A simple score to identify the sickest normotensive patients with acute pulmonary embolism

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The SIMpLe score can be applied to identify the sickest normotensive patients with acute PE and to support shared decision-making https://bit.ly/4qCgMoB

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Background Emerging evidence suggests that various prognostic factors should be combined to identify normotensive patients with pulmonary embolism (PE) at intermediate–high risk for a short-term complicated course. We proposed and externally validated a pragmatic score to identify those patients.
Methods The SIMpLe risk score contained vital Signs, IMaging testing and Laboratory tests. For the primary outcome of 30-day all-cause mortality and the secondary outcome composed of clinical deterioration or PE-related mortality, three independent cohorts from sites in Europe were used to assess overall score performance, discrimination, calibration and prediction.
Results The participants had a median (interquartile range) age of 72 (59–80) years in the PROTECT derivation cohort, 73 (66–82) years in TELOS and 69 (59–81) years in the Ramón y Cajal external validation cohorts. Women comprised 51–58% of each cohort. The SIMpLe score had areas under the curve of 0.69, 0.78 and 0.71 in the PROTECT, TELOS and Ramón y Cajal cohorts for the primary outcome, respectively. The score had good calibration. Using a threshold of a 15% probability of 30-day all-cause mortality, the risk score created a binary test with a positive predictive value of 23.5% in PROTECT, 26.7% in TELOS and 27.0% in Ramón y Cajal. For the composite secondary outcome, the risk score created a binary test with a positive predictive value of 23.5% in PROTECT, 26.7% in TELOS and 28.6% in Ramón y Cajal.
Conclusions The SIMpLe score can be applied to identify the sickest normotensive patients with acute PE and to support shared decision-making.

Introduction

Once the diagnosis of acute symptomatic pulmonary embolism (PE) is objectively confirmed, accurate risk stratification assists with the selection of appropriate initial therapy and treatment setting [1–3]. Multiple models have been developed for the initial risk assessment of patients presenting with acute PE. Some of them are used to identify low-risk patients for whom outpatient treatment may be appropriate, while others aim at identifying haemodynamically stable patients who are at higher risk of PE-related adverse events (*i.e.*, intermediate–high-risk PE) who may need closer observation with additional supportive care and/or pharmacological or mechanical circulatory support [4].

Traditionally, guidelines have recommended the combination of right ventricle (RV) enlargement/dysfunction and myocardial injury to identify intermediate–high-risk patients with acute PE [4]. However, previous research showed relatively low event rates among patients who met these criteria [5], prompting investigators to propose models with a higher positive predictive value [6–9]. Nonetheless, these models have certain practical limitations. The vast majority include a limited number of prognostic tests to risk classify patients with acute symptomatic PE and these criteria may appear insufficient for providing personalised treatment recommendations [6–9]. Furthermore, they employ fixed risk thresholds to identify patients who might benefit from reperfusion therapies with different risk–benefit ratios [6–9]. Consequently, it remains uncertain whether these scores might be clinically useful to drive decision-making toward advanced therapy for patients with PE.

Considering the limitations of the aforementioned prognostic models and to fill a key knowledge gap, we derived and aimed to externally validate a new pragmatic score for predicting key outcomes in haemodynamically stable patients with acute symptomatic PE.

Methods

We followed the TRIPOD (Transparent Reporting of a Multivariable Prediction Model for Individual Prognosis or Diagnosis) statement for reporting multivariable prediction model development and validation [10].

Derivation and validation cohorts

The risk score was derived using data from the PROgnosTic valuE of Computed Tomography scan (PROTECT) study, which recruited participants from 12 sites in Spain and was conducted from January 2009 until May 2011 [11]. Briefly, individuals were eligible for inclusion in PROTECT if they had acute PE diagnosed by multidetector computed tomographic pulmonary angiography (CTPA) and haemodynamic stability at presentation (*i.e.*, without cardiogenic shock, systolic blood pressure <90 mmHg or use of inotropic support). Exclusion criteria were need for immediate reperfusion treatment at the time of PE diagnosis, life expectancy less than 3 months, pregnancy, geographic inaccessibility and severe renal insufficiency.

