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Enhancing Pulmonary Embolism Risk Stratification: The National Early Warning Score and its Integration into the European Society of Cardiology Classification

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Abstract

Background Pulmonary embolism (PE) requires accurate risk assessment. We investigated the prognostic performance of the National Early Warning Score (NEWS) in emergency department patients with PE.

Methods We included patients $\geq$ 18 years from our PE registry (2017 to 2021), excluding patients after cardiac arrest or intubation before admission. The primary outcome was a composite of 30-day all-cause mortality or the need for advanced therapy (i.e., systemic or catheter-directed thrombolysis). We used logistic regression and the Cox proportional hazards models to estimate associations. The Pulmonary Embolism Severity Index (PESI) and the European Society of Cardiology (ESC) classification served as covariates. The overall score performances were quantified using receiver operating characteristic analysis.

Results We included 524 patients. Each increase in NEWS points increased the odds of the primary outcome by 69% (odds ratio: 1.69, 95% confidence interval [CI]: 1.51–1.89, $p < 0.001$) and 30-day mortality by 44% (hazard ratio: 1.44, 95% CI: 1.30–1.60, $p < 0.001$). Within the ESC intermediate–high and high-risk group, the 30-day mortality rate was higher in patients with a NEWS $\geq$ 7 compared with NEWS $<$ 7 (24 vs. 1%, $p < 0.001$). With a NEWS $\geq$ 7, 30-day mortality was lower in patients who received advanced therapy (18 vs. 39%) but not significantly. The NEWS predicted the primary outcome better than the PESI (area under the curve: 0.853 vs. 0.752, $p < 0.001$).

Conclusion The NEWS was associated with 30-day mortality and the need for advanced therapy. Incorporating the NEWS into the ESC classification could help to assess patient outcomes early and thus support timely treatment decisions.

Keywords
- pulmonary embolism
- risk assessment
- mortality
- emergency medicine
- thrombolytic therapy

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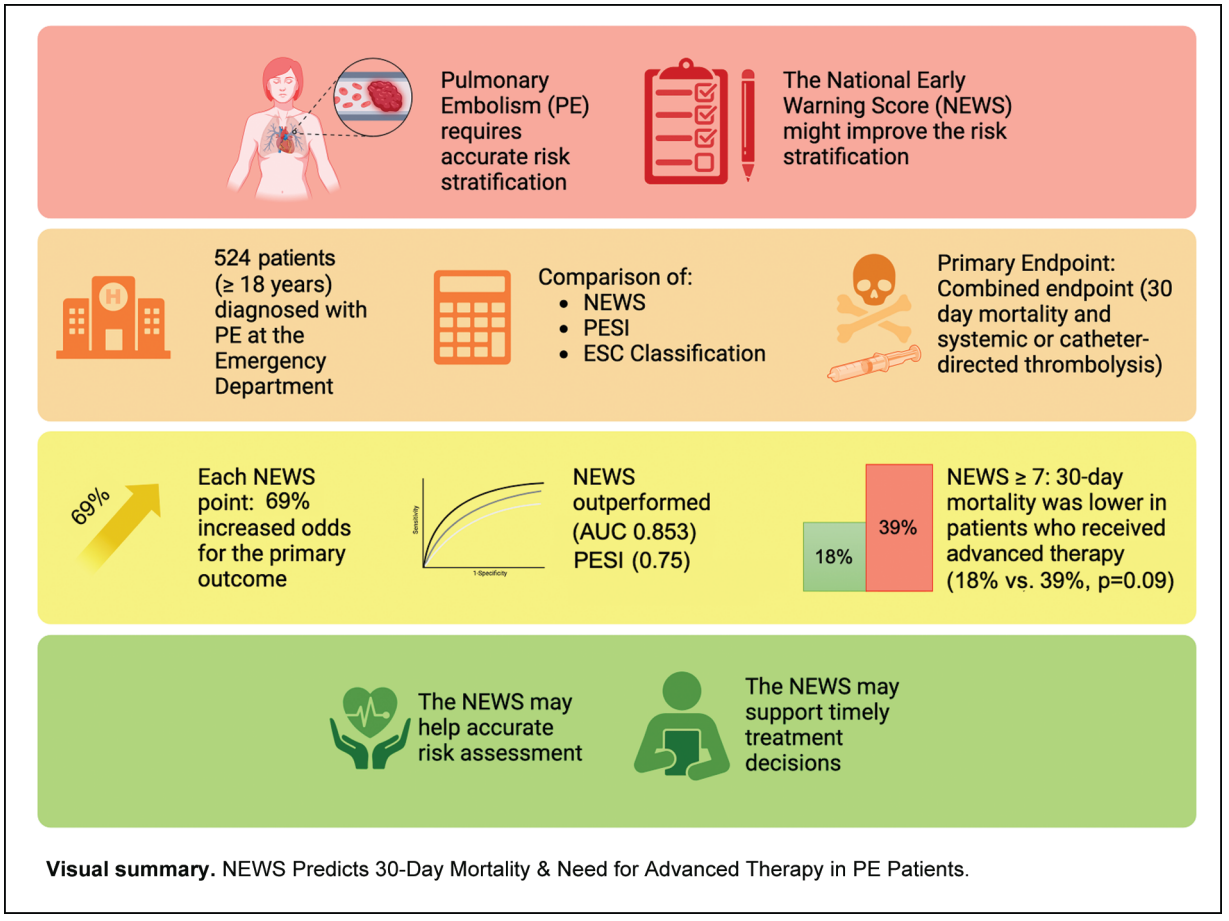

Visual summary. NEWS Predicts 30-Day Mortality & Need for Advanced Therapy in PE Patients.

