mortality (Roy et al, 2005).

Computed tomography pulmonary angiogram

Computed tomography pulmonary angiogram is the modality of choice for investigating pulmonary embolism and allows adequate visualisation of pulmonary arteries down to at least segmental level. The PIOPED II study found a computed tomography pulmonary angiogram sensitivity of 83% and specificity of 96% for pulmonary embolism diagnosis (Stein et al, 2006). Figure 2 demonstrates acute saddle pulmonary embolism with bilateral emboli and enlarged pulmonary trunk.

Computed tomography pulmonary angiogram requires 100–150 ml contrast media. In patients at high risk of nephropathy, Doppler leg ultrasound scan or lung scintigraphy may be more appropriate first-line investigations. The radiation effective dose is 3–10 mSv. Increasing accessibility of computed tomography pulmonary angiogram imaging is leading to overuse, resulting in a reduction in diagnostic yields; Mountain et al (2016) demonstrated a population yield of 14.3%.

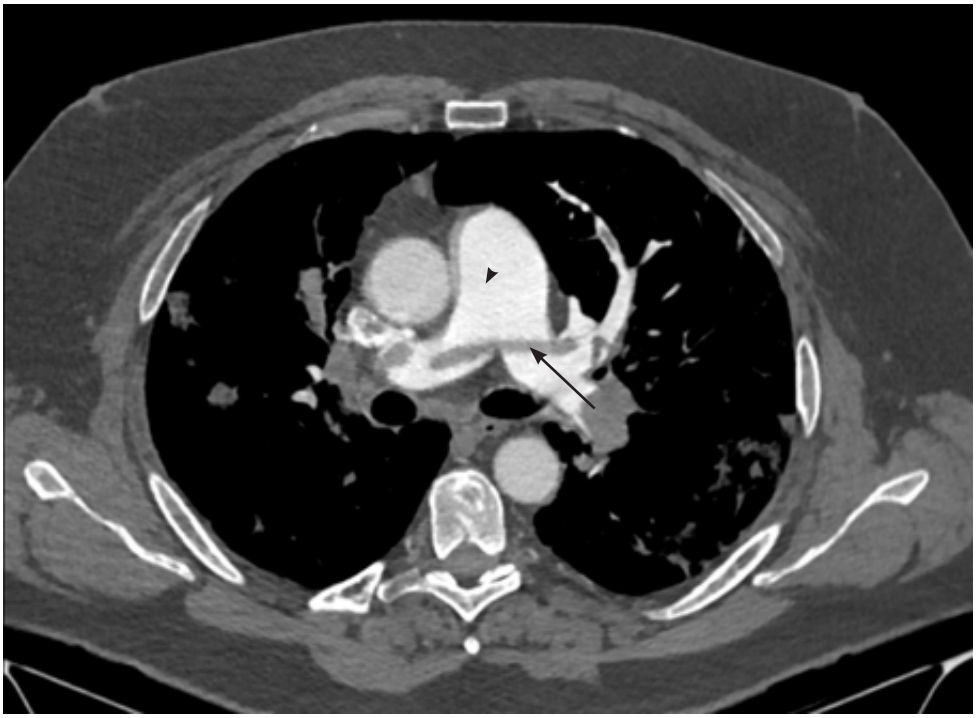

Figure 2. Computed tomography pulmonary angiogram demonstrating saddle pulmonary embolism with extensive clot burden bilaterally (black arrow) and an enlarged pulmonary trunk (black arrowhead) in a patient with COVID-19 infection.

Lung scintigraphy

The planar ventilation/perfusion scan is an established and safe diagnostic test for suspected pulmonary embolism. In acute pulmonary embolism, ventilation is expected to be normal in hypoperfused segments (mismatched). Planar lung scan results should be reported using a three-tier system: normal scan (excluding pulmonary embolism), high-probability scan (considered diagnostic of pulmonary embolism in most patients), and non-diagnostic scan (Glaser et al, 2011). The high frequency of non-diagnostic scans is a significant limitation. Performing only a perfusion scan might be acceptable in patients with a normal chest X-ray; any perfusion defect in this situation would be considered a mismatch.

The ventilation/perfusion scan requires lower radiation (approximately 2 mSv) than computed tomography pulmonary angiogram and does not require contrast medium, making it preferential in those with a normal chest X-ray, younger patients, pregnant women, contrast allergy, and renal failure (Reid et al, 2009).

Ventilation/perfusion single-photon emission computed tomography is a promising new method of scintigraphic acquisition that requires further validation (Phillips et al, 2015).

