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Abstract

Pulmonary embolism (PE) can present with a range of severity. Prognostic risk stratification is important for efficacious and safe management. This review article discusses the management of high, intermediate, and low risk PE. We discuss strategies to identify patients suitable for urgent outpatient care in addition to identification of patients who would benefit from thrombolysis. We discuss specific subgroups of patients where optimal treatment differs from the usual approach and identify emerging management paradigms exploring new therapies and subgroups.

Manuscript Text

INTRODUCTION

Combined with deep vein thrombosis (DVT), pulmonary embolism (PE) is the third most common acute cardiovascular syndrome. The condition has an estimated incidence of 39 to 115 per 100,000 population per year – a rate which increases annually [1]. In the context of improved disease awareness and greater access to diagnostic tests, the balance of early diagnosis and intervention versus over-investigation is challenging. Most PE cases presenting to the Emergency Department (ED) are low risk, and the estimated mortality for missed or untreated disease at less than 5% [2].

Management of PE is focussed on arresting clot growth, providing physiological support and preventing recurrence. However, treatment comes with a risk of serious adverse events. The narrative of progress in PE management is less about the application of new therapeutic agents and more about improvements in detecting which patients may benefit from existing interventions.

DEFINING RISK

The clinical presentation and prognosis of acute PE is variable. Even with treatment, high risk PE has a mortality rate as high as 65%, while low risk PE has a mortality rate less than 1% [3]. Severity assessment is crucial to determine correct treatment. Risk stratification tools can reliably predict 30-day mortality risk.

Historically, PE was divided into massive, sub-massive and non-massive PE. This division was initially based on anatomy and clot burden, but later encompassed physiological parameters [4]. These definitions were vague and inconsistently applied. More practical classifications have now been issued from several international bodies, but these vary. The National Institute for Health and Care Excellence (NICE) dichotomises PE into those with or without cardiovascular instability [5]; the European Society of Cardiology (ESC) divides patients with PE into low, moderate and high risk; and the American College of Chest Physicians (ACCP) uses screening tools to identify low risk patients safe for outpatient management, and high risk patients for thrombolysis **[Table 1]**. All guidelines agree that high risk is defined primarily by refractory hypotension.

Table 1:

	ESC [1]	ACCP [6,7]	NICE [8]
High risk	Shock, RV dysfunction and myocardial injury Tx: emergency thrombolysis, embolectomy, admission	Hypotension (systolic blood pressure <90 mmHg) Tx: thrombolysis	Haemodynamic instability Tx: UFH infusion and consider thrombolysis
Intermediate risk	RV dysfunction, or myocardial injury, or both. No shock or hypotension. Tx: anticoagulation and admission	No specific definition of intermediate risk, but strongly recommend against thrombolysis in PE not associated with hypotension Tx: anticoagulation	No haemodynamic instability Tx: anticoagulation, consider early discharge or ambulation
Low risk	No shock, hypotension, RV dysfunction or myocardial injury Tx: anticoagulation, early	Clinically low risk patients Tx: anticoagulation, consider treatment at	

	discharge, or ambulation	home	

ACCP: American College of Chest Physicians; CT: computer tomography; ESC: European Society of Cardiology; NICE: National Institute for Health and Care Excellence; PESI: Pulmonary Embolism Severity Index; RV: right ventricular; sPESI: simplified Pulmonary Embolism Severity Index; Tx: Treatment; UFH: Unfractionated Heparin

Assessing right ventricular dysfunction

Moderate risk PE is defined by the presence of right ventricular (RV) dysfunction. RV dilatation can be directly correlated with mortality risk and is used by the ESC as a tool for risk stratification [9]. Increasing RV:LV ratio on CT imaging is associated with higher mortality, even in patients otherwise assessed as low risk by other clinical markers [10]. CT can also identify other indicators of severity such as contrast reflux into the IVC and abnormal volumetric analysis of the heart chambers [1]. Point of care ultrasound (POCUS) may identify RV dysfunction (particularly dilatation) in the hands of trained emergency clinicians.