Introduction

Pulmonary embolism (PE) is one of the most common cardiovascular diseases. The prognosis at the time of presentation is decisive for clinical treatment. While hemodynamic status at the time of the acute event is the most reliable predictor of the short-term outcome, the long-term outcome is mainly determined by age and underlying diseases, such as cancer.

According to Keller et al, approximately 9.0% of PE patients are in shock or require cardiopulmonary resuscitation. It is generally accepted that hemodynamically unstable patients require immediate reperfusion therapy. However, it has been reported that this is not always the case, and only a minority of these patients receive advanced treatment (i.e., systemic thrombolysis).[1]

The majority of patients with PE present with stable hemodynamics. Accurately identifying those who require hospitalization and advanced therapy is crucial. Current practice follows the European Society of Cardiology (ESC) guidelines and the proposed risk stratification integrating the Pulmonary Embolism Severity Index (PESI).[2] However, whether this risk score allows for optimal patient management is controversial.

We aimed to evaluate the National Early Warning Score (NEWS) as an alternative or adjunct to the PESI and ESC risk stratification. The NEWS is based on a simple clinical assessment[3–5] and was primarily developed to identify deteriorating patients in the hospital or emergency department (ED) at an early stage.[6] Several studies reported that NEWS allows early identification of patients with severe sepsis and septic shock at triage[7] and prediction of disease severity and 90-day survival in patients with acute dyspnea.[8] A post hoc analysis of the YEARS study[9] found that the NEWS adequately predicted 7-day intensive care unit (ICU) admission and 30-day mortality in hemodynamically stable patients with confirmed PE.[5]

In this study, we aimed to evaluate the performance of the NEWS in predicting a composite outcome of 30-day all-cause mortality or the need for advanced therapy (e.g., systemic- or catheter-directed thrombolysis [CDT]) in patients with PE in an ED and to compare it with the PESI and ESC classification.

Methods

Setting

The setting for this study was the Vienna General Hospital at the Medical University of Vienna, a 2,200-bed tertiary care center. The Department of Emergency Medicine treats around 80,000 patients annually, including 100 to 150 patients with PE. The department has its own intensive care unit, intermediate care unit, and outpatient ward.

Study Design and Study Population

The study data were retrieved from a prospectively compiled PE registry that was approved by the local ethics committee. This registry includes all patients ≥ 18 years of age who have

been treated in our department for confirmed PE. We included all cases from January 2017 to December 2021. Patients who required intubation or cardiopulmonary resuscitation before admission were excluded.

Risk Classification

We used three prognostic scores: the NEWS,[10] the PESI,[11] and the ESC classification.[2] The patient's vital signs were assessed on arrival at the ED. The NEWS uses seven variables to determine the likelihood of a patient's condition deteriorating, with each variable being assigned a score from 0 to 3 points. The total score, which ranges from 0 to 20, indicates the degree of risk, with a higher score indicating a greater likelihood of deterioration.[10] We differentiated three NEWS risk groups—low risk (0–4 points), medium risk (5–6 points), and high risk ($\geq$7 points). The PESI comprises 11 variables for classifying patients with confirmed PE according to their mortality risk. Class I indicates a very low 30-day mortality risk (0–1.6%) and class IV has a very high mortality risk (10.0–24.5%).[11] We also categorized patients, according to the ESC, into low, intermediate–low, intermediate–high, and high mortality risk.[2]

Outcomes

The primary outcome was a composite of all-cause 30-day mortality or need for advanced therapy, defined as systemic thrombolysis or CDT, using the EkoSonic Endovascular System.[12] Secondary outcomes included the all-cause mortality rate within 7 and 30 days and subgroup analysis for the ESC intermediate-risk group and cancer patients. For troponin measurements, we used the Cobas E602-Module ECLIA (Roche Diagnostics GmbH, Mannheim, Germany) with a reference level of 0 to 14 ng/L and a coefficient of variation of 5.7%.

Statistical Methods

We calculated the mean, standard deviation or median, and interquartile range (IQR) for continuous variables and absolute and relative frequencies for categorical variables. Univariate differences between groups were assessed with the Mann–Whitney U test or the chi-square test, as appropriate.

We used logistic regression analysis to estimate the association between the scores (NEWS, PESI, and ESC), the combined endpoint, 7-day mortality, 30-day mortality, and advanced therapy. We used a Cox proportional hazards model to assess the effects of the scores on 7- and 30-day mortality. Using the likelihood ratio test, we tested for deviation from linearity and modeled the scores as linear predictors where appropriate. We included other scores into the model simultaneously as covariates to adjust the estimates onto each other. We used the Wald test to test the H_0: Regression Coefficient = 0. The discrimination was evaluated using receiver operating characteristic (ROC) analysis, and the results were presented as the area under the curve (AUC).

No imputation for missing data was performed. All analyses were performed using the R statistical software environment (R Foundation for Statistical Computing, Vienna, Austria, http://www.R-project.org, version 3.6.2) and GraphPad Prism (version 9.4.0). We considered a two-sided p-value < 0.05 statistically significant.