We externally validated the new score in two independent cohort studies of haemodynamically stable patients with acute PE, namely the Thrombo-Embolism Lactate Outcome Study (TELOS) cohort [9] and an academic hospital registry [12]. Details of the recruitment and study designs have been previously reported. Briefly, TELOS was a longitudinal cohort of patients with PE enrolled at a tertiary teaching hospital in Italy. Consecutive adults presenting to the emergency department were enrolled if they had acute PE diagnosed by CTPA or by lung scan and were haemodynamic stable at presentation [9]. The Ramón y Cajal Hospital database is a large, prospective registry of patients with acute PE [12]. For this analysis, investigators excluded patients with haemodynamic instability (defined as cardiogenic shock, systolic blood pressure <90 mmHg or need of inotropic support), those in whom fibrinolytic therapy was indicated by decision of the attending physician and those with a diagnosis of COVID-19-associated PE. Briefly, a total of 1389 adults with acute symptomatic PE were enrolled between 1 January 2017 and 31 December 2024.

Predictor variables

Candidate variables were selected based on subject matter knowledge. We combined the variables included in the composite pulmonary embolism shock (CPES) score (tachycardia, echocardiographic RV dysfunction, saddle PE, concomitant deep vein thrombosis (DVT), troponin elevation and brain natriuretic peptide (BNP) elevation) [13] with additional prognosticators (mild hypotension, oxygen desaturation and lactate elevation) associated with short-term PE-related complications [9, 14]. Therefore, the SIMpLe risk score contained vital Signs (heart rate (⩾110 bpm *versus* other), systolic blood pressure (<100 mmHg *versus* other) and oxyhaemoglobin saturation (<90% *versus* other)), IMaging testing (CTPA (saddle PE or PE in the main pulmonary arteries *versus* other), echocardiography (RV dysfunction *versus* other) and lower limb ultrasound (concomitant proximal DVT *versus* other)) and Laboratory tests (troponin, BNP and lactate elevation *versus* other) (eTable 1).

For calculation of the SIMpLe score, in accordance with the clinical application of prognostic models [15], we assumed for the main analyses that missing values were normal.

Imaging testing

Local radiologists identified the presence of saddle PE when PE was at the level of the bifurcation of the pulmonary trunk and extended into the right and left main pulmonary arteries [16]. eTable 2 shows the

echocardiographic criteria that were used to define RV dysfunction in each of the study cohorts [9, 17]. Lack of compressibility was the diagnostic criterion for DVT.

Biomarkers

For derivation (PROTECT) and external validation in the Ramón y Cajal registry, the cardiac troponin (cTnI) test was considered abnormal in case of levels of troponin higher than >0.05 ng·mL^{-1}. TELOS used a troponin concentration of 0.10 ng·mL^{-1} to identify myocardial injury. For BNP, concentration of 100 pg·mL^{-1} was established as distinguishing between normal and elevated biomarker levels in acute PE in the three cohorts. The plasma lactate concentration was determined on arterial blood samples at the time of PE diagnosis. Plasma lactate values ⩾2 mmol·L^{-1} were considered abnormal in the derivation and validation cohorts.

Outcome measures

This study used 30-day all-cause mortality as the primary outcome. Secondary outcomes were PE-related mortality, haemodynamic collapse (or clinical deterioration) and the composite of PE-related mortality or collapse within 30 days from the diagnosis of PE. eTable 2 shows individual definitions of haemodynamic collapse for each of the cohorts.

Statistical analysis

To compare categorical variables, the analyses used chi-squared or Fisher's exact tests. Continuous data were tested for a normal distribution with the Kolmogorov–Smirnov test. Continuous data that did not follow a normal distribution were compared with the Mann–Whitney U test.

The regression coefficients from PROTECT were used to calculate risk scores separately in TELOS and Ramón y Cajal (eTable 3). We defined the following thresholds for the risk score: low (predicted all-cause death of less than 1%), intermediate–low (1–15%) and intermediate–high (more than 15%) [18, 19].

The performance of the SIMpLe score in the derivation and validation cohorts was assessed using the following parameters: 1) Brier score [20], with lower values indicate higher overall performance; 2) discrimination, using the area under the receiver operating characteristic curve; 3) calibration, by visual inspection and reporting the intercept and slope after plotting the predicted probability against the observed frequency in deciles of the predicted mortality [21]; and 4) prediction, with positive predictive values.

