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Recent advances

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How to predict the prognosis in patients with acute pulmonary embolism? Recent advances

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ABSTRACT
Pulmonary embolism (PE) is the third most frequent cardiovascular disease, characterised by a wide range of presentations and clinical course. Prognostic assessment is a cornerstone of PE management as it determines the choice of both diagnostic and therapeutic strategies. During the last decades significant efforts have been made to safely select patients for early-discharged or home-treatment, but the appropriate risk-stratification, particularly of intermediate-risk patients, remains challenging. In addition to the guidelines recommended clinical prediction rules, such as PESI, sPESI and/or Hestia Criteria, a multimodality approach based also in biomarkers and cardiac imaging is crucial for risk-stratification and to select the appropriate management of the patients. In this review article we discuss the current methods for predicting
short and long-term prognosis in patients with PE, focusing on the current guidelines, but also in the most recently proposed clinical prediction rules, biomarkers and imaging parameters.

**Key words:** pulmonary embolism; risk-stratification; venous thromboembolism; prognosis; mortality

**INTRODUCTION**

Pulmonary embolism (PE) is the third most frequent cardiovascular disease, accounting for approximately 300,000 deaths in Europe every year [1, 2]. It has various presentations, ranging from an asymptomatic incidental finding to circulatory collapse. In the past, patients with PE were traditionally hospitalised due to the indication of intravenously anticoagulation and concerns about the high risk of death [3]. Since oral anticoagulants demonstrated efficacy and safety, PE can nowadays often be treated on an outpatient basis. However, appropriate patient selection remains under debate. Risk-stratification is a cornerstone in managing several conditions, including PE. It determines the need for urgent reperfusion therapy in high-risk patients and identifies low-risk patients that could be safely treated at home. The major challenge in managing PE patients is for the remaining group of intermediate-risk patients, which is highly heterogeneous. Although most of those patients experienced a favourable outcome, a small, albeit significant, proportion will need rescue reperfusion [4].

In this article, we discuss the current models for predicting short- and long-term prognosis for patients with PE and the decision-making process of PE management, particularly regarding the decision on inpatient vs outpatient treatment.

**INSTRUMENTS USED FOR PROGNOSIS ASSESSMENT IN PE**

**Clinical scores**

The Pulmonary Embolism Severity Index (PESI) and the Geneva score were the first to be proposed and validated for acute PE risk-stratification.

The Geneva prediction rule was developed to identify patients with PE who are at low risk of death, recurrent venous thromboembolism (VTE) or major bleeding at three months [5]. This score is based on six predictors, including cancer, heart failure, previous deep vein thrombosis (DVT), documented DVT, systolic blood pressure (SBP) < 100 mmHg, and arterial PaO₂ <60 mm Hg (8 kPa). A score of two or less represents about two-thirds of patients and is associated with a 2% risk of adverse outcomes.
The Pulmonary Embolism Severity Index (PESI) comprises 11 clinical variables and stratifies patients into five severity classes [6]. A simplified PESI score (sPESI) version includes only six variables and two risk classes [7]. A PESI risk of I or II indicates a low-risk population (as does a simplified PESI of zero), with the 30-day mortality rate being less than 3%. According to a meta-analysis including 50,021 patients, the area under the curve (AUC) of sPESI was 0.79 for all-cause mortality with a pooled sensitivity and specificity of 0.92 and 0.38, respectively, being similar to the original PESI score [8]. This study documented a pooled mortality of 2% among patients with PESI class I or II, and 1.8% among patients with 0 points on sPESI [8].

The Hestia Criteria represents an alternative approach to identify low-risk patients and select those safely treated at home [9]. This approach consists of eleven criteria regarding the patient's clinical presentation, comorbidities, and familial and social factors. In a prospective study, 90-day mortality was 1% for patients with acute PE and no Hestia Criteria for hospitalisation who were managed as outpatients.

Table 1 summarises the most frequently used clinical prognostic scores.

To re-stratify patients with intermediate risk, several scores have been developed. One of the most used is the BOVA score, which includes parameters such as heart rate (HR), SBP, biomarkers and transthoracic echocardiography (TTE) [10]. The primary composite outcome was PE-related death, hemodynamic collapse, or recurrent PE at 30 days. Thirty-day complications differed significantly across categories of the model (0–2 points: 4%; 3–4 points: 11%; >4 points: 29%), with an AUC of 0.73 (95% confidence interval [CI], 0.68–0.77). Other scores, such as TELOS, CAPE and SHIeLD score, were also developed for additional risk-stratification in normotensive patients [11–13]. The variables comprised in those scores are summarised in Table 2.