Results

Baseline Characteristics

We screened 576 cases of patients with PE between 2017 and 2021. After excluding 48 patients due to cardiopulmonary resuscitation and four intubated patients on arrival, 524 patients remained (►**Table 1**). The mean age of the patients was 62 years (standard deviation: 16), and 49% ($n = 254$) were female.

Table 1 Baseline characteristics

	Patients diagnosed with acute PE ($n = 524$)
Age in years, mean (SD)	62.2 (16)
Female, *n* (%)	254 (49)
Pregnancy, *n* (%)	2 (0.4)
Smoking, *n* (%)	167 (32)
Vital parameters	
Alert, *n* (%)	518 (98.9)
Respiratory rate, mean (SD)	14 (4)
Heartrate in bmp, mean (SD)	97 (21)
Systolic blood pressure in mm Hg, mean (SD)	138 (24)
Peripheral oxygen saturation in percentage, mean (SD)	94 (5.3)
Temperature in °C, mean (SD)	36.7 (0.8)
Pulmonary embolism	
Central pulmonary embolism, *n* (%)	240 (46)
D-Dimer[a] in µg/mL, mean (SD)	10.4 (32.6)
Troponin[b] in ng/L, mean (SD)	55 (97)
Right ventricular strain, *n* (%)	225 (43)
Oxygen supplementation, *n* (%)	121 (23)
Comorbidities, *n* (%)	
Hypertension	236 (45)
Venous thromboembolism	167 (32)
Chronic Heart Disease	67 (13)
Cancer as part of medical history	154 (29)
Chronic pulmonary disease	55 (11)
Heart failure	49 (9)
ESC classification	
Low	171 (32.6)
Intermediate–low	154 (29.4)
Intermediate–high	182 (34.7)
High	17 (3.2)

Abbreviations: ESC, European Society of Cardiology; PE, pulmonary embolism; SD, standard deviation.
[a]$n = 440$.
[b]$n = 445$.

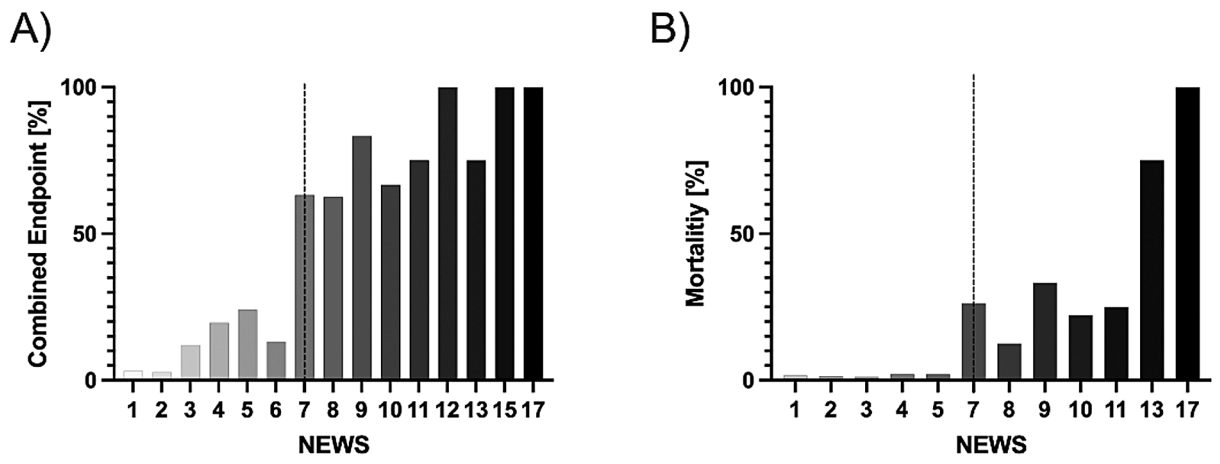

Fig. 1 Relative frequency of combined endpoint (**A**) and the 30-day mortality rate (**B**) grouped by NEWS. The dotted line in A and B marks the cutoff for a high NEWS (i.e., ≥7). If no patients scored within a NEWS category, the category was omitted on the *x*-axis. NEWS, National Early Warning Score; Combined endpoint, all-cause 30-day mortality, systemic thrombolysis, or use of the catheter-directed thrombolysis.

The primary outcome was present in 79 (15%) patients. Twenty-one (4%) patients died within the first 30 days, and 13 of them (62%) died within the first 7 days. ►**Fig. 1** shows the relative frequency of the combined endpoint and the 30-day mortality rate grouped by NEWS. Systemic thrombolysis was applied in 32 (6%) patients, and CDT was performed in 31 (6%) cases.

The NEWS was significantly higher in patients who reached the primary outcome than the other patients (median: 6, IQR: 4–9 vs. median: 2, IQR: 1–4, $p < 0.001$). The same was true for the PESI (median: 117, IQR: 98–143 vs. median: 85, IQR 68-107, $p < 0.001$). The NEWS distribution in our population and the median NEWS and primary outcome rates categorized by the ESC classification can be found in the ►**Supplementary Fig. S1** (available in the online version only).

Patients who died within 30 days showed a significantly higher NEWS (median: 7, IQR: 5–10 vs. 2, IQR: 1–4, $p < 0.001$) and PESI (median: 147, IQR: 121–173 vs. 88, IQR: 69–110, $p < 0.001$). The 30-day mortality was significantly higher in patients with a history of cancer compared with those without cancer (7.8 vs. 2.4%, $p = 0.004$).