Biomarkers also allow identification of RV dysfunction in the setting of acute PE, usually through indication of myocardial injury. Elevated troponin is significantly associated with short term mortality (odds ratio [OR] 5.24; 95% CI, 3.28 to 8.38) and is predictive of higher mortality even in haemodynamically stable patients [11]. Raised B-natriuretic peptide (BNP) is also correlated with early PE related mortality, with an OR of 3.71 (95% CI, 0.81– 17.02) [12]. Although the association between a raised troponin or BNP with RV dysfunction and worse prognosis is clear, the role of these biomarkers in the acute setting is not yet established. The ESC include troponin as part of their risk adjusted management strategy flow chart in non high-risk PE whilst natriuretic peptides are only mentioned as a potential consideration as part of 3-6 month follow up. There is not sufficient evidence to dictate treatment. However, in a deteriorating patient these markers may enable individualised decision making to thrombolyse or admit to higher level care. Equally, normal biomarkers in a stable patient, may support CTPA or echocardiography evidence of normal RV function, and aid a decision not to thrombolyse or admit to higher level care an intermediate-high risk patient.

Outpatient therapy

Around 95% of patients diagnosed with PE can be categorized as non-high risk who may be eligible for outpatient treatment [13]. Managing patients at home may reduce hospital costs and result in improved patient satisfaction [14,15]. Three validated decision-making tools are available for the emergency physician: the Pulmonary Embolism Severity Index (PESI), simplified PESI (sPESI), and HESTIA scores [16] **[Table 2].** All three scores accurately identify patients with < 2.5% risk of death in the coming 30 days. [16,17] The ESC recommends using sPESI or HESTIA to stratify patients and determine suitability of outpatient management, ACCP suggests using a computerised clinical decision-support system based on the PE Severity Index (PESI) score and pragmatic exclusion criteria [18] while NICE guidelines do not recommend any specific decision tool.

Table 2:

	PESI [19]	sPESI [20]	HESTIA [21]
Role	Predicts risk of 30-day all-cause mortality for patients presenting with acute PE, using variables identified from a large retrospective cohort	Predicts risk of 30-day all-cause mortality using a selection of variables from PESI	A set of exclusion criteria to identify whether patients are unsuitable for treatment at home for acute PE
Components	Age (in years) Male sex (+10) History of cancer (+30) History of heart failure (+30) History of chronic lung disease (+10) Heart rate ≥ 110 (+20) Systolic BP <100mmHg (+30) Respiratory rate ≥30 (+20) Temperature <36ºC (+20) Altered mental status (+60) O_2 saturations <90% (+20)	Age >80 years History of cancer History of chronic cardiopulmonary disease Heart rate ≥110 Systolic BP <100 O_2 saturations <90%	Haemodynamic instability Thrombolysis or embolectomy Active or high risk of bleeding PE diagnosed during anticoagulation treatment > 24 hours supplemental oxygen to maintain saturations > 90% Severe pain requiring intravenous analgesia Medical or social reason for admission for over 24 hours Creatinine clearances of < 30mL/min Severe liver impairment Pregnancy History of HIT
Interpretation	Total score assigns patients to specific risk categories: ≤65 Very low risk 66-85 Low risk 86-105 Intermediate risk 106-125 High risk >125 Very high risk Widely validated, including	Score one for each variable met. 0 Low risk ≥1 High risk Good agreement with PESI and validated in prospective	If any criteria present, the patient should be admitted for treatment. Otherwise, they can be treated at home. Validated in prospective studies [22].

	in a randomised trial.	studies.	

PESI: Pulmonary Embolism Severity Index; sPESI: Simplified Pulmonary Embolism Severity Index

Derived from a retrospective database and the most widely validated tool [16], the Pulmonary Embolism Severity Index (PESI) predicts 30-day all-cause mortality for patients with acute PE and is based on 11 clinical criteria with weighted score. The simplified tool (sPESI) is an equally weighted 6-question tool which has been demonstrated to be as accurate as PESI, [22] and provides a binary outcome. This and the fact that it incorporates many of the factors which are immediately relevant to the emergency physician such as the bleeding risk, the need for supplemental oxygen, intravenous analgesia, the social situation, and renal impairment, makes it of particular utility in ED.