The shock index (SI) incorporates information about the patient's HR and SBP (shock index = HR/SBP) to assess hemodynamic status. A SI ≥0.9 represents a high-risk population. Shock index demonstrated to be an independent predictor of 30-day mortality and to perform better than SBP alone for discrimination of low-risk patients [14]. However, while the SI had a higher sensitivity compared to SBP (31% vs. 14% for SBP <100 mm Hg and 8% for SBP <90 mm Hg, respectively), it was associated with lower specificity (86% vs. 93 and 97%, respectively) [15]. The sPESI demonstrated to outperformed SI in predicting 30-day mortality [16].

Biomarkers
Biomarkers were traditionally included as part of the risk-stratification of PE patients. Although in initial studies, elevated troponin was associated with poor outcomes, including mortality, subsequent studies have questioned its predictive value. Nowadays, the recommendation is that it should be combined with other prognostic markers [17, 18]. The prognostic value of natriuretic peptides has also been demonstrated, and it seems to have an additive predictive value when combined with troponin measurements. In the PROTECT study, the combination of sPESI with troponin and N-terminal prohormone B-type natriuretic peptide (NTproBNP) measures had a higher positive predictive value for adverse outcomes than the sPESI alone [19]. Current guidelines recommend employing NT-proBNP to identify normotensive patients with an expected benign disease course.

Elevated plasma lactate signalises patients with organ dysfunction and is associated with increased mortality in patients with acute PE [13, 20]. The FAST score is a clinical predicting rule that includes heart fatty acid-binding protein (H-FABP), syncope and HR. The positive predictive value was 20.5%, and the AUC was 0.85 (95% CI, 0.75–0.95). A meta-analysis of 9 studies including 1680 patients found that elevated H-FABP levels were associated with 30-day PE-related mortality [21]. Although a promising biomarker, H-FABP is not routinely available. Other biomarkers, such as copeptin, have also been studied but are less extensively validated and not readily available in clinical practice [22–24].

**Cardiac imaging**

Right ventricular (RV) dysfunction has been associated with an increased risk of death [4]. Computed tomography pulmonary angiography (CTPA) has the advantage of combining both diagnostic and prognostic features at once [4]. CTPA signs of RV dysfunction include septal bulging, pulmonary artery enlargement, elevated right-to-left ventricular end-diastolic diameter ratio and retrograde contrast reflux into the vena cava [4]. CTPA also assesses PE extension, and due to high sensitivity, it contributes to an increased incidence of subsegmental PE diagnosis. The clinical significance of subsegmental PE remains uncertain, and recommendations are extrapolated mainly from historical ventilation-perfusion lung scan trials. In the PIOPED study, 17% of patients had defects isolated to the subsegmental pulmonary arteries [25]. A systematic review and meta-analysis showed no difference between patients with subsegmental PE treated with anticoagulation and those not treated for the pooled outcomes of a 3-month incidence of recurrent VTE and all-cause mortality [26]. Thus, the indication of anticoagulation should be individualised in patients with incidentally diagnosed PE who have no additional risk factors such as cancer.
TTE is a readily available tool which can be easily performed at the patient’s bedside. Although according to the European Society of Cardiology (ESC) guidelines on PE, TTE is not a mandatory part of the routine diagnostic workup in hemodynamically stable patients, several parameters have been proposed for risk stratification [4]. Prognostic markers include the increased right-to-left ventricular ratio, ratio of tricuspid annular plane systolic excursion (TAPSE) to pulmonary arterial systolic pressure, 60/60 sign, and RV wall hypokinesis (including the McConnell’s sign) [27]. Considering that TAPSE cannot be measured in some patients, the subcostal echocardiographic assessment of tricuspid annular kick (SEATAK) was demonstrated to be an accurate alternative, reflecting RV systolic function and demonstrating prognostic value [28].