Primary Outcome

The NEWS showed a significant association with the primary outcome (crude NEWS odds ratio [OR]: 1.69, 95% confidence interval [CI]: 1.51–1.89, $p < 0.001$). It was independent of the PESI (NEWS adjusted OR: 1.61, 95% CI: 1.42–1.83, $p < 0.001$; PESI adjusted OR: 1.006, 95% CI: 0.998–1.02, $p < 0.001$).

Furthermore, the association was independent of D-dimer, lactate and troponin levels ($n = 319$, NEWS adjusted OR: 1.49, 95% CI: 1.26–1.76, $p < 0.001$, ►**Supplementary Table S1**, available in the online version only).

We calculated the regression analysis for patients in the intermediate-risk group according to the ESC classification ($n = 335$) as a sensitivity analysis. The NEWS showed a significant association with the combined endpoint (crude NEWS OR: 1.48, 95% CI: 1.31–1.67, $p < 0.001$).

Mortality

The NEWS was able to predict 30-day all-cause mortality (crude NEWS hazard ratio [HR]: 1.44, 95% CI: 1.30–1.60, $p < 0.001$), independent from the PESI (NEWS HR: 1.23, 95% CI: 1.10–1.37, $p < 0.001$, PESI HR: 1.03, 95% CI: 1.01–1.04, $p < 0.001$). Furthermore, it did so independently from D-dimer, lactate and troponin (adjusted NEWS HR: 1.46, 95% CI: 1.21–1.75, $p < 0.001$, ►**Supplementary Table S2**, available in the online version only).

We calculated the Cox regression analysis for patients in the intermediate group according to the ESC classification ($n = 335$) as a sensitivity analysis. The NEWS predicted 30-day mortality alone (crude NEWS HR: 1.35, 95% CI: 1.17–1.57, $p < 0.001$).

The NEWS also predicted mortality within the first seven days (crude HR: 1.47, 95% CI: 1.31–1.66, $p < 0.001$). It did so independently from the PESI (NEWS adjusted HR: 1.23, 95% CI: 1.07–1.40, $p = 0.003$, ►**Supplementary Table S3**, available in the online version only) and independently from D-dimer, lactate and troponin (NEWS adjusted HR: 1.50, 95% CI: 1.11–1.78, $p = 0.005$ ►**Supplementary Table S4**, available in the online version only).

Advanced Therapy

The NEWS showed a significant association with the administration of advanced therapies (crude NEWS OR: 1.50, 95% CI: 1.35–1.65, $p < 0.001$). It was independent of the PESI (NEWS adjusted OR: 1.52, 95% CI: 1.35–1.71, $p < 0.001$, ►**Supplementary Table S5**, available in the online version only). Furthermore, the NEWS was significantly associated with CDT (crude NEWS OR: 1.35, 95% CI: 1.22–1.50, $p < 0.001$) and systemic thrombolysis (crude NEWS OR: 1.37, 95% CI: 1.24–1.52, $p < 0.001$).

Receiver Operating Characteristic Analysis

Receiver Operating Characteristic Combined Endpoint

The AUC for the prediction of the combined endpoint was 0.853 (95% CI: 0.809–0.897) for the NEWS and 0.752 (95% CI:

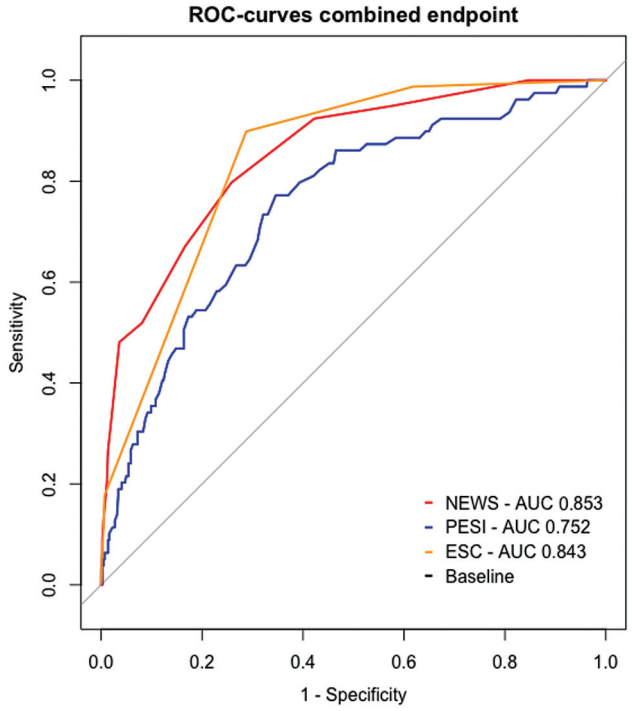

Fig. 2 The AUC for predicting the combined endpoint (i.e., all-cause 30-day mortality or the need for advanced therapy, which was defined as systemic thrombolysis or the use of the catheter-directed thrombolysis) for NEWS, PESI, and ESC scoring in the overall patient population ($n = 524$). AUC, area under the curve; NEWS, National Early Warning Score; PESI, Pulmonary Embolism Severity Index.

0.694–0.810) for the PESI, with a statistically significant difference ($p < 0.001$, ►**Fig. 2**). The AUC for the ESC classification was 0.843 (95% CI: 0.808–0.878). When the NEWS was added as covariable to the ESC classification in the binary logistic regression model, the AUC improved significantly (AUC: 0.894, 95% CI: 0.862–0.926, $p < 0.001$). In the intermediate-risk group, according to the ESC guidelines, the AUC for the NEWS was 0.764 (95% CI: 0.701–0.827), and 0.657 (95% CI: 0.584–0.731) for the PESI. The AUC for the NEWS was significantly higher than the AUC for the PESI ($p = 0.006$).