We performed several secondary analyses. First, subgroup analyses were carried out according to age (>65 years *versus* younger), sex (female *versus* male) and cancer (present *versus* absent). Second, we repeated all analyses for the secondary end-points. We evaluated the prognostic performance of a simplified version of the SIMpLe score, in which only one point is assigned to the presence of each variable. For the simplified score, we defined a threshold of ⩾5 points to identify intermediate–high-risk patients. We repeated the analyses after removal of the variable "concomitant proximal deep vein thrombosis" and replacement of echocardiographic RV dysfunction by CT-assessed RV enlargement in the score. Finally, we evaluated the prognostic performance of the SIMpLe score in the subgroup of patients with a positive simplified PE Severity Index (sPESI) score.

Comparisons were considered significant if the two-sided p-values were less than 0.05. We used Stata, version 16.0 for all analyses (StataCorp LLC).

Results

Characteristics of the cohorts

A total of 848 haemodynamically stable patients with acute PE were included in the PROTECT derivation cohort and 1702 (313 in TELOS and 1389 in the Ramón y Cajal cohorts) in the external validation cohorts (eFigure 1). The median age of participants ranged from 69 to 73 years, the mean baseline systolic blood pressure was 134 mmHg, the mean baseline heart rate was 94 bpm and more than two thirds had a positive sPESI score. Compared to patients in the PROTECT derivation sample, patients in TELOS were older and had a higher frequency of female gender. They more frequently had cancer, central PE, RV dysfunction and elevated levels of BNP, troponin and lactate; and less frequently chronic lung disease, recent surgery, chest pain or dyspnoea (table 1). Baseline characteristics were largely similar between the PROTECT cohort and the Ramón y Cajal registry, though the proportion of patients with recent surgery, previous venous thromboembolism, chronic lung disease, RV dysfunction and elevated biomarkers was higher in the derivation cohort (table 1).

TABLE 1 Baseline characteristics for normotensive patients with acute symptomatic pulmonary embolism (PE)

	PROTECT derivation n=848	TELOS external validation n=313	Ramón y Cajal external validation n=1389
Clinical characteristics, n (%)			
Age, years, median (25th–75th percentiles)	72 (59–80)	73 (66–82)	69 (59–81)
Age >80 years	184 (21.7)	97 (31.0)	361 (26.0)
Male gender	416 (49.0)	131 (41.9)	637 (45.9)
Risk factors for VTE, n (%)			
Cancer[#]	144 (17.0)	118 (37.7)	233 (16.8)
Recent surgery[¶]	89 (10.5)	13 (4.2)	108 (7.8)
Previous VTE	121 (14.3)	53 (16.9)	155 (11.2)
Immobilisation[+]	167 (19.7)	46 (14.7)	287 (20.7)
Comorbid diseases, n (%)			
COPD	108 (12.7)	18 (5.8)	105 (7.6)
Congestive heart failure	51 (6.0)	16 (5.1)	71 (5.1)
Clinical symptoms and signs at presentation, n (%)			
Syncope	128 (15.1)	32 (10.2)	222 (16.0)
Chest pain	410 (48.3)	48 (15.3)	656 (47.2)
Dyspnoea	680 (80.2)	171 (54.6)	1037 (74.7)
Heart rate ⩾110 bpm	176 (20.8)	67 (21.4)	339 (24.4)
Arterial oxyhaemoglobin saturation by pulse oximetry <90%	185 (21.8)	67 (21.4)	379 (27.3)
Systolic blood pressure <100 mm Hg	34 (4.0)	12 (3.8)	60 (4.3)
Simplified PESI			
Low-risk	313 (36.9)	79 (25.2)	431 (31.0)
High-risk	535 (63.1)	234 (74.8)	958 (69.0)
Clot burden			
Saddle PE or PE in the main pulmonary arteries	149 (17.6)	104 (33.2)	263 (18.9)
Concomitant proximal DVT	375 (44.2)	146 (46.6)	736 (53.0)
Echocardiography and biomarkers, n (%)			
RV dysfunction (echocardiogram)	192 (22.6)	122 (39.0)	223 (16.1)
Elevated BNP	380 (44.8)	204 (65.2)	361 (26.0)
Elevated cTnI	139 (16.4)	99 (31.6)	335 (24.1)
Elevated lactate	145 (17.1)	94 (30.0)	107 (7.7)
Treatment			
Insertion of an IVC filter	8 (0.9)	NA	40 (2.9)