Pulmonary angiography

Pulmonary angiography is an invasive procedure, previously considered to be the gold standard for diagnosis of pulmonary embolism, but is now rarely used. Diagnostic accuracy is similar to computed tomography pulmonary angiogram (Qanadli et al, 2000), but risks are higher, with 0.5% mortality, 1% major and 5% minor complication reported (Stein et al, 1992). High radiation doses of 10–20 mSv are required.

Risk stratification

Following diagnosis of pulmonary embolism, risk stratification can be used to identify low-risk individuals who may be suitable for early discharge or ambulatory management, or those who may require invasive or high dependency care. Table 5 summarises some of these models.

The Pulmonary Embolism Severity Index (PESI) predicts risk of 30-day mortality based upon 11 predefined variables (Aujesky et al, 2005). Patients are grouped into one of five risk

Table 5. Pulmonary embolism severity index (PESI), subsequent simplified pulmonary embolism severity index (sPESI) and Hestia criteria for risk stratification and identification of low-risk individuals who may be suitable for outpatient investigation and management

	Scoring system – points per item					
Variable	**PESI**		**sPESI**		**Hestia**	
Age	Age in years		>80	1 point		
Male sex	10 points					
Cancer	30 points		1 point			
Chronic heart failure	10 points		1 point			
Chronic lung disease	10 points					
Severe liver impairment					1 point	
Creatinine clearance <30 ml/min						
Heart rate (beats per minute)	≥ 110	20 points	≥ 110	1 point	≥ 100	1 point
Systolic blood pressure <100 mmHg	30 points		1 point			
Needing intensive care unit or of clinical concern						
Respiratory rate >30/min	20 points					
Temperature <36.0 °C	20 points					
Altered mental status	60 points					
Arterial oxygen saturations <90%	20 points		1 point		>24 hours on supplemental oxygen	1 point
Thrombolysis or embolectomy					1 point	
Active or high-risk of bleeding*					1 point	
Pulmonary embolism while anticoagulated					1 point	
Pain requiring >24 hours intravenous analgesia					1 point	
Medical or social reason for admission >24 hours					1 point	
History of heparin-induced thrombocytopaenia					1 point	
Pregnant					1 point	
Risk outcome						
Scoring system	**PESI**		**sPESI**		**Hestia**	
Suitable for outpatient management	≤65 very low		0 points		0 points	
	66–85 low					
Not suitable for outpatient management	86–105 intermediate		≥1 point		≥1 point	
	106–125 high					
	>125 very high					

** Gastrointestinal bleeding/surgery in last 2 weeks, stroke in last month, bleeding disorder, platelet count <75x109/litre, uncontrolled hypertension, clinical concern. From Aujesky et al (2005); Jiménez et al (2010); Zondag et al (2011); Konstantinides et al (2019)*

categories with predicted mortality ranging from 1.1% for class I (very low) to 24.5% for class V (very high). The simplified PESI (sPESI) (Jiménez et al, 2010) was subsequently

developed using six criterion which provide either low (1.1%) or high (8.9%) risk of 30-day mortality. The Hestia criteria is another prediction model (Zondag et al, 2011).

The European Society of Cardiology prognosticates risk of early death (in-hospital or 30 day), which can be used to identify high-risk patients for emergency investigation and consideration of reperfusion (Table 6). Intermediate-high risk cases require intensive monitoring to identify those at risk of impending haemodynamic instability (Konstantinides et al, 2019).

Management

Pulmonary embolism-associated severe hypoxia may require high-flow oxygen and consideration of invasive ventilation, but the latter may worsen haemodynamic instability. Managing oxygenation or haemodynamic compromise invasively only serves as a bridge to reperfusion.

Anticoagulation

Anticoagulation should be started in patients with high- or intermediate probability pulmonary embolism while awaiting further investigation if there are no immediate contraindications (Konstantinides et al, 2019). Options for initial anticoagulation include unfractionated heparin, low-molecular weight heparin, fondaparinux and direct oral anticoagulants. Ongoing anticoagulation following confirmation of pulmonary embolism is with the above agents or vitamin K antagonists. Table 7 summarises the advantages and disadvantages of each.