Receiver Operating Characteristic Mortality

In the ROC analysis, the NEWS showed an AUC of 0.840 (95% CI: 0.736–0.943) when predicting 30-day mortality (►**Supplementary Fig. S2**, available in the online version only) and an AUC of 0.908 (95% CI: 0.827–0.989) when predicting 7-day mortality. The AUC for the PESI predicting 30-day mortality did not differ significantly (AUC: 0.896, 95% CI: 0.844–0.937, compared with NEWS: $p = 0.108$). The AUC for the ESC risk stratification was 0.736 (95% CI: 0.632–0.839). When the NEWS was added as a covariable to the ESC risk stratification in the Cox regression model, the AUC improved significantly (AUC: 0.845, 95% CI: 0.748–0.943, $p = 0.046$). When analyzing the prediction of mortality in the intermediate-risk group according to the ESC guidelines, the AUC for the NEWS was 0.730 (95% CI: 0.564–0.895) and 0.841 (95% CI: 0.757–0.925) for the PESI with a statistically significant difference ($p = 0.040$). The ROC analysis for the 7-day mortality can be found in the ►**Supplementary Fig. S3** (available in the online version only).

Clinical Prediction

►**Supplementary Table S6** and ►**Supplementary Fig. S4** (available in the online version only) show the predicted and observed values for the 30-day mortality. In patients with a high NEWS (i.e., NEWS $\geq$ 7, $n = 54$), the rate of advanced therapy was 52% ($n = 28$). In those patients undergoing advanced therapy ($n = 28$), the 30-day all-cause mortality rate was 18% compared with 39% in patients who did not undergo advanced therapy (►**Fig. 3A**). This difference was not statistically significant ($p = 0.091$). Patients who scored a high PESI ($n = 169$) showed a 22% ($n = 37$) rate for advanced therapy. There was no difference in the mortality rate, regardless of the use of advanced therapy ($n = 37$, 30-day mortality rate 13.5%) or not ($n = 132$, 30-day mortality rate 9.8%, $p = 0.523$, ►**Fig. 3B**).

►**Table 2** shows the CDT, systemic thrombolysis, advanced therapy, 30-day all-cause mortality, 7-day mortality rates, and combined endpoint rates grouped by the ESC classification and NEWS categories. In patients who scored high in the NEWS and ESC score ($n = 16$), the 30-day

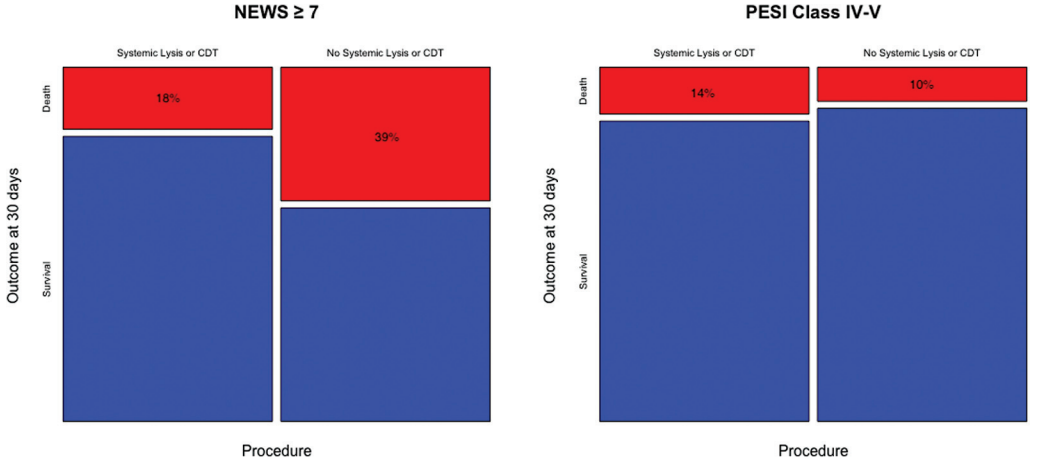

Fig. 3 (**A**) Outcome at 30 days in patients with a NEWS $\geq$ 7 (**A**) or a PESI $\geq$ 106 (**B**). (**B**) Outcome at 30 days in patients with a NEWS $\geq$ 7 (**A**) or a PESI $\geq$ 106 (**B**). CDT, catheter-directed thrombolysis; PESI, Pulmonary Embolism Severity Index; NEWS, National Early Warning Score.