A clot in transit, defined as a free-floating thrombus within cardiac chambers, represents a potential source of recurrent embolism and is associated with higher short-term all-cause mortality and PE-related mortality [29]. Prevalence of TTE detection of right heart thrombi was 3.1% (95% CI, 2.8–3.4) [29]. Besides the prognostic value, there was no significant difference in outcomes between treatment with anticoagulation alone or reperfusion strategy in these patients [30]. A multicentre prospective cohort study including 490 normotensive PE patients managed according to the current ESC guidelines proposed the optimal definition of RV dysfunction for prognostic assessment. In this study, the multivariable analysis identified SBP, right-to-left ventricular ratio and TAPSE as independent predictors of adverse outcomes or rescue thrombolysis within the first 30-days [21].

New echocardiographic parameters have reinforced the role of TTE in risk assessment of acute PE. Right ventricular outflow tract velocity time integral <9.5 cm was associated with increased PE-related mortality [31]. RV strain assessed with speckle-tracking echocardiography is an independent prognostic marker for in-hospital events in patients with acute non-massive PE [31]. The ratio of tricuspid annular plane systolic excursion to pulmonary arterial systolic pressure (TAPSE/PASP) predicts adverse outcome in PE better than each measurement individually [31]. Pulmonary artery systolic pressure/left ventricle stroke volume (PASP/LVSV) performs better compared to BOVA and PESI in predicting adverse events in intermediate PE [32].

Although markers of RV dysfunction have a consistent association with short-term mortality, they have poor diagnostic performance when used as a stand-alone test, requiring combination with other parameters [33]. In some patients with suspected acute PE, TTE and CTPA may be useful tools to identify findings of pre-existing chronic thromboembolism pulmonary hypertension [4].
**Electrocardiogram**

The electrocardiogram (ECG) is a quickly interpretable, low-cost and widely available tool that could be used for prognostic stratification of patients with PE. The Daniel score was developed as a scoring system for the severity of pulmonary hypertension in patients with PE. However, since its publication, several studies have investigated the use of ECG as a risk-stratification tool for PE. A systematic review and meta-analysis identified S1Q3T3, complete right bundle branch block and right axis deviation as the best predictors for in-hospital mortality [15]. T wave inversion and atrial fibrillation were also identified as predictors of negative outcome [15].

**RISK-STRATIFICATION OF PE PATIENTS**

**Identification of high-risk patients**

Identifying high-risk mortality patients should be the first step in PE risk-stratification. According to the ESC criteria, high-risk patients correspond to those who present with cardiac arrest, hemodynamic instability (defined as SBP inferior to 90 mm Hg for more than 15 minutes in the absence of other explanation), and/or the need of vasopressors in combination with end-organ hypoperfusion, or persistent hypotension not caused by new-onset arrhythmia, hypovolemia or sepsis [4]. This subgroup of patients corresponds to 4% of PE patients, with a documented short-term mortality of 16% to 19% [34, 35]. These patients' management relies on organ support and prompt reperfusion with thrombolytic therapies or thrombectomy.

In a haemodynamically compromised patient with suspected PE, if immediate CTPA is not possible, bedside TTE echo is the most useful test to evaluate signs of RV pressure overload. Some specific TTE findings (60/60 sign, McConnell sign, or right- heart thrombi) justify emergency reperfusion treatment for PE, without further tests.

**Identification of low-risk patients**

Low-risk PE corresponds to about 40% of acute PE patients [36]. Although historically, all patients with acute PE were admitted to the hospital, last decades, several prediction rules have since been developed to identify patients that can be safely treated as outpatients [3]. Home-treatment seems feasible in approximately 30% of the normotensive patients with acute PE [37].