BNP: brain natriuretic peptide; cTnI: cardiac troponin I; DVT: deep vein thrombosis; IVC: inferior vena cava; NA: not applicable; PESI: Pulmonary Embolism Severity Index; RV: right ventricle; VTE: venous thromboembolism. [#]: Active or under treatment in the last year. [¶]: In the previous month. [+]: Immobilised patients defined as nonsurgical patients with limited mobility (*i.e.*, total bed rest with bathroom privileges) for ⩾4 days in the month prior to PE diagnosis.

Outcomes

eTable 4 summarises the outcomes for study patients. Overall mortality was lower in the PROTECT derivation cohort than in both validation cohorts. Of 848 patients in the PROTECT derivation cohort, 38 (4.5%, 95% CI 3.1–5.9%) died during the 30-day follow-up. Mortality rates in the TELOS validation and Ramón y Cajal validation cohorts were 5.8% (n=18) and 7.0% (n=97), respectively (eTable 4). During follow-up, PE-related death occurred in 1.3%, 3.2% and 2.7% of patients in the PROTECT derivation, TELOS and Ramón y Cajal validation cohorts, respectively. The rates of haemodynamic collapse in the derivation cohort were 3.3% (n=28), while rates in the TELOS validation and Ramón y Cajal validation cohorts were 5.4% (n=17) and 7.1% (n=98), respectively (eTable 4).

Model derivation

Coefficients and odds ratios of the newly developed SIMpLe risk score are shown in table 2. The underlying formulas are presented in eTable 3. The predictive performance of the SIMpLe score in the derivation cohort was moderate. For the total population of 848 patients, the area under the curve for 30-day all-cause mortality was 0.693 (95% CI 0.604–0.781) and the Brier score was 0.042±0.180 (figure 1). Visual inspection of the calibration plot indicated that the score was generally well calibrated, with slopes closer to 1 and intercepts closer to 0 across all outcomes. Based on the SIMpLe risk score, patients were categorised as having low (n=0; 0%), intermediate–low (n=831; 98.0%) or intermediate–high (n=17; 2.0%)

TABLE 2 Prediction models for primary and secondary outcomes

Predictor	All-cause mortality		Haemodynamic collapse or PE-related mortality	
	Odds ratio (95% CI)	Chi^2 statistic	Odds ratio (95% CI)	Chi^2 statistic
Vital signs				
Systolic blood pressure <100 mmHg	1.37 (0.37–5.13)	0.32	1.46 (0.42–5.07)	0.38
Heart rate ⩾110 bpm	1.19 (0.55–2.57)	0.18	1.86 (0.90–3.82)	0.62
Oxygen saturation <90%	1.59 (0.76–3.32)	0.46	1.05 (0.49–2.26)	0.05
Imaging testing				
RV dysfunction	1.14 (0.51–2.54)	0.13	2.16 (1.00–4.65)	0.77
Concomitant DVT	1.79 (0.91–3.52)	0.58	2.70 (1.30–5.59)	0.99
Saddle PE or PE in the main pulmonary arteries	2.58 (0.70–9.50)	0.95	2.41 (0.76–7.60)	0.88
Laboratory tests				
Elevated troponin	1.03 (0.44–2.43)	0.03	2.16 (0.99–4.75)	0.77
Elevated BNP	2.19 (1.02–4.70)	0.79	1.65 (0.74–3.72)	0.50
Elevated lactate	1.08 (0.49–2.38)	0.08	1.85 (0.96–3.57)	0.61

BNP: brain natriuretic peptide; DVT: deep vein thrombosis; PE: pulmonary embolism; RV: right ventricle.

risk for 30-day all-cause mortality. Of 831 patients with intermediate–low risk according to the SIMpLe risk score, 34 (4.1%) died during the 30-day follow-up. Of 17 patients with intermediate–high risk according to the SIMpLe risk score, four (23.5%) died during the 30-day follow-up (eTable 5). For predicting all-cause mortality, the score (predicted probability 15%) had a positive predictive value of 23.5% (95% CI 7.8–50.2%), a specificity of 98.4% (95% CI 97.2–99.1%) and a positive likelihood ratio of 6.56 (95% CI 2.24–19.17) (table 3).