The duration of anticoagulation should be determined for each patient on an individualised risk/benefit basis, considering patient preference to aid compliance. Pulmonary embolism or venous thromboembolism should be treated for a minimum of 3 months (National Institute for Health and Care Excellence, 2020), but initial duration of anticoagulation will not offset risk of recurrence following cessation of treatment (Couturaud et al, 2015). In the presence of a reversible major risk factor, the risk of recurrence of venous thromboembolism is low (1% in first year, and 0.5% per subsequent years) and anticoagulation can be stopped after 3 months or when the risk factor is no longer applicable (Agnelli et al, 2003). Patients with venous thromboembolism in the absence of reversible risk factors should be considered for lifelong anticoagulation because there is a 10% risk of recurrence in the first year with 5% risk per year subsequently (Kearon et al, 2016). The risk of venous thromboembolism should be balanced against bleeding risk with lifelong anticoagulation.

Table 6. Prognostic risks of 30-day mortality

		Indicator			
Risk of 30-day mortality		**Haemodynamic instability**	**PESI intermediate, high or very high or simplified PESI ≥1 / clinically severe pulmonary embolism**	**Right ventricular dysfunction on imaging (computed tomography pulmonary angiogram or transthoracic echocardiogram)**	**Elevated troponin level**
High		Yes	-	Yes	-
Intermediate	Intermediate-high	No	Yes	Yes	Yes
	Intermediate-low	No	Yes	Either or none	
Low		No	No	No	No (assessment optional)

In high risk cases of confirmed pulmonary embolism with haemodynamic instability and evidence of right ventricular dysfunction, PESI score and troponin are not necessary to determine risk category; however, if measured, both are likely to be raised. Patients who have elevated troponin levels or right ventricular dysfunction on imaging who would otherwise be low-risk should be elevated to intermediate-low risk. PESI = pulmonary embolism severity index. Adapted from Konstantinides et al (2019)

Table 7. Comparison of anticoagulation types with examples for use

Type of anti-coagulation	Route of administration	Examples	Dose*	Advantages	Disadvantages	Specific cases for use
Unfractionated heparin	Intravenous infusion		Loading dose (75 u/kg) then maintenance (18 u/kg/hr) with adjustment by activated partial thromboplastin time ratio	■ Rapid onset ■ Rapid offset ■ Monitoring based dosing	■ High risk of heparin-induced thrombocytopaenia ■ Higher risk of major bleeding compared with low-molecular weight heparin ■ Requires monitoring for dosing ■ Continuous intravenous infusion	■ Haemodynamic instability with high likelihood of progression to thrombolysis ■ High bleed risk or need for imminent reversal ■ Creatinine clearance <30 ml/min ■ Severe obesity
Low-molecular weight heparin	Subcutaneous injection	Dalteparin sodium	200 u/kg OD, max 18 000 units or 100 u/kg BD†	■ Rapid onset	■ Lower risk of heparin induced thrombocytopaenia ■ Use with caution or avoid in those with reduced renal function, eg estimated glomerular filtration rate <30 ml/min	■ Pregnancy ■ Luminal or high-bleed risk malignancy
		Enoxaparin sodium	1.5 mg/kd OD or 1mg/kd BD†			
		Tinzaparin sodium	175u/kd OD			
Fondaparinux	Subcutaneous infection		5 mg OD (<50 kg), 7.5 mg OD (50–100 kg), 10 mg OD (>100 kg)	■ Rapid onset, alternative parenteral anticoagulation to heparin	■ Caution in reduced renal function	■ History of heparin-induced thrombocytopenia
Direct oral anticoagulant	Oral	Apixaban	10 mg BD for 7 days then 5 mg BD	■ Rapid onset ■ Fixed dose without routine monitoring ■ Reduced bleeding risk compared with warfarin ■ Low-dose direct oral anticoagulant can be used for longer term anticoagulation after initial phase ■ Reversal agents becoming licenced ■ Fewer drug interactions than warfarin	■ Dabigatran needs loading with parenteral anticoagulation first ■ Some drug interactions ■ Some requirements for taking with food ■ Reversal agent not widely available	■ Edoxaban and rivaroxaban can be used in non-luminal malignancy ■ Typically first choice in patients without contraindications
		Dabigatran	150 mg BD (110 mg >80 years age) after 5 days treatment with parenteral anticoagulation			
		Edoxaban	30 mg if <61 kg, 60mg if ≥61 kg			
		Rivaroxaban	15 mg BD then 20 mg OD			

British Journal of Hospital Medicine | 2021 | https://doi.org/10.12968/hmed.2021.0286a

Table 7. (Continued)