Although initially designed to stratify risk in hospitalised patients, these tools are now commonly used to indicate suitability for outpatient treatment [23]. The Hestia criterion also identifies low-risk PE patients suitable for outpatient PE treatment. Patients with no Hestia criteria have low all-cause mortality, and the Hestia score has been used to reliably identify patients safe for discharge [24]. Comparisons between the sPESI and Hestia scores suggest that the Hestia score allows for safe discharge in a greater portion of patients than the sPESI [25].

It is important to note that PESI and sPESI were developed to predict 30 days all-cause mortality and do not differentiate between patients whose mortality risk is related to their PE and those whose mortality risk reflects their underlying comorbidities. Whatever the risk score, the clinician must first ask the question of whether inpatient admission will improve overall prognosis or comfort. Many patients will wish to participate in the decision to be admitted or discharged and shared-decision making can be important. Patients with a higher risk of 30-day mortality based on comorbidities such as cancer may still choose outpatient care if they are fully informed and have the required home supports. Rapid, reliable follow up will be important in this instance. Others at low risk of mortality may not feel comfortable being discharged directly home.

ANTICOAGULATION

Most patients with acute PE require therapeutic anticoagulation as the primary treatment strategy. The choice of anticoagulant is determined by a range of factors such as bleeding risk, comorbidities, co-prescribed medications, and patient preference as listed in **Table 3.** Patients diagnosed with PE are often started on either direct oral anticoagulants (DOACs) or subcutaneous low molecular weight heparin (LMWH) to ensure effective early anticoagulation.

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144 Table 3:

Therapeutic option	Advantages	Considerations	Patient Group	Contraindications	Pregnancy
Apixaban 10 mg twice daily for 7 days followed by 5 mg twice daily for a minimum of 3 months	Fixed dosing		Most patients	Severe renal impairment (creatinine clearance < 15 ml/min) Pregnancy and breast feeding Co-prescription of strong inhibitors or inducers of P-glycoprotein and CYP 3A4*. In-situ gastrointestinal tumour. Recent gastrointestinal bleeding. Relative contra-indication: urothelial cancer.	Passed by placenta and breast milk
Rivaroxaban 15 mg twice and day for 21 days followed by 20 mg daily for a minimum of 3 months	Fixed dosing	Manufacturer suggests consideration of dose reduction in renal impairment	Most patients	Severe renal impairment (creatinine clearance < 15 ml/min) Pregnancy and breast feeding Co-prescription of strong inhibitors or inducers of P-glycoprotein and CYP 3A4* In-situ gastrointestinal tumour. Recent gastrointestinal bleeding. Relative contra-indication: urothelial cancer.	Low level evidence, possible increased rate of miscarriage and foetal abnormality [23]
Tinzaparin, Enoxaparin Dalteparin		Injected once or twice daily by the patient	In-situ gastrointestinal cancer Recent gastrointestinal bleeding Urothelial cancer Pregnant or breast feeding Intermediate risk patients (signs of right heart strain) during initial treatment phase	Severe renal function creatinine clearance < 30 ml/min	Safe in pregnancy and breastfeeding
Edoxaban 60 mg daily or dabigatran 150 mg twice daily with initial LMWH lead in (5 days)		Edoxaban dose is reduced to 30 mg daily in patients who meet any of the following criteria: creatinine clearance 15-50 mL/min, ≤ 60 kg or concomitant use of potent P-glycoprotein inhibitors (such as erythromycin, cyclosporine, dronedarone, quinidine, or ketoconazole).	Most patients	Edoxaban is not contraindicated in patients with creatinine clearance < 15 mL/min, whereas dabigatran is contraindicated in patients with creatinine clearance < 30 mL/min. Pregnancy and breast feeding Co-prescription of strong inhibitors or inducers of P-glycoprotein and CYP 3A4* for dabigatran and CYP 3A4 for edoxaban In-situ gastrointestinal tumour Recent gastrointestinal bleeding Relative contra-indication: urothelial cancer	Both edoxaban and dabigatran have showed toxicity in animal studies

Warfarin dosed according to the INR with initial concurrent LMWH until target INR ≥ 2.0		Requires regular INR blood tests	On medications interacting with DOACs Renal impairment precluding DOAC prescription Antiphospholipid antibody syndrome	In severe renal dysfunction, LMWH is contraindicated Pregnancy or breast feeding	Passed by placenta and breast milk, teratogenic
IV Unfractionated Heparin (UFH)	Short half life	Given IV so patient must be admitted into hospital May be long delays until therapeutic anticoagulation achieved	Initial treatment in patients with a very high bleeding risk or renal failure	Heparin induced thrombocytopenia	Safe in pregnancy and breastfeeding.