The safety of these scoring systems was further investigated in the HOME-PE (Hospitalization or Out-treatment Management of PE) study, which directly compared the sPESI and Hestia
Criteria. This study demonstrated that both strategies had similar safety and effectiveness and may be used for PE risk-stratification. In this study, Hestia criteria identified a lower proportion of patients candidates for home treatment compared to sPESI (39.4% vs. 48.4%). Still, the proportion of patients actually managed at home was similar in the two-triaging group (38.4% vs 36.3% in the Hestia and sPESI group, respectively) [37]. The incidence of recurrent VTE, major bleeding or death in patients who qualified for home treatment by the Hestia or sPESI strategy and were treated at home was as low as 1.3% and 1.1%, respectively. 30-days mortality was 0.27% and 0.28%, respectively [37]. The HOT-PE (Home Treatment of Patients with Low-risk PE with the Oral Factor Xa inhibitor Rivaroxaban) trial investigated the safety and efficacy of home treatment of PE using rivaroxaban in low-risk patients, defined by the adapted Hestia criteria and the absence of RV enlargement or dysfunction, and of free-floating thrombi on TTE or CTPA. From the reported initial population of 2854 patients with objectively confirmed PE, 300 patients had either RV dysfunction or free-floating thrombi despite not meeting any of the Hestia criteria. A recent meta-analysis of 3295 patients from 21 studies showed that RV dysfunction, primarily defined by RV pressure overload assessed on imaging tests, alternatively by elevated cardiac biomarkers, may have a significant impact on the early prognosis of patients classified as low-risk based on PESI, sPESI or Hestia criteria [21]. Thus, outpatient treatment appears to be safe for truly low-risk patients identified by PESI, sPESI or Hestia criteria combined with the exclusion of RV dysfunction by either imaging studies or cardiac biomarkers. In fact, data show that these instruments are similarly reliable in identifying low-risk patients in terms of prognosis [38].

Re-stratifying intermediate-risk patients

The intermediate-risk patients represent a highly heterogenous group of patients, with a 30-day mortality risk varying between 5% and 15% [6, 7]. Data from the FLASH (FlowTriever All-Comer Registry for Patient Safety and Hemodynamic) registry revealed that over one-third of these patients were in normotensive shock, described as the presence of SBP higher than 90 mmHg in patients with a cardiac index \( \leq 2.2l/min/m^2 \) (invasive evaluation). This subgroup of patients is at higher risk of hemodynamic deterioration and in-hospital mortality. For this reason, in the last decade, efforts have been made to identify the subgroup of patients at higher risk who mainly benefit from close in-hospital monitoring. Several markers have been investigated as potential tools to stratify intermediate-risk patients, such as troponin and natriuretic peptides and detection of RV dysfunction. However, when considered isolated, none
of those markers exceeded a specificity of 70% (ranging from 56% for CT-documented RV dysfunction to 70% for natriuretic peptides) [3]. Based on experts' opinions, current guidelines proposed a subdivision into intermediate-high and intermediate-low risk patients, as the first represents a high 30-day mortality risk subgroup (10% vs. 4%) [39]. Normotensive patients with sPESI <1 or PESI II-II are considered low-risk patients without further risk stratification; those with an sPESI ≥ 1 or those with either RV dysfunction or elevated cardiac biomarkers are considered intermediate-low-risk patients; and those with sPESI ≥1 and both RV dysfunction and elevated cardiac biomarkers are considered intermediate-high risk patients. However, the currently available tools for the stratification of this subgroup of patients still have some limitations. The PESI and sPESI score have a high negative predictive value but a low positive predictive value. It does not adequately identify among the normotensive patients who are at a higher risk, requiring intensive monitoring [3, 26]. For this purpose, alternative scores such as the BOVA, TELOS and CAPE scores, seems more appropriate [26].

The TELOS score was derived from a prospective cohort of 496 patients and includes RV dysfunction, troponin and plasma lactate elevation as predictors of death or hemodynamic collapse at 7 days. In a prospective validation of this score, 5.9% of patients were allocated to the intermediate-high-risk category, with a cumulative incidence of death or hemodynamic collapse at 7 days of 21% [3, 40].

The CAPE (Calgary Acute Pulmonary Embolism) score consists of a simple four-variable risk score (comprising computed tomography right to left ventricle ratio ≥1.5, presence of central clot, HR ≥100 beats per minute and SBP <90–100 mm Hg), and demonstrated high predictive value for adverse outcomes in normotensive patients [12].

The SHIeLD score was created and validated to predict 30-days PE-related mortality and/or rescue thrombolysis, and comprises four prognostic factors: shock index ≥ 1, hypoxemia, lactate and cardiovascular dysfunction (defined as elevated troponin and NT-proBNP and right-to-left ventricular ratio >1) [11].