External validation cohorts

The predictive performance of the SIMpLe score in the external validation cohorts was moderate. For the TELOS and Ramón y Cajal cohorts, the area under the curve for 30-day all-cause mortality was 0.782 (95% CI 0.665–0.889) (Brier score: 0.050±0.179) and 0.710 (95% CI 0.656–0.763) (Brier score: 0.060 ±0.197), respectively (figure 1). For the external validation cohorts, the proportion of patients categorised as having low, intermediate–low or intermediate–high risk for 30-day all-cause mortality, and the death rates within each risk class are shown in eTable 5. In TELOS, the score (predicted probability 15%) had a positive predictive value of 26.7% (95% CI 13.0–46.2%), a specificity of 92.5% (95% CI 88.8–95.2%) and a positive likelihood ratio of 5.96 (95% CI 3.10–11.47) for the primary outcome (table 3). In the Ramón y Cajal registry, the score (predicted probability 15%) had a positive predictive value of 27.0% (95% CI 19.7–35.8%), a specificity of 92.9% (95% CI 91.3–94.2%) and a positive likelihood ratio of 4.92 (95% CI 3.52–6.88) for the primary outcome (table 3).

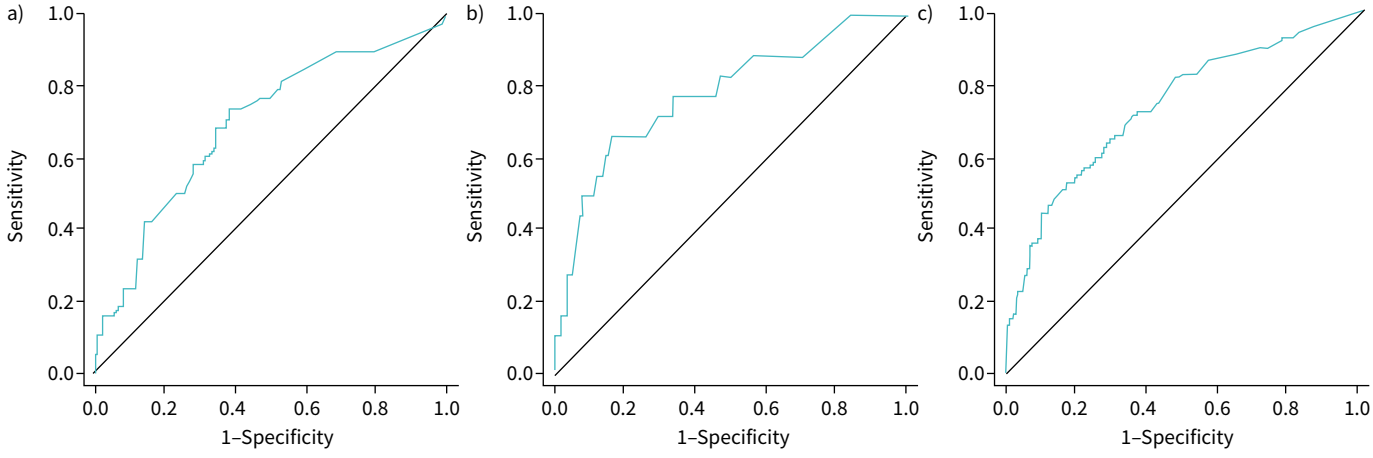

FIGURE 1 C-statistic for 30-day all-cause mortality. a) PROTECT cohort. b) TELOS cohort. c) Ramón y Cajal cohort.