Table 2 Catheter-directed thrombolysis, systemic lysis, advanced therapy, 30-day and 7-day mortality in patients with ESC low, intermediate–low, intermediate–high, high, and NEWS low, intermediate, high absolute numbers and percentages

CDT		ESC				
		Low	**Int–Low**	**Int–High**	**High**	
NEWS	Low	0/164 (0%)	1/137 (1%)	10/96 (10%)	0/0 (0%)	11/397 (3%)
	Intermediate	0/6 (0%)	0/14 (0%)	7/52 (13%)	0/1 (0%)	7/73 (10%)
	High	0/1 (0%)	0/3 (0%)	7/34 (21%)	6/16 (38%)	13/54 (24%)
		0/171 (0%)	1/154 (0.6%)	24/ 182 (13%)	6/17 (35%)	
Systemic lysis		**ESC**				
		Low	**Int–Low**	**Int–High**	**High**	
NEWS	Low	0/164 (0%)	0/137 (0%)	10/96 (10%)	0/0 (0%)	10/397 (3%)
	Intermediate	0/6 (0%)	0/14 (0%)	7/52 (13%)	0/1 (0%)	7/73 (10%)
	High	0/1 (0%)	0/3 (0%)	10/34 (29%)	5/16 (31%)	15/54 (28%)
		0/171 (0%)	0/154 (0%)	27/182 (15%)	5/17 (29%)	
Advanced therapy		**ESC**				
		Low	**Int–Low**	**Int–High**	**High**	
NEWS	Low	0/164 (0%)	1/137 (1%)	20/96 (21%)	0/0 (0%)	21/397 (5%)
	Intermediate	0/6 (0%)	0/14 (0%)	14/52 (27%)	0/1 (0%)	14/73 (19%)
	High	0/1 (0%)	0/3 (0%)	17/34 (50%)	11/16 (69%)	28/54 (52%)
		0/171 (0%)	1/154 (0.6%)	51/182 (28%)	11/17 (65%)	
30-d mortality		**ESC**				
		Low	**Int–low**	**Int–high**	**High**	
NEWS	Low	0/164 (0%)	3/137 (2%)	2/96 (2%)	0/0 (0%)	5/397 (1%)
	Intermediate	0/6 (0%)	1/14 (7%)	0/52 (0%)	0/1 (0%)	1/73 (1%)
	High	1/1 (100%)	2/3 (67%)	6/34 (18%)	6/16 (38%)	15/54 (28%)
		1/171 (0.6%)	6/154 (4%)	8/182 (4%)	6/17 (35%)	
7-d mortality		**ESC**				
		Low	**Int–Low**	**Int–High**	**High**	
NEWS	Low	0/164 (0%)	0/137 (0%)	1/96 (1%)	0/0 (0%)	1/397 (0.3%)
	Intermediate	0/6 (0%)	1/14 (7%)	0/52 (0%)	0/1 (0%)	1/73 (1%)
	High	1/1 (100%)	1/3 (33%)	4/34 (12%)	5/16 (31%)	11/54 (20%)
		1/171 (0.6%)	2/154 (1%)	5/182 (3%)	5/17 (29%)	
Combined endpoint		**ESC**				
		Low	**Int–Low**	**Int–High**	**High**	
NEWS	Low	0/164 (0%)	4/137 (3%)	22/96 (23%)	0/0 (0%)	26/397 (7%)
	Intermediate	0/6 (0%)	1/14 (7%)	14/52 (27%)	0/1 (0%)	15/73 (21%)
	High	1/1 (100%)	2/3 (67%)	21/34 (62%)	14/16 (88%)	38/54 (70%)
		1/171 (0.6%)	7/154 (5%)	57/182 (31%)	14/17 (82%)	

Abbreviations: CDT, Catheter-directed thrombolysis; ESC, European Society of Cardiology; NEWS, National Early Warning Score; int–low, intermediate–low risk; int–high, intermediate–high risk.

mortality rate was 38% ($n = 6$). When both scores were low ($n = 164$), the 30-day mortality rate was 0%. Patients with a NEWS score < 7 ($n = 470$) showed a low 30-day mortality rate with an average of 1.3% and a maximum of 7% (one out of 14 patients), regardless of the ESC risk category. Patients with NEWS ≥ 7 ($n = 53$) showed a significantly higher 30-day mortality rate with an average of 27.8% ($p < 0.001$), with a range of 18 to 100% (one out of one patient). In the ESC intermediate–high and high-risk group ($n = 199$), patients with a NEWS ≥ 7 had a 30-day mortality rate of 24%, and

patients with NEWS < 7 had a mortality rate of 1% ($p < 0.001$). Of note, the two patients who died within the ESC intermediate–high-risk group and low NEWS group were 103 and 92 years old. Interestingly, the 30-day mortality rate in the ESC intermediate–low-risk group was 67% (2 out of 3 patients) when the NEWS was ≥ 7.

The performance metrics of the NEWS for 30-day mortality (sensitivity, specificity, negative predictive value [NPV], positive predictive value [PPV]) can be found in ►**Supplementary Table S7**, ►**Supplementary Fig. S5** (available in the online version only). A NEWS of 5 is the threshold with a balanced sensitivity and specificity (sensitivity: 0.762, specificity: 0.779, PPV: 0.126, NPV: 0.987). A NEWS of 3 is the threshold for high sensitivity (sensitivity: 0.857, specificity: 0.517, PPV: 0.069, NPV: 0.989). NPV decreases slightly as cutoffs increase but remains consistently high (>0.96) even at high cutoffs. A NEWS of 7 as a cutoff represents a good trade-off between specificity and maintaining a high NPV (sensitivity = 0.714, Specificity = 0.922, PPV: 0.278, NPV = 0.987). A cutoff of 13 also achieves a good PPV while maintaining high specificity and reasonable sensitivity compared with very high cutoffs (specificity: 0.996, sensitivity: 0.190, PPV: 0.667, NPV: 0.967). However, only six patients in our dataset show a NEWS ≥ 13. A NEWS ≥ 11 was present in 12 patients. This cutoff balances higher sensitivity while maintaining acceptable PPV (specificity = 0.986, sensitivity = 0.238, PPV = 0.417, NPV = 0.969). The 30-day mortality rate was 42%.