Furthermore, both biomarkers and cardiac imaging can be useful for additional risk-stratification [12]. In a cohort of 688 normotensive patients with acute PE, NT-proBNP and echocardiography had a prognostic impact on top of the sPESI. The risk of adverse outcome in patients with sPESI ≥ 1 with normal NT-proBNP and normal echocardiography was 2.5%, while the risk increased to 5.8% and 5.6% in patients with either NT-proBNP elevation or evidence of RV dysfunction, respectively. For those with both elevated NT-proBNP and RV dysfunction, the risk increases to 10.8%. In the PROTECT study, normotensive patients with
sPESI \geq 1, the risk of adverse event was 6.1\% in patients with normal biomarkers, 13.8\% in patients with elevated BNP and 20.4\% in patients with both elevated troponin and natriuretic peptides [19].

Despite current advances, re-stratification of the intermediate-risk patients remains challenging and an important area of research as, in addition to the decision about if in versus out-of-hospital care, it may impact the treatment decision. The use of systemic thrombolysis among normotensive patients considered as being at high-risk of decompensation has been evaluated in several trials. The European Pulmonary Embolism Thrombolysis (PEITHO) trial included 1005 patients with intermediate-high risk PE, defined by the evidence of myocardial injury (documented by elevated troponin) and RV dysfunction on imaging. It demonstrated that the incidence of hemodynamic collapse or death within one week was substantially lower among patients who performed tenecteplase plus unfractionated heparin (UFH) compared to those who performed UFH alone (2.6\% vs. 5.6\%; \( P = 0.02 \)). However, this benefit was mainly driven by reducing the risk of hemodynamic decompensation, while mortality did not significantly differ. In addition, the risk of major bleeding was significantly higher in patients who performed thrombolysis. Based on these findings, the potential benefit of full-dose systemic thrombolysis seems to be outweighed by bleeding risks, highlighting that more refined strategies are necessary to re-stratify patients at higher risk. The ongoing trial PEITHOS-3 will evaluate whether a reduced dosage of alteplase may be superior to heparin without an excess risk of major bleeding in these patients [41].

One possibly safer alternative to systemic thrombolysis in intermediate-risk PE patients, may be catheter-directed PE treatment using lower thrombolytic doses, which have been the focus of recently published small randomised and cohort studies. The results are promising, although only surrogate endpoints were used [42–45]. The larger randomised ongoing ultrasound-facilitated, catheter-directed thrombolysis vs anticoagulation alone for acute-intermediate-high-risk pulmonary embolism (HI-PEITHO) study will evaluate catheter-directed treatment (CDT), and particularly ultrasound-assisted CDT versus isolated anticoagulation in selected patients with intermediate-high risk acute PE [46]. In this trial, the investigators are using the National Early Warning Score (NEWS), an objective assessment and monitoring of each patient’s vital status to enable the early detection of patients who may benefit of prompt institution of rescue therapy before hemodynamic collapse occurs.

**BLEEDING RISK AS AN ADDITIONAL PROGNOSTIC FACTOR**
Aside from the thrombotic risk, bleeding risk also impacts the prognostic of patients with PE. Major bleeding was identified as a predictor of short and midterm-mortality in the Rejestr ZATorowości płucnej w POLsce (ZATPOL) and as a predictor of 1-year mortality in the Registro Informatizado Enfermedad TromboEmbolica (RIETE). The VTE-BLEED score was developed in the dabigatran arms of the pooled RE-COVER studies and identified six variables as predictors of major bleeding in patients with VTE on stable oral anticoagulation: active cancer, males with uncontrolled hypertension, anaemia, history of bleeding, age $\geq 60$ years and renal dysfunction. This score was externally validated in the HOKUSAI-VTE, and its prognostic value was further demonstrated in a real-world prospective cohort study [47].

A systematic review evaluated the ability of different bleeding risk tools to predict major bleeding. Most scores showed a moderate ability to predict major bleeding events in patients with VTE. The VTE-BLEED score was the most sensitive to forecast major bleeding events in patients treated with direct oral anticoagulants [48].

**SPECIFIC POPULATIONS: PATIENTS WITH CANCER**

Venous thromboembolism is a frequent complication in patients with cancer and represents the second cause of death after cancer itself. Pulmonary embolism attributable to a neoplasia is associated with 3-fold increased mortality compared to a non-neoplastic condition [49,50]. Approximately 80% of patients with acute PE attributable to cancer died after 1 year of follow-up [49]. Although it is associated with significant mortality, there is considerable heterogeneity in prognosis, and prognostic tools adapted to this population are lacking.