GI: gastro-intestinal; INR: international normalised ration; IV: intravenous; VTE: venous thromboembolism. * Examples of are phenytoin, carbamazepine, phenobarbital, primidone, eslicarbazepine, rifampicin, ‘azole antifungals (such as ketoconazole, voriconazole), HIV protease inhibitors (such as ritonavir).

DOACs are the treatment of choice for most patients on discharge. They are simpler to take than warfarin with fixed dosing, no food restrictions and minimal monitoring requirements (usually 6-12 monthly assessments of renal function). Although all DOACs are effective treatment for PE, apixaban and rivaroxaban have the added advantage of requiring no LMWH lead in treatment, making either well suited to prescribing in the ED. In contrast, warfarin is challenging to initiate in the ED due to the need for serial monitoring and dose titration. Warfarin must be started with a minimum of five days of LMWH (continued until the INR $\geq$ 2.0). Important DOAC contraindications include in-situ gastrointestinal tumours, bladder tumours, and a number of interacting medications [24].

Obesity

Patients weighing more than 120kg present a further challenge to achieve effective anticoagulation. In such cases, NICE guidelines recommend using an anticoagulant which can be monitored for efficacy, such as warfarin or LMWH. However, emerging evidence suggests both apixaban and rivaroxaban may be safe and effective in obese patients [25,26] at the standard dose [27].

Pregnancy

For pregnant patients, prevention of iatrogenic harm to the foetus and breast-feeding infant is paramount (see **Table 3).** LMWH is a safe anticoagulant for pregnant patients and should be given in doses titrated against the woman's booking or early pregnancy weight [28]. There is no evidence to suggest superiority between once daily and twice daily LMWH dosing regimens. Treatment should continue throughout pregnancy until 6 weeks post-partum and 3 months total of treatment has been given. These patients tend to be induced with their LMWH held for 24 hours pre-delivery. When a patient is diagnosed with PE within two weeks of delivery, they are often changed to unfractionated heparin (UFH) in the days prior to delivering. This reduces the period of time when their anticoagulant therapy is held and in the context of significant haemorrhage, can be held because of its short half-life.

Renal Impairment

Apixaban, rivaroxaban and edoxaban can be prescribed for patients with renal impairment as long as the creatinine clearance is > 15 ml/min. The dose of edoxaban should be reduced with a creatinine clearance < 50 ml/min. PE patients with a creatinine clearance of < 15 ml/min should be commenced on IV heparin followed by warfarin anticoagulation [29].

MANAGEMENT OF SUBSEGMENTAL PE

Subsegmental PE (SSPE) affects the 4th division and more distal pulmonary arterial branches. Increasing use of computer tomography pulmonary angiography (CTPA) and improved sensitivity of diagnostic imaging have resulted in higher rates of SSPE diagnosis. There is also more subjectivity in diagnosis; higher inter observer variability is seen on CTPA for diagnosis of subsegmental than for proximal PE [30].

A prospective cohort study [31] enrolling 292 patients diagnosed with SSPE (without cancer) found 28 (9.6%) had DVT at baseline or on repeat ultrasound a week later. Among 266 patients (without DVT at baseline or one week) managed without anticoagulation, 3.1% (95% CI 1.6-6.1) were diagnosed with recurrent VTE within 90 days [32]. This first prospective study only supports withholding anticoagulation for all patients with SSPE with normal serial bilateral leg ultrasounds, although shared decision making with the patient would be necessary to withhold anticoagulation. Further research is ongoing including a randomised controlled trial (NCT04727437).