Discussion

In the present study, we investigated the prognostic performance of the NEWS in patients diagnosed with PE in the ED. We found that the NEWS can predict the composite endpoint of 30-day all-cause mortality and the need for advanced therapy (i.e., systemic thrombolysis or CDT). Although the observed reduction in 30-day all-cause mortality among patients with a high NEWS (i.e., ≥ 7) who received advanced therapy is noteworthy (18 vs. 39%), it should be interpreted with caution due to the lack of statistical significance and the study's observational nature. The NEWS predicted the composite endpoint better than the PESI.

Our findings are consistent with recent studies on adult PE patients in the ED, showing that the NEWS on admission can reliably predict adverse outcomes, regardless of age and comorbidities.[13–16] These outcomes included the need for ICU admission and mortality.[17] In contrast, we used a combined outcome encompassing not only all-cause 30-day mortality but also the requirement for advanced therapy, such as systemic thrombolysis or CDT (i.e., EkoSonic Endovascular System). The NEWS demonstrated independent predictive ability for the combined outcome, irrespective of the PESI and biomarkers, including troponin, D-dimer, and lactate. Troponin showed a crude significant association with the primary endpoint (OR: 1.005, 95% CI: 1.002–1.007, $p = 0.001$). However, when controlling for confounding variables, troponin levels did not show a significant association. This finding may be attributed to the time delay in troponin elevation. Previous studies have shown that cardiac troponin levels have limited specificity and PPV for early mortality in normotensive patients with PE. Still, they exhibit a high NPV in this context.[18]

A 10-year cross-sectional study conducted by Bumroongkit et al in Southeast Asia with 696 patients showed that the NEWS can predict 30-day all-cause mortality.[19] Similarly, in their study of 352 hemodynamically stable patients with confirmed PE, Bavalia et al found that the NEWS could adequately predict 7-day ICU admission and 30-day mortality.[5] Consistent with these findings, our study corroborates the predictive value of the NEWS. We observed that the NEWS independently predicted all-cause 30-day mortality and 7-day mortality, with an AUC of 0.840 (95% CI: 0.736–0.943) for 30-day mortality prediction, comparable to the AUC reported in previous studies.[5] The Cox regression showed a 30-day mortality increase of 44% (HR: 1.44, 95% CI: 1.30–1.60, $p < 0.001$) for each NEWS point. Although the NEWS was judged to be an unreliable predictor of mortality beyond 24 hours when used in all ED patients,[14] our results support the utility of the NEWS as a predictor of 30-day mortality in patients with PE.

Determining an optimal threshold for the NEWS in PE patients remains challenging and has yet to be definitively answered. Different studies have proposed various thresholds for 30-day mortality prediction, with some suggesting a threshold of ≥ 3 points[5] and others suggesting a threshold of ≥ 9.[19] In our dataset, we observed that patients with a high NEWS (i.e., NEWS ≥ 7, $n = 54$) exhibited higher 30-day mortality (18% and above, with an average of 28%) than those with a NEWS < 7 (average of 1.3% and a maximum of 7%), regardless of the ESC classification. In patients with a NEWS ≥ 7 and an ESC high-risk classification ($n = 16$), the 30-day mortality rate was 38% ($n = 6$). In our data, a cutoff value of 7 showed an NPV of 98.7% while remaining acceptable values for sensitivity (71.4%) and specificity (92%). When both scores were low (i.e., NEWS 0–4 and ESC low-risk classification, $n = 164$), the 30-day mortality rate was 0%. Of note, the 30-day mortality rate in the intermediate–low-risk ESC group was 67% when the NEWS was ≥ 7, which may warrant closer monitoring for potential worsening of the condition in these patients. In addition, patients in the ESC intermediate–high-risk group also showed a higher 30-day mortality rate when the NEWS was ≥ 7 (18 vs. 1.4%).

Regarding therapeutic decisions, patients with a NEWS ≥ 7 might benefit from advanced therapy. The 30-day all-cause mortality rate in these patients was 39% in patients without advanced treatment compared with 18% in patients who received advanced therapy. Although not statistically significant and certain limitations may be considered (e.g., in patients with hemodynamical instability that is most likely not caused by a PE, such as a subsegmental PE), future investigations might be worthwhile.

Mortality of acute PE depends on the performance of the right ventricle, which in turn is determined by the extent of embolized clots and the cardiopulmonary reserve of the patient.[20] The clinical picture ranges from sudden death before arrival to the hospital to an incidental finding in an asymptomatic patient.[21] The ESC working group defined four stages of severity according to the hemodynamic situation, the performance of the right ventricle, and the vitals and risk factors of a patient assessed by the PESI. It is evident that a hemodynamically unstable patient needs more aggressive treatment, and those without any compromise might be managed in an outpatient setting. Between these extremes, optimal management is still under discussion. Especially in patients with intermediate–high-risk, according to the ESC guidelines, a prediction tool is warranted to identify patients with the highest risk to decide whether advanced treatment could prevent deterioration or not.[22] Our results show that the NEWS is also a reliable predictor in the intermediate-risk group. It could predict the combined endpoint and the 30-day mortality or advanced therapy. We observed that the 30-day mortality was low in the ESC intermediate–high-risk group (8 out of 182 patients, 4%), but when the category was divided by the NEWS, we found a mortality rate of up to 18% (6/34), when the NEWS was $\geq$7. This might be one possible clinical use for the NEWS to select at-risk patients in this ESC group.