TABLE 3 Test characteristics of the SIMpLe (vital Signs, IMaging testing, and Laboratory tests) score for predicting 30-day all-cause mortality in the derivation and validation cohorts

Parameter	PROTECT derivation	TELOS external validation	Ramón y Cajal external validation
Positive patients			
n/total	17/848	30/313	126/1389
% (95% CI)	2.0 (1.2–3.2)	9.6 (6.6–13.4)	9.1 (7.6–10.7)
Specificity[#]			
n/total	797/810	273/295	1200/1292
% (95% CI)	98.4 (97.2–99.1)	92.5 (88.8–95.2)	92.9 (91.3–94.2)
Positive predictive value[¶]			
n/total	4/17	8/30	34/126
% (95% CI)	23.5 (7.8–50.2)	26.7 (13.0–46.2)	27.0 (19.7–35.8)
Positive likelihood ratio[+]			
Value (95% CI)	6.56 (2.24–19.17)	5.96 (3.10–11.47)	4.92 (3.52–6.88)

[#]: Percentage of patients who correctly test negative over those who do not experience a complicated course. [¶]: Percentage of patients who experience a complicated course over those who test positive. [+]: Change in the odds of experiencing a complicated course in patients with a positive test.

Sensitivity analyses

The results were consistent in analyses of the pre-defined subgroups (eTable 6). The performance of the SIMpLe score for predicting secondary outcomes in the derivation and validation cohorts is shown in eTable 7. In the three cohorts (*i.e.*, PROTECT, TELOS and Ramón y Cajal), the score had positive predictive values for the composite of 30-day PE-related mortality or collapse above 20% (23.5% *versus* 26.7% *versus* 28.6%) (eTable 7).

For the development of a clinical prediction rule suitable for use in busy emergency departments, we evaluated the prognostic performance of a simplified version of the SIMpLe score, in which one point is assigned to the presence of each variable. For the simplified score, we defined a threshold of ⩾5 points to identify intermediate–high-risk patients. As the score increased, the proportion of patients designated as positive according to the score decreased, while the proportion of patients experiencing complications increased (figure 2). With a cutoff score ⩾5, the proportions of patients designated as positive were 8.5%, 22.7% and 7.3% in the PROTECT, TELOS and Ramón y Cajal cohorts, respectively. For predicting 30-day all-cause mortality, the SIMpLe score (score ⩾5) had positive predictive values of 11.1%, 14.1% and 22.6% in the PROTECT, TELOS and Ramón y Cajal cohorts, respectively (eTable 8). eTables 9 and 10 show positive predictive values for 30-day all-cause mortality across a range of point cutoffs with the simplified and the modified versions of the SIMpLe score, respectively. The results were consistent in analyses of the subgroup of patients with a positive sPESI (eTable 11).

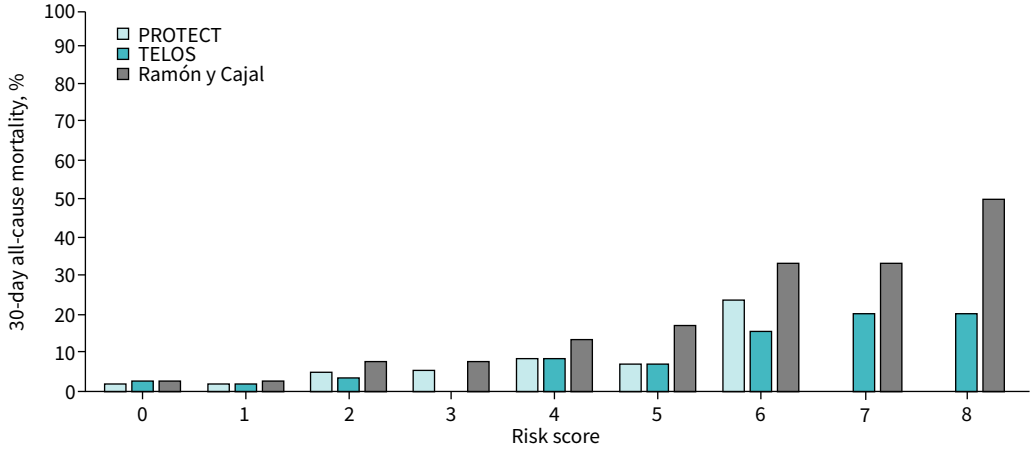

FIGURE 2 Proportion of patients with a 30-day outcome as a function of SIMpLe (vital Signs, IMaging testing and Laboratory tests) score.