Type of anti-coagulation	Route of administration	Examples	Dose*	Advantages	Disadvantages	Specific cases for use
Vitamin K antagonist	Oral	Warfarin Synthrone	Minimum 5 days low-molecular weight heparin bridge and in target international normalised ratio range: International normalised ratio 2.5 (2–3) for pulmonary embolism or 3.5 (3–4) with deep vein thrombosis or pulmonary embolism on anticoagulation	Reversal agent available Can use for treatment of venous thromboembolism while on anticoagulation Can be used in reduced renal function	Dose monitoring required Multiple drug interactions Loading alongside low-molecular weight heparin required	Anti-phospholipid syndrome Deep vein thrombosis or pulmonary embolism while anticoagulated
Thrombolytics	Intravenous: peripheral, central or catheter directed	Alteplase	10 mg over 1–2 minutes then 90 mg over 2 hours (max 1.5 mg/kg)	Rapid reperfusion Reversal of haemodynamic compromise	Acute risk of haemorrhage including fatal bleeding No reversal once given	High risk pulmonary embolism patients with haemodynamic instability Cardiac arrest
		Strepto-kinase	250 000 u over 30 minutes then 100 000 u/hr for 24 hours			
		Urokinase	4400 u/kg over 10–20 minutes then 4400 u/kg/hr for 12 hours			

**Always follow local guidelines, doses given are for example only and do not include specific cautions, eg renal impairment or interactions. †Dose in patients with increased bleed risk. BD = twice daily; OD = once daily. From Konstantinides et al (2019); National Institute for Health and Care Excellence (2021)*

Anticoagulation for isolated subsegmental pulmonary embolism is controversial with limited evidence both supporting and opposing its use (Carrier et al, 2010). den Exter et al (2013) suggested that symptomatic pulmonary embolism may act more similarly to larger clots and convey recurrent venous thromboembolism risk. There is insufficient evidence for a universal anticoagulation strategy and therefore the risk–benefit of anticoagulation needs to be decided with patients on an individualised basis.

Thrombolysis

In patients with haemodynamic instability secondary to acute pulmonary embolism, thrombolysis is indicated to reperfuse the pulmonary vasculature and prevent circulatory collapse. Thrombolysis achieves greatest benefit in the first 48 hours of symptoms, although it may have advantages up to 14 days (Daniels et al, 1997). Meta-analysis of systemic thrombolysis has shown reduction in overall mortality and pulmonary embolism recurrence in patients with haemodynamic instability. The improved outcome was offset by increased bleed risk, including 9.9% risk of major haemorrhage and 1.7% risk of intracranial haemorrhage (Marti et al, 2015).

Konstantinides et al (2019) defined haemodynamic instability as:

- Cardiorespiratory arrest
- Systolic blood pressure <90 mmHg, or requiring inotropic support to maintain ≥90 mmHg despite euvolaemia and evidence of end organ dysfunction (eg altered mental status, raised lactate, hypoperfusion, reduced urine output)
- Sustained hypotension (>15 minutes) of blood pressure <90 mmHg or reduced by ≥40 mmHg, not attributable to sepsis, hypovolaemia or arrhythmia.

The pulmonary embolism thrombolysis (PEITHO) trial examined the use of thrombolysis with heparin vs heparin and placebo in intermediate risk patients. Patients in the thrombolysis arm had significantly reduced 7-day risk of death or haemodynamic compromise (2.6%) compared with standard anticoagulation (5.6%), but with a significantly increased rate of intracranial haemorrhage (2.0%) and major extracranial haemorrhage (6.3%) (Meyer et al, 2014).

In intermediate-risk patients, the risks of haemorrhage and impending cardiovascular collapse or death needs to be weighed up. Risk of haemorrhage appears to increase with age, with meta-analysis of thrombolysis vs standard anticoagulation trials showing no significant difference in the rate of major bleeding in patients 65 years and under (Chatterjee et al, 2014). Table 8 shows absolute and relative contraindications to systemic thrombolysis for pulmonary embolism.

Surgical embolectomy and catheter-directed thrombolysis

Embolectomy and catheter-directed thrombolysis may be treatment options for patients who have contraindications to systemic thrombolysis, or those who have persistent haemodynamic instability following initial systemic thrombolytic therapy.

Surgical embolectomy may carry an increased mortality risk compared to catheter-directed therapies. An American cohort analysis of 2709 patients found that inpatient mortality was 27.2% following surgical pulmonary embolectomy (Kilic et al, 2013). Centres that offer extracorporeal membrane oxygenation may offer better outcomes (Malekan et al, 2012).

