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Full Length Article

Risk stratifying emergency department patients with acute pulmonary embolism: Does the simplified Pulmonary Embolism Severity Index perform as well as the original?

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ABSTRACT

Introduction: The Pulmonary Embolism Severity Index (PESI) is a validated prognostic score to estimate the 30-day mortality of emergency department (ED) patients with acute pulmonary embolism (PE). A simplified version (sPESI) was derived but has not been as well studied in the U.S. We sought to validate both indices in a community hospital setting in the U.S. and compare their performance in predicting 30-day all-cause mortality and classification of cases into low-risk and higher-risk categories.

Materials and methods: This retrospective cohort study included adults with acute objectively confirmed PE from 1/2013 to 4/2015 across 21 community EDs. We evaluated the misclassification rate of the sPESI compared with the PESI. We assessed accuracy of both indices with regard to 30-day mortality.

Results: Among 3006 cases of acute PE, the 30-day all-cause mortality rate was 4.4%. The sPESI performed as well as the PESI in identifying low-risk patients: both had similar sensitivities, negative predictive values, and negative likelihood ratios. The sPESI, however, classified a smaller proportion of patients as low risk than the PESI (27.5% vs. 41.0%), but with similar low-risk mortality rates (<1%). Compared with the PESI, the sPESI overclassified 443 low-risk patients (14.7%) as higher risk, yet their 30-day mortality was 0.7%. The sPESI underclassified 100 higher-risk patients (3.3%) as low risk who also had a low mortality rate (1.0%).

Conclusions: Both indices identified patients with PE who were at low risk for 30-day mortality. The sPESI, however, misclassified a significant number of low-mortality patients as higher risk, which could lead to unnecessary hospitalizations.

Abbreviations: PE, pulmonary embolism; PESI, Pulmonary Embolism Severity Index; sPESI, simplified Pulmonary Embolism Severity Index; ED, emergency department; MAPLE, management of acute pulmonary embolism; KP, Kaiser Permanente; ICD, International Classification of Disease; CPT®, Current Procedural Terminology; VTE, venous thromboembolism; DVT, deep venous thrombosis.

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1. Introduction

Pulmonary embolism (PE) is the third most common cause of death from cardiovascular disease after heart attack and stroke and places a large burden on society and the healthcare system [1]. Depending on the size and location of the PE and the patient's underlying cardiopulmonary reserve, the clinical presentation can register anywhere across the spectrum of severity, ranging from mild symptoms with normal vital signs on the one hand to life-threatening hemodynamic instability on the other [2].

Given the historically high case fatality rate, most emergency department (ED) patients with acute PE have been hospitalized for at least several days to initiate anti-coagulation and demonstrate sufficient cardiopulmonary stability prior to discharge home. Growing evidence, however, suggests that a sizeable proportion of ED patients with acute PE are at exceedingly low risk for short-term clinical deterioration and may be safely discharged home directly from the ED [3–5].

Several risk stratification instruments have been developed to assist physicians in identifying patients who are eligible for outpatient care [6,7]. Few instruments have been used in randomized trials to safely select ED patients for outpatient care [8,9]. Of these, the PE Severity Index (PESI) is the most extensively studied and widely validated [10]. The PESI is comprised of 11 weighted clinical variables and stratifies patients into 5 risk classes, each higher class associated with an ascending incidence of 30-day all-cause mortality [11].

Because PESI can be difficult to calculate at the bedside, a simplified version (sPESI) was derived [12]. It contains 6 unweighted variables and dichotomizes patients into low- and higher-risk classes. Although validated in many countries, the sPESI has not been well studied in large contemporary U.S. populations [13–15].

Both the European Society of Cardiology and the American College of Chest Physicians recommend using either the PESI or the sPESI to help identify low-risk patients who may be eligible for outpatient management [16–18]. Although both indices may be safely employed for this purpose, they may not be entirely interchangeable [13,19–22]. Some studies suggest that the sPESI identifies a lower proportion of truly low-mortality patients as low risk [13,21], although this finding has not been replicated in a more contemporary multicenter U.S. community setting. Moreover, the implications of sPESI's risk classification for site-of-care decision making have not been well explored and may result in overly conservative recommendations for inpatient care. We undertook this study in order to evaluate the performance of both the PESI and the sPESI in a large U.S. integrated delivery system and to assess the misclassification rate of sPESI when compared to the PESI.