The most frequently used non-cancer-specific prediction rules, such as PESI, sPESI and Geneva score, include cancer as a relevant predictor of mortality, even though these patients may be at low risk and successfully treated as outpatients [26]. Those prediction rules fail to account for cancer-specific disease characteristics by including cancer as a generic variable. Particularly, sPESI automatically classifies all cancer patients as high-risk individuals, limiting its usefulness in this setting. In fact, previous studies have demonstrated that the performance of those non-cancer specific clinical prediction rules could not be relied on to predict 30-day mortality in cancer patients with acute PE [51]. Recognising that the existing clinical prediction rules likely require modification in cancer patients, Carmona-Bayonas et al. [51] adapted the commonly used Hestia, PESI and sPESI by replacing the typical “history of cancer” variable with “metastatic cancer”. While these scores adaptations demonstrated acceptable predictive accuracy, these rules only categorise a small portion of patients at low risk [51, 52].
As an alternative to the generic risk scores, there are two cancer-specific risk-stratification rules: the RIETE and the POMPE-C scores. The RIETE score uses six variables (age >80 years, HR ≥110/min, SBP <100 mm Hg, weight <60 kg, immobilisation, and presence of metastases) [7]. The POMPE-C calculates a probability of death based on respiratory rate, O₂ saturation, weight, pulse, altered mental status, respiratory distress, do not resuscitate status and unilateral limb swelling [53]. In their original studies, both rules classified 22% to 38% of patients as low risk with a sensitivity >95%. When cancer-specific risk-stratification tools were compared to cancer-adapted generic prediction rules (adapted PESI and sPESI), RIETE and POMPE-C demonstrated better discriminatory ability [51].

A meta-analysis performed to assess the prognostic accuracy of clinical prediction rules for mortality in patients with cancer and PE, concluded that the highest sensitivity was observed with Hestia (98.1%; 95% CI, 75.6%–99.9%) criteria [54]. Other clinical prediction rules, such as POMPE-C, PESI, sPESI, modified PESI and RIETE, displayed a sensitivity between 87.8% and 93.8% [54]. Considering all the clinical prediction rules with sensitivity equal to or higher than 95%, all had a specificity lower than 33% [54]. Thus, further studies are necessary to define specific predictors of mortality in this heterogeneous group of patients.

**LONG TERM PROGNOSIS**

In addition to minimising short-term mortality, PE management should focus on long-term prognosis and reducing the risk of VTE recurrence. Although the risk of recurrence is low during anticoagulant treatment, it increases after interruption of anticoagulation to as high as 10% in the first year and more than 30% within five years. Currently, most guidelines recommend balancing the risk of bleeding with the risk of recurrence after an initial treatment period of three to six months based on the aetiology and presence of modifiable risk factors. The provoked (e.g., by a transient risk factor such as major surgery) or unprovoked nature of PE also impacts prognosis, as patients with an unprovoked PE are at a higher risk of recurrence and represents a heterogeneous subgroup of patients, in which further Risk-stratification is needed.

Previous studies have suggested that D-dimer testing after three to six months of treatment can help identify patients with an unprovoked PE with a low risk of VTE recurrence. The PROLONG study demonstrated that patients with elevated D-dimer levels after an initial treatment period and stopped using anticoagulation had an annualised PE recurrence of 11%. In comparison, the rate was 2% among patients who resumed treatment [55].
The Vienna model is a prediction model for assessing the risk of recurrence in patients with unprovoked VTE, which comprises the male sex and the absolute D-dimer level as predictors. Based on this score, the expected rate of recurrent VTE at one year is below 5%, 5-10% and > 10% for patients with low, moderate or high risk, respectively [56].

THE APPLICATION OF ARTIFICIAL INTELLIGENCE

Artificial intelligence (AI) is having a significant impact on healthcare. In the past few years, investigation of new AI-based PE tools has focused on diagnosis, using deep-learning models to improve time and diagnostic accuracy based on CTPA and also ECG-signals [57–59]. Fewer studies are available regarding the use of AI models for risk-stratification, although they demonstrate that machine learning models have the notable potential for PE prediction [21]. Based on the knowledge that the clot burden is related to the prognosis of acute PE, Liu la et al. [21] developed a deep framework based on U-Net to conduct pulmonary emboli segmentation and quantification on CTPA. Thus, artificial intelligence is giving the first steps, but they already shown promising results in this field, aiming at new applicability in the future.