No study has compared open surgical embolectomy vs catheter-directed thrombolysis, but both provide satisfactory outcomes (Kuo et al, 2015; Loyalka et al, 2018).

Early discharge and outpatient pathways

Risk stratification

With reduced burden on healthcare provisions and overall cost savings, outpatient management of pulmonary embolism is increasingly popular (Condliffe, 2016). Early discharge or ambulatory management may be considered if the following criteria are met:

1. The risk of serious complications and early pulmonary embolism-related mortality is low
2. There is no serious comorbidity which would require inpatient care
3. Robust outpatient care and anticoagulant treatment can be provided.

Table 8. Absolute and relative contraindications to systemic thrombolysis for pulmonary embolism. Risk–benefit comparison must be undertaken on a case-by-case basis

Absolute contraindication	■ CNS neoplasm ■ Previous intracranial haemorrhage ■ Ischaemic stroke within last 6 months ■ Active bleeding ■ Recent trauma, surgery or head injury in preceding 3 weeks ■ Bleeding diathesis
Relative contraindication	■ Uncontrolled hypertension (systolic blood pressure >180 mmHg, diastolic blood pressure >110 mmHg) ■ Recent non-intracranial bleed ■ Recent surgery or invasive procedure ■ Transient ischaemic attack in last 6 months ■ Anticoagulation ■ Traumatic cardiopulmonary resuscitation ■ Pregnancy or within 1 week postpartum ■ Pericarditis ■ Age >75 years ■ Low body weight ■ Advanced liver disease ■ Peptic ulcer disease ■ Non-compressible puncture sites ■ Infective endocarditis

Adapted from Kearon et al (2012), Konstantinides et al (2019)

The PESI, sPESI or Hestia scores can be used in risk stratification to outpatient care as outlined in Table 9.

Management

Patients should be assessed and investigated on the same day as presentation. If pulmonary embolism is confirmed and the patient is stratified as low risk, initiation of treatment with low-molecular weight heparin or direct oral anticoagulant should be commenced. Patient education regarding treatment, signs and symptoms or recurrence, major bleeding and other complications is essential. Follow up in specialist pulmonary embolism clinics should be in place to review any screening investigations, assess treatment duration and rule out long-term complications. If same day investigation is unavailable, anticoagulation should be commenced (either direct oral anticoagulant or low-molecular weight heparin) with outpatient investigation to be arranged within 24 hours (Howard et al, 2018).

Conclusions

Managing pulmonary embolism requires a multifactorial approach involving risk stratification, determining appropriate diagnostics and selecting individualised therapy. Clinical presentation and outcomes can be extremely varied. Overinvestigation of pulmonary embolism places further pressure on an already stretched NHS. Adopting evidence-based approaches with less invasive investigations reduces the use of diagnostic imaging to exclude pulmonary embolism.

Table 9. Use of pulmonary embolism severity index (PESI), subsequent simplified pulmonary embolism severity index (sPESI) and Hestia in risk stratification

PESI	sPESI score	Hestia	Risk	Outcomes
Class I/II	0	Negative	Low	Consider outpatient management
Class III	>0	Positive	High	Inpatient management

From Howard et al (2018); Konstantinides et al (2019)

Key points

- The pulmonary embolism rule-out criteria can help prevent overinvestigation of pulmonary embolism in low or very low-risk populations.
- D-dimer should only be used in combination with clinical assessment and standardised pre-test probability scoring.
- Mortality risk stratification should be based on a combination of the pulmonary embolism severity index, haemodynamic stability, features of right ventricular dysfunction on imaging, and troponin level.
- Patients with haemodynamic instability should be considered for thrombolysis. This includes patients in cardiorespiratory arrest or those with sustained systolic blood pressure <90 mmHg (or reduced by ≥40 mmHg) not attributable to sepsis, hypovolaemia or arrhythmia.
- Pulmonary embolism should be treated with anticoagulation for a minimum of 3 months. Patients with no identifiable risk factors for venous thromboembolism should be considered for lifelong anticoagulation after balancing risk of recurrence against bleeding risk.

Risk stratification should also be used to guide therapeutic management. The emergence of direct oral anticoagulation over the past decade allows safer extended treatment in higher risk groups.

Despite medical advances, pulmonary embolism remains clinically challenging because of its potential life-threatening consequences. Balancing the risk of missed diagnosis against overinvestigation continues to be problematic. Future research is needed to develop targeted interventions and strategies.

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Conflicts of interest

The authors declare that they have no conflicts of interest.

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