2. Methods

2.1. Study design and setting

This retrospective cohort study, the Management of Acute Pulmonary Embolism (MAPLE) Study, was conducted in 21 community medical centers across Kaiser Permanente (KP) Northern California, an integrated healthcare delivery system that provides comprehensive medical care for >3.9 million health plan members with over 1.2 million annual ED visits [23]. In 2014, the 21 medical centers had inpatient bed capacities ranging from 50 to 325, and each had an intensive care unit. KP members represent approximately 33% of the insured population in areas served and are highly representative of the surrounding population [24,25]. KP Northern California uses a comprehensive integrated electronic health record (Epic, Verona, Wisconsin) in which inpatient- and outpatient-level clinical data are electronically accessible within hierarchical databases [26,27]. The study was approved by the Kaiser Foundation Research Institute's Northern California Institutional Review Board.

No standardized clinical care pathway for the management of patients with acute PE was in place during the study period; treatment was at the discretion of treating board-certified physicians. Patients diagnosed with acute PE in the outpatient clinic setting were referred to the ED for definitive care. Physicians discharging patients with PE from the ED or inpatient units commonly employed a standard computerized discharge order set for venous thromboembolism, which at the time recommended warfarin with bridging therapy using enoxaparin. Direct, or "novel," oral anticoagulants were rarely prescribed during the study period. Outpatient warfarin dosing was managed by each facility's pharmacy-led anticoagulation service. The percent time in therapeutic range for the international normalized ratio during the study period varied by facility and ranged from 69% to 74%, calculated with a 6-month look-back period using the Rosendaal linear interpolation method [28]. Follow-up for patients with PE discharged home directly from the ED or after a short observational stay was usually arranged within seven days [29].

2.2. Study population

2.2.1. Cohort assembly via database query

The study included all patients ≥18 years of age with acute objectively confirmed PE with at least one eligible ED visit throughout the study period. We assembled the cohort by first electronically identifying adults with an ED or inpatient discharge diagnosis (primary or not) of non-gravid PE (*International Classification of Disease, Ninth Edition* [ICD-9], codes: 415.11, 415.13, 415.19, 673.20, 673.21, 673.22, 673.24) from January 2013 through April 2015 who underwent a venous thromboembolism imaging study (Current Procedural Terminology [CPT®] codes: spiral computed tomography [71275, 71260, and 71270], pulmonary angiogram [75743 and 75746], a ventilation-perfusion lung scan [78579, 78580, 78582, 78584–78588, 78591, 78593, and 78594], a magnetic resonance angiogram [71555], or a venous duplex Doppler/compression ultrasound [93970 and 93971]) in the ED or in the 12 h prior to registration. The 12-h window allowed for the inclusion of cases in which a positive outpatient diagnostic imaging test precipitated a referral to the ED for definitive care. We electronically excluded cases with an earlier ED or inpatient PE diagnosis with associated venous thromboembolism imaging (listed above) in the 30 days prior to their index ED encounter. We also electronically excluded cases lacking an ED PE diagnosis whose inpatient PE diagnosis was neither primary nor present on admission (after manual validation of ineligibility of a cohort of 50 cases). Cases with acute PE who did not have sustained health plan membership for at least 30 days following their index ED visit were also excluded to ensure complete 30-day outcomes.

2.2.2. Diagnostic confirmation via manual chart review

We manually reviewed the electronic health records of all cases for the presence of acute objectively confirmed PE. Diagnostic confirmation was based on the final interpretation by a board-certified radiologist (or nuclear medicine physician, as indicated). This required a new contrast-filling defect on spiral computed tomography or pulmonary angiography, or a new high-probability ventilation-perfusion lung scan. The diagnosis of PE was also confirmed in patients with a compression ultrasound positive for proximal deep vein thrombosis with concurrent pulmonary symptoms suggestive of acute PE, as other outpatient PE research studies have done [8,30,31]. Cases were manually excluded from the cohort if the patient was known to be pregnant, had received a diagnosis of acute venous thromboembolism in the prior 30 days, was designated in the ED to receive only comfort care, was transferred outside the system, or left the ED against medical advice. Fig. 1 depicts the cohort assembly.