MANAGEMENT OF PE IN HIGH-RISK CASES

Overall mortality for high-risk PE patients with cardiovascular instability is estimated to range from 18% to 30%[3]. When progression to cardiac arrest occurs mortality can be as high as 65% [3,33]. Whilst the evidence for thrombolysis improving outcomes is relatively weak, outcomes in high-risk patients with cardiovascular instability are so poor that most international guidelines recommend systemic thrombolysis [1,7,8]. For intermediate risk patients, there is little evidence that systemic thrombolysis improves overall mortality or longer term outcomes while increasing the risk of major bleeding including hemorrhagic stroke. [34,35]. In this situation, guidelines suggest deferring systemic thrombolysis unless the patient develops cardiovascular decompensation [6].

Management of cardiac arrest due to PE

PE represents between 2% to 5% of out of hospital cardiac arrests [36], and at least 6% of in-hospital cardiac arrests [37]. In cases of known or suspected PE, systemic thrombolysis during CPR increases 30-day survival [38] [39]. Thrombolysis must be given as soon as possible to increase the likelihood of a positive outcome. When the cause of cardiac arrest is unknown, empiric thrombolysis does not appear to improve clinical outcomes [40]**.**

A key challenge often lies in identifying patients for whom PE is the most likely cause of arrest, particularly where no collateral history is available. Whilst 25 to 50% of first time PE patients have no risk factors [41], recent medical history (recent hospitalisation, abdominal or pelvic surgery) and family history may influence differential diagnosis. Identification of DVT on POCUS may provide evidence of acute VTE, making PE as a cause of arrest more likely [42]. The most common PE arrest rhythm is PEA [43] and PE can be associated with low end tidal CO_2 readings due to increased dead space, although this finding is non-specific [44]. Prognosis following cardiac arrest is likely to be poor, even with thrombolysis [45].

Thrombolysis is achieved using a tissue plasminogen activator (TPA) agent, such as alteplase or tenecteplase. Treatment harms are significant with 10% of intermediate risk PE patients experiencing a major bleeding event after thrombolysis and 1.5% having haemorrhagic stroke. These risks increase with age [34].

Extracorporeal membrane oxygenation (ECMO)

Patients identified as likely to benefit from ECMO use following massive PE can see up to a 65% rate of survival to decannulation, but outcomes are worse for PE patients who progress to cardiac arrest [46]. Delay to initiation of ECMO for more than 30 minutes during PE related arrest is associated with a less than 10% survival rate [47].

Management of unstable high-risk PE

Systemic thrombolysis versus alternatives

International guidelines (ESC, ACCP, CHEST) recommend systemic thrombolysis for high-risk PE patients with cardiovascular instability, to rapidly reperfuse pulmonary arteries and reduce RV dysfunction. A meta-analysis has demonstrated effectiveness of systemic thrombolysis for high-risk patient groups, with a reduction in mortality or recurrence from 19% to 9.4% compared to treatment with heparin alone [48]. Many contraindications exist

and there is a statistically significant increase in major and clinically relevant non major bleeding events compared to treatment with heparin alone, with a NNT of 10 and NNH of 8 [48].

Departments with immediate access to interventional radiology and relevant techniques such as catheter directed thrombolysis and/or clot retrieval, may consider their use in high risk patients [49]. Patients who undergo direct intra-arterial thrombolysis receive lower doses of thrombolytic agent with a theoretical reduced bleeding risk [50]. There are no clear contraindications to catheter directed thrombolysis and for patients with recent surgery, trauma, or pregnant women, such techniques may be lifesaving. Intravascular therapy is only effective for proximal pulmonary artery thromboses. Such services must be set up through the development of intradepartmental protocols and require an on-call rota of interventional radiologists with expertise who can be rapidly mobilised. In a highly functioning system, one study reports a pooled estimate for clinical success of catheter directed thrombolysis of 81.3% and a 30-day mortality estimate was 8.0%. The incidence of major bleeding was 6.7% [51]. There is insufficient evidence to recommend catheter directed therapies over systemic thrombolysis at present [52]. Surgical embolectomy may be considered in patients with haemodynamic instability despite anticoagulation treatment, as an alternative to “rescue thrombolysis” [1]. Surgical embolectomy is highly unlikely to be first choice therapy and there is insufficient evidence to recommend embolectomy over catheter directed therapy or systemic thrombolysis.