Cancer patients with acute PE represent a unique group that requires distinct treatment strategies due to the increased risk of recurrence and the management considerations for incidental PE. Studies have emphasized the importance of managing incidental PE in the same manner as symptomatic cases in this patient population.[23,24] Our study found that the NEWS demonstrated good predictive ability in predicting the combined outcome also in cancer patients with acute PE.

Incorporating the NEWS into risk stratification and management protocols may aid health care professionals in identifying individuals who could benefit from closer monitoring or more intensive interventions.

Utilizing the NEWS offers several advantages in predicting outcomes without needing detailed patient history. This simplifies the prognostic assessment process, relying instead on a straightforward clinical evaluation and vital sign measurements. Our study results support the notion that the NEWS can provide valuable guidance for determining the need for advanced therapy, surpassing the sole reliance on blood pressure and lactate levels, as we found that the 30-day mortality increased with a NEWS $\geq$ 7, regardless of the ESC classification. In patients with NEWS $\geq$ 7, the 30-day mortality rate was 28% (15 out of 54 patients), whereas the 30-day mortality rate was 1% in patients with NEWS $<$ 7 (6 out of 470 patients). In the case of a NEWS $\geq$ 7, most patients (50 out of 54, 93%) scored within the ESC intermediate–high or high-risk. This could help identify patients at increased risk earlier without waiting for the echocardiography or laboratory assessment and could be used at the triage level. A high NEWS could identify patients who will deteriorate despite normal blood pressure in patients within the ESC intermediate–high-risk group. Furthermore, those in the intermediate–high-risk group with a high NEWS should be evaluated as candidates for advanced therapy, considering their high 30-day mortality rate. Although we observed a spike in 30-day morality in the ESC intermediate–low-risk and NEWS high group (67%), conclusions should be drawn cautiously because of the low patient number (two out of three patients died).

Adding the NEWS to the ESC classification significantly improved the combined endpoint and 30-day mortality prediction. The simplicity of the NEWS empowers nurses to seek senior medical assistance promptly and facilitates smoother patient referrals, reducing potential conflicts.[25] Additionally, monitoring the NEWS over time enables health care providers to track patients' progress or deterioration, prompting timely clinical reviews and appropriate escalation of care.[26] Notably, the NEWS has undergone extensive validation and is widely recognized as the most well-validated early warning score in clinical practice.[16]

The study has several limitations. This was an observational study, and confounding cannot be ruled out. The single-center design limits the generalizability of our findings. The mortality rate was low (although comparable to previous studies), which may affect the accuracy of the estimates. Given the low mortality rate, predictive values should be interpreted with caution. Given the retrospective nature of this study, the reasons for the complex decision for treatment (including the use of systemic thrombolysis or CDT) are challenging to obtain and were at the treating physician's discretion. Even though the analysis of mortality reveals similar results to those of the combined endpoint, an interaction between advanced therapy and mortality cannot be ruled out. To address a potentially harmful overuse of advanced therapy within the ESC intermediate–high-risk group, eight patients died within the first 30 days. One patient received CDT and one patient received systemic thrombolysis. Both patients died from a fulminant recurrent embolic event. This study was conducted before the introduction of aspiration thrombectomy at our center, which became available in early 2022. As a result, this technique was not considered in the treatment options. Admission to the intensive care unit could not be used as an outcome measure, as our department has its own intensive care unit.

Conclusion

The study results suggest that the NEWS may be useful in predicting unfavorable outcomes (30-day mortality or advanced therapy) in patients with PE admitted to the ED. Incorporating the NEWS into the ESC risk classification could support early and timely treatment decisions. Further research should focus on testing the NEWS in different subgroups of

patients with PE and investigating the impact of NEWS-based risk stratification on clinical treatment strategies.

What is known about this topic?

- Pulmonary embolism (PE) is a serious condition requiring accurate risk stratification to guide treatment decisions.
- The National Early Warning Score (NEWS) assesses the severity of various conditions, but its specific prognostic value in PE patients has been less well-studied.
- The Pulmonary Embolism Severity Index (PESI) and the ESC classification are established tools for assessing PE risk, but their predictive power has limitations.

What does this paper add?

- This study demonstrates that NEWS outperforms PESI and ESC classification in predicting 30-day mortality and the need for advanced therapy (i.e., systemic or catheter-directed thrombolysis) in PE patients.
- The study provides evidence that a higher NEWS is associated with significantly increased odds of adverse outcomes, supporting its use in PE management.
- Integrating NEWS into the ESC classification could improve early risk assessment and help guide timely treatment decisions for patients with PE.

Data Availability Statement

The article's data will be shared at a reasonable request by the corresponding author.

Authors' Contribution

K.J.: Conceptualization, data collection and supervision, writing—original draft preparation; A.J.L.: literature review, data collection, data validation; A.M.: data collection, data validation, manuscript review; M.M.: data collection, data validation, manuscript review; U.A.: clinical expertise, literature review, manuscript review; H.H.: methodology refinement, statistical analysis, data interpretation, manuscript review; M.S.: project supervision, data interpretation, critical evaluation, manuscript editing; J.G.: conceptualization, statistical analysis, data interpretation, manuscript writing—review and editing.

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Conflict of Interest

None declared.

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