CONCLUSION

The management of patients with acute PE requires accurate step-by-step risk stratification. Hemodynamic instability allows identifying high-risk patients who will benefit from thrombolytic therapy, while the clinical prediction rules such as PESI, sPESI and Hestia criteria will enable identifying low-risk patients who can safely be treated as outpatients. The approach to intermediate-risk patients could be most challenging, and no single parameter could be recommended. In these patients, a multimodal approach should be encouraged based on PESI, sPESI or Hestia Criteria, biomarkers, and cardiac imaging.

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REFERENCES


**Table 1.** Summary of prognostic clinical scores for pulmonary embolism

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<td>Cancer</td>
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<td>Cancer</td>
<td>Hemodynamic instability</td>
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<tr>
<td>Heart failure</td>
<td>Chronic heart Failure</td>
<td>Chronic heart failure or chronic pulmonary disease</td>
<td>Need for thrombolysis or embolectomy</td>
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<tr>
<td>Previous DVT</td>
<td>Chronic pulmonary disease</td>
<td>Pulse rate ≥110 bpm.</td>
<td>Active bleeding or high bleeding risk</td>
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Documented DVT

Male sex

SBP <100 mm Hg

Arterial PaO₂ <60 mm Hg (8 kPa)

SBP <100 mm Hg

Arterial oxyhaemoglobin saturation <90%

Arterial oxyhaemoglobin saturation <90%

Respiratory rate >30 breaths per minute

Pulse rate ≥110 bpm

Temperature <36° C

Altered mental status

Age in years

SBP <100 mm Hg

Arterial oxyhaemoglobin saturation <90%

Age >80 years

Oxygen supply to maintain oxygen >90% for >24 hours

PE diagnosed during anticoagulant treatment

Severe pain needing IV medication >24 hours

Medical or social reasons for treatment in hospital

Creatinine clearance <30 ml/min

Severe liver impairment or disease

Pregnancy

Table 2. Summary of the prognostic clinical scores for normotensive patients with pulmonary embolism

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<tr>
<td>SBP 90–100 mm Hg</td>
<td>SBP 90–100 mm Hg</td>
<td>Elevated lactate</td>
<td>Lactateab</td>
</tr>
<tr>
<td>HR ≥100 bpm</td>
<td>HR ≥100 bpm</td>
<td>HR ≥100 bpm</td>
<td>Shock index ≥1.0</td>
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<tr>
<td>RV dysfunctiona</td>
<td>Right-to-left ventricle ratio</td>
<td>RV dysfunctionb</td>
<td>Cardiovascular dysfunctionc</td>
</tr>
<tr>
<td>1.5c</td>
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Abbreviations: DVT, deep vein thrombosis; SBP, systolic blood pressure; PE, pulmonary embolism; IV, intravenous; HIT, heparin-induced thrombocytopenia
Cardiac troponin elevation\textsuperscript{b}
Presence of central pulmonary artery clot
Hypoxaemia (PaO\textsubscript{2}/FiO\textsubscript{2} ratio)

\textsuperscript{a}RV dysfunction defined as echocardiographic assessment RV/LV >0.9, systolic pulmonary artery pressure >30 mm Hg, RV end-diastolic diameter >30 mm, RV dilatation or RV free-wall hypokinesis; or on CT scan as RV/LV ratio > 1 \[10\]. \textsuperscript{b}Based on standard manufacturer assays and cut-off values \[10\]. \textsuperscript{c}Evaluated on cardiac CT \[12\]. \textsuperscript{d}Elevated plasma lactate is defined as plasma lactate levels ≥2 mmol/l \[40\]. \textsuperscript{e}RV dysfunction defined as the presence of at least one of the following: (1) RV dilatation (end-diastolic diameter ≥30 mm or right-to-left ventricular end-diastolic diameter ≥ 1 in apical four-chamber view; (2) pulmonary hypertension (estimated RV-right atrial gradient over 30 mm Hg; (3) Hypokinesis of the RV free wall \[40\]. \textsuperscript{f}Absolute value in mmol/l \[11\]. \textsuperscript{g}Cardiovascular dysfunction is defined as the cumulative presence of elevated troponin, elevated NTproBNP and RV/LV ratio ≥1.0 \[11\]

Abbreviations: SBP, systolic blood pressure; HR, heart rate; RV, right ventricle; LV, left ventricle; CT, computed tomography