Management of intermediate-risk PE

The PEITHO trial found no significant difference in mortality at 7 days and 30 days with systemic thrombolysis in intermediate risk PE, and a significant increased bleeding risk with systemic thrombolysis [34]. Guidelines suggest against use of systemic thrombolysis for intermediate risk PE, but promote use of systemic thrombolysis for patients who deteriorate to become high risk [6]. Unlike myocardial infarction, there is no evidence to suggest benefit of short door-to-needle times, so systemic thrombolysis can be reserved over the entire phase of acute admission for those patients who deteriorate.

Intravascular thrombolysis and therapy may also be effective for intermediate risk PE patients, however there is insufficient evidence supporting catheter directed therapy over standard treatment of therapeutic anticoagulation. Low molecular weight heparin is a

common treatment of choice for intermediate risk PE and there are no trials comparing its efficacy to the DOACs.

Systemic thrombolysis in pregnant patients

For pregnant patients with life threatening PE and haemodynamic compromise, the Royal College of Obstetricians and Gynaecologists (RCOG) suggest initial therapy with UFH, noting the importance of individual case assessment. They advocate consideration of systemic thrombolysis or surgical thrombectomy for deteriorating patients. Catheter directed therapies may be a future option, but benefit has not yet been established [53]. The evidence is low quality [54,55] and individual patient decisions have to be made balancing therapeutic availability, time to treatment, haemodynamic stability, and individualised risk.

SPECIAL CIRCUMSTANCES

Cancer patients

In cancer associated thrombosis, guidelines support DOAC therapy [7,8]. These agents demonstrate potential benefits such as reduced bleeding risk and comparable safety and efficacy profile compared to LMWH, and lower lifestyle burden [56]. However, in gastrointestinal or bladder malignancy where bleeding risk is greater, guidelines advise avoiding DOACs which are associated with a greater risk of gastrointestinal bleeding and haematuria.

Recurrent PEs

VTE recurrence following a provoked clot is approximately 3% per patient-year after stopping anticoagulant therapy [57]. This risk is higher (at least 8%) in patient groups such as those with cancer or antiphospholipid syndrome, and in those with no provoking cause for their PE [58].

True ‘anticoagulation failure’ is rare, occurring in 2.0% of patients on DOACs and 2.2% of patients on warfarin for VTE [59]. An ED safe approach to patients who are diagnosed with PE while being prescribed an anticoagulant is to change them onto full dose LMWH. Early discussion with specialists is sensible, as there is little evidence to guide management.

PE FOLLOW UP

Patients diagnosed with PE should be reviewed in a specialist clinic as soon as practical. Patients should be given important information about PE and anticoagulation treatment. This is also an opportunity to perform a limited cancer screen. Previously routine, thrombophilia testing is not longer performed in most cases. PE is treated for a minimum of three months and in cases with persistent symptoms, long term medication may be required. All patients are assessed for their risk of recurrent VTE [1]. In general, patients with a strong, transient provoking factor for their PE (such as hip replacement surgery, hospitalisation for acute illness, trauma) can discontinue their anticoagulation at 3 months. Patients with a weak provoking factor or no provoking factor have a higher risk of recurrence. A decision rule such as the HERDOO2 rule can individualize the estimated risk of recurrent VTE which helps with shared decision making [60]. For example, men remain at high risk of recurrence following unprovoked PE and are usually offered long term anticoagulation. Patients with active cancer and antiphospholipid syndrome have the highest risk for recurrence and are recommended to continue long term.

EMERGING MANAGEMENT STRATEGIES AND CONTROVERSY

Multidisciplinary hospital PE teams

Multidisciplinary PE response teams (PERT) aim to bring clinicians from several different specialties, including cardiology, respiratory, haematology, vascular and cardiothoracic surgery together to provide emergency evaluation and rapidly determine optimal management. An important aspect of this team is availability 24 hours a day with remote access to patient details and the ability to meet immediately. Most examples are seen in the United States, and tend to focus on intermediate, high risk and complex patients. Retrospective data have signalled improved outcomes associated with implementation of these teams [61].