Discussion

We used information from three large cohorts of normotensive patients with acute PE (PROTECT, TELOS and Ramón y Cajal) to develop and validate a SIMpLe risk score for short-term clinical deterioration and/or death. We found that the set of predictors developed in PROTECT (nine risk factors including higher heart rate, lower systolic blood pressure, lower oxyhaemoglobin saturation, saddle PE or PE in the main pulmonary arteries, echocardiographic RV dysfunction, concomitant DVT, as well as troponin, BNP and lactate elevation) also identified normotensive patients with acute PE in the TELOS and Ramón y Cajal cohorts with an increased probability of significant deterioration and/or death.

Previously published prediction models had important limitations that we sought to address, including complexity, combination of a small number of prognosticators and the use of fixed risk thresholds that may jeopardise clinical relevance [6–9, 22]. In the development of a clinical prediction rule suitable for use by PE response teams [23], we sought to include variables that should correlate independently with the prognosis of PE, be easily measurable and serve as a surrogate for other potentially important variables. We believe that the SIMpLe score is useful because it includes predictors (heart rate and systolic blood pressure) that express the clinical haemodynamic consequences of PE, two predictors that quantify RV stress/dysfunction (BNP and echocardiography), predictors that reflect hypoxia (oxygen saturation and lactate), one that captures myocardial injury (troponin) and two predictors (saddle PE or PE in the main pulmonary arteries and concomitant residual DVT) that reflect clot burden.

Surprisingly, the area under the receiver operating curve (ROC) of the SIMpLe score (0.74) did not outperform previous clinical prediction models, which achieved values ranging from 0.70 to 0.72 [24]. Nonetheless, ROC analysis explores the tradeoff between sensitivity and specificity. The overall positive predictive value and positive likelihood ratio of the SIMpLe score were higher than those reported for other scoring systems used to identify intermediate–high-risk patients with acute symptomatic PE [24, 25]. Therefore, the SIMpLe score could be considered accurate for identifying intermediate–high-risk patients with acute PE in real-world clinical situations.

Our study has important implications for patients with haemodynamically stable PE. Using readily available data, we identified several risk factors for deterioration short after initiation of anticoagulant therapy. These specific risk factors can be used to identify those patients who may possibly benefit from close monitoring and consideration for advanced treatments. In addition, the simplified version makes the SIMpLe score easier to calculate at bedside and more attractive for clinicians. Use of higher thresholds had a better positive predictive value than lower thresholds for identifying patients with an intermediate–high risk of complicated course after the diagnosis of PE. Therefore, clinicians might consider various thresholds when selecting recanalisation procedures with different risk of bleeding- and procedure-related complications (*e.g.*, systemic thrombolysis and percutaneous thrombectomy) [26, 27].

Some strengths of the present study included use of three large cohorts of normotensive patients with acute symptomatic PE, routine utilisation of standard anticoagulation alone (*i.e.*, no immediate reperfusion treatment of the PE) for every patient and evaluation of clinical (*i.e.*, not haemodynamic) outcomes. Some study methodology limitations affect the findings and interpretation of the study and future studies could further address these issues. First, the new model was not directly compared with other scores that might be used to identify patients with intermediate–high-risk PE [6–9]. Second, the new score was not developed to classify patients with PE into categories of increasing risk of mortality and should not be used to identify patients estimated to be at low risk who could be discharged early or managed entirely as outpatients. Third, though the score is simple to calculate and the variables are easy to remember, it requires an echocardiogram and lower limb ultrasound testing. Expert teams providing care for sick patients with acute PE should have ready access to these tests for fine-tuning risk stratification and this should not affect the simplicity of the score. Even if those tests are not readily available, our results suggest that clinicians can still use an eight-item (*i.e.*, without lower limb ultrasound) score and replace echocardiographic RV dysfunction by CTPA-assessed RV enlargement in SIMpLe to identify patients with an increased probability of significant deterioration and/or death. Finally, the use of predictors as continuous variables could have been a more accurate approach. However, from a clinician's point of view, the relevant question is when a test is "normal" *versus* abnormal in order to determine which patients are at low risk and which are at elevated risk. This is why in the present study we validated (and confirmed) the prognostic relevance of predefined cutoff values for continuous predictors.

In summary, we validated a simple risk score for identification of severe normotensive PE. This model should help clinicians weigh the risks and benefits of reperfusion therapies and will allow for enrichment of prospective studies and trials designed to treat PE.

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