2.3. Data collection and definitions

All chart abstractors were practicing emergency physicians, who received standardized training on data collection methods and use of the electronic data collection instrument, which was modified to its final

form after pilot testing. The principal investigator (DRV) answered and arbitrated all coding questions and monitored data collection activities by reviewing each abstractor's performance at ten regular intervals throughout the abstraction period. Abstractors were blind to the sPESI score and to the nature of this study's analysis.

We adopted our definitions of the variables of the original PESI from the initial derivation and validation study by Aujesky et al. (Table 1) [11]. The derivation study included the most abnormal vital sign value in the direction in question on the day of presentation. For our calculation we used the most abnormal vital sign documented in the ED record to simulate the data available to the treating physician at the time of disposition. Our retrospective calculation of the PESI score at the time of ED disposition followed a two-step process described elsewhere [32]. Briefly, we electronically pre-populated the computerized data collection tool with the 11 variables of the PESI extracted from structured data from the electronic health record. The physician abstractors then confirmed or corrected the data using information in the electronic health record available to the treating physicians at the time of the index ED assessment. To do this, abstractors expanded the scope of source data to include unstructured values documented in the records of the emergency physician and consulting hospitalist (if present), including abnormal vital signs and mental status findings from the index ED encounter as well as any immediate pre-arrival assessments, particularly emergency medical services and outpatient clinic visits. We did not review the original pre-arrival records. If a pre-arrival abnormal finding was not documented in the emergency or admitting records, it was not included in the data set. As in the derivation study, missing ED vital signs were assumed to be normal [11]. The definition of the sPESI was adopted from Jimenez et al. [12]. Low-risk classification is defined in the PESI as ≤85 points (Classes I and II) and in the sPESI as 0 points (Table 1).

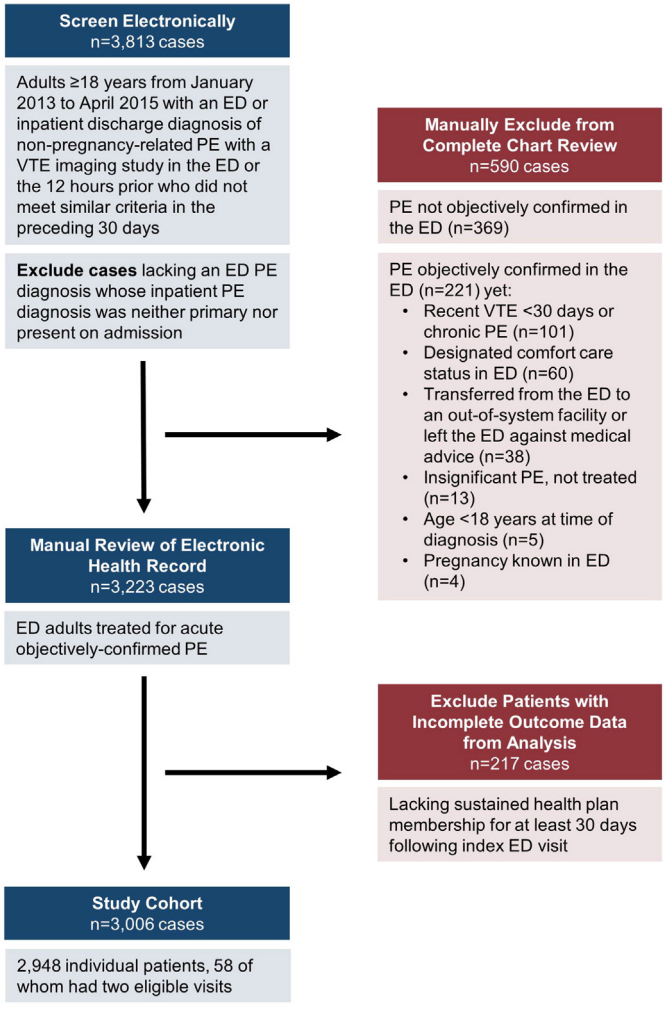

Fig. 1. Cohort assembly for the Management of Acute Pulmonary Embolism (MAPLE) study.

Table 1
Original and simplified Pulmonary Embolism Severity Indices.