Reduced-dose thrombolysis

The use of reduced-dose systemic thrombolysis (0.5 to 0.6 mg/kg alteplase) might reduce the risk of major bleeding or intracranial bleeding. A recent network meta-analysis suggests no difference in efficacy between full dose and reduced-dose thrombolysis, and reduced-dose thrombolysis may have a net benefit with a reduced bleeding risk [62]. A trial is currently

underway to prospectively evaluate low dose thrombolysis in the setting of intermediate risk PE (NCT04430569).

PE in SARS-CoV-2 Patients

As many as 35% of hospitalised SARS-CoV-2 patients are diagnosed with VTE and 60% have VTE at autopsy [63,64]. VTE risk correlates with disease severity with 21% in intensive care units (ICU) having VTE. This compares to 8% of influenza ICU patients [65]. The exact pathophysiological process is not yet fully understood but growing consensus indicates a direct effect of SARS-CoV-2 on vascular endothelium along with predisposing prothrombotic factors like hypoxia, severe inflammation, and immobilization [66]. An elevated D-dimer and thrombocytopenia correlate with increasing VTE risk, disease severity and mortality [67,68]. VTE diagnosis, risk assessment and treatment in COVID-19 patients is currently the same as with standard protocols, with no current evidence supporting alternative management [69].

Prophylactic treatment of hospitalised SARS-CoV-2 patients with anticoagulation (using treatment or prophylactic dose LWMH [75]) improves survival, although VTE risk remains despite anticoagulation particularly in the critically unwell [70,71]. An enhanced anticoagulation regime with close monitoring has demonstrated survival benefit in critically unwell patients [72], However, in level two or three patients, NICE suggests the LMWH dose should be reduced to a locally agreed intermediate or standard dose as treatment dose has not been shown to prevent deaths or reduce duration of intensive care but is associated with an increased risk of bleeding [75].

Even greater uncertainty exists for VTE risk management in non-hospitalised patients. The IMPROVE VTE study suggests an individualised risk assessment to determine if extended treatment is required on discharge [73]. The ACA and CHEST guidance concurs with patient specific risk assessment, while National Institute of Health (NIH) suggests against routine screening for VTE in SARS-CoV-2 patients [72]. NICE guidance also recognises lack of evidence here, and suggests assessment of both VTE and bleeding risks and to consider pharmacological prophylaxis if the risk of VTE outweighs the risk of bleeding [74].

Patient Centred Care

Patient involvement is increasingly recognised as central to providing good care for patients with PE. The Canadian Venous Thromboembolism Clinical Trials and Outcomes Research Network, in conjunction with the James Lind Alliance, is undertaking a priority setting partnership for VTE and is set to chart the direction of future research in this area towards questions important to patients and the public [75]. Shared decision making in the ED is particularly important in areas of uncertainty around PE management, for example decisions around admission, choice of anticoagulant and long term anticoagulation. Successful shared decision making in PE is grounded in a good understanding of the evidence behind treatment strategies, acknowledgement and communication of uncertainty, and use of plain language summaries like those produced by Thrombosis UK [76].

SUMMARY

The approach to managing PE starts with risk stratification and use of validated scoring systems. High risk patients should receive systemic thrombolysis when suitable and low risk patients should be assessed for home management. Most PE patients are suitable for outpatient treatment. Emergency physicians should be familiar with anticoagulant prescribing tailored to individual patient need and aware of the relevant contraindications for specific anticoagulants.

Competing interests

JC, PS, KdW and MR have no conflicts of interest to declare.
DH was a topic expert for NICE NG158 and QS201, regarding the diagnosis and management of venous thromboembolic disease and venous thromboembolism in adults, respectively. DH was also a co-author on the BTS guidelines for the outpatient management of pulmonary embolism and the accompanying national quality standards.

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Table legends

Table 1: Comparison of commonly used national and international classification tools for PE with associated treatment guidance.

Table 2: Commonly used scoring tools to identify low risk PEs

Table 3: comparison of various anticoagulation choices

Contributorship statement

PS, JC and MR devised the concept and planned the review. PS and JC drafted the manuscript. KdW, DH and MR provided critical review and redrafted the work. MR is guarantor.

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