Predictors	Pulmonary Embolism Severity Index	
	Original score[a]	Simplified score[b]
Demographic characteristics		
Age	+1 per year	
Age >80 years	–	+1
Male sex	+10	–
Comorbid Illnesses		
Cancer (active or history of)	+30	+1
Heart failure (systolic or diastolic)	+10	+1[c]
Chronic lung disease (includes asthma)	+10	
Clinical findings[d]		
Pulse ≥110/min beats per min	+20	+1
Systolic blood pressure <100 mmHg	+30	+1
Respiratory rate ≥30 breaths per min	+20	–
Temperature <36 °C	+20	–
Altered mental status[e]	+60	–
Arterial oxygen saturation <90%[f]	+20	+1

[a] A total point score for a given patient is obtained by summing the patient's age in years and the points for each applicable prognostic variable. Point scores correspond with the following classes that estimate escalating risks of 30-day mortality: ≤65 Class I; 66–85 Class II; 86–105 Class III; 106–125 Class IV; >125 Class V. Patients with 85 points or less (Classes I and II) are considered low risk.
[b] A total point score for a given patient is obtained by summing the points for each applicable prognostic variable. Patients with 0 points are considered low risk.
[c] The two variables were combined into a single category of chronic cardiopulmonary disease, that is, a patient is awarded one point for having either heart failure or chronic lung disease.
[d] The most abnormal vital signs in the direction of interest from the emergency department record are used.
[e] Acute or pre-existing disorientation, lethargy, stupor, or coma.
[f] With or without supplemental oxygenation.

We defined massive PE by the presence of sustained hypotension, that is, a systolic blood pressure <90 mmHg on at least two measurements 15 or more minutes apart [16,18,33]. The patients who remained after excluding those with massive PE constituted our normotensive subgroup.

Non-PESI variables also manually abstracted from the electronic health record included coronary artery disease and cerebrovascular disease. We queried the health plan's administrative and clinical databases for the following additional variables: race/ethnicity, body mass index, prior venous thromboembolism, chronic severe renal failure, active smoking, Charlson Comorbidity Index score [34], and mode of ED arrival.

The primary study outcome was 30-day all-cause mortality, which we used to determine the performance metrics of each index. Thirty-day major hemorrhage and recurrent venous thromboembolism were secondary outcomes [3,8,35]. Major hemorrhage was defined in keeping with the International Society on Thrombosis and Haemostasis as bleeding at high-risk anatomic locations (intracranial, intraspinal, intraocular, retroperitoneal, intra-articular, pericardial, or intramuscular with compartment syndrome), or overt bleeding with either a reduction of hemoglobin ≥2 g/dL or a transfusion of two or more units of packed red blood cells [36]. Recurrent venous thromboembolism was defined as a new or expanded abnormality on imaging in a symptomatic patient. Deaths were identified using a healthcare system mortality database that links to the Social Security death master file and the California State Department of Vital Statistics to identify both in-system and out-of-system deaths. We also identified claims for out-of-system medical encounters in order to improve capture of all heath care visits related to our 30-day outcomes.

We used the PESI as the comparative standard of risk classification. The rate of sPESI misclassification was calculated in both

directions: PESI low-risk patients classified as higher risk by the sPESI were considered overclassified and PESI higher-risk patients classified as low risk by the sPESI were considered underclassified. We determined the 30-day all-cause mortality rates of these two groups of misclassified patients to assess how well the terms underclassified and overclassified correlate with mortality outcomes.

A second reviewer independently collected specified variables on a randomly selected subset of 90 cases in order to measure interrater reliability via kappa statistic and percent agreement. Variables included the PESI risk class (low vs higher) and the three 30-day adverse outcomes: all-cause mortality, major hemorrhage, and recurrent venous thromboembolism.

2.4. Statistical analysis

We compared the proportions of patients classified as low versus higher risk between the PESI and sPESI and estimated 30-day all-cause mortality within each risk group. To assess accuracy of both indices to predict mortality, we calculated sensitivity, specificity, predictive values, and likelihood ratios for low-risk versus higher-risk patients. We also compared the indices' discriminative power by calculating the area under the receiver operating characteristic curve. We used a Kaplan–Meier survival curve for both indices to present time to death. We also compared rates of secondary outcomes between the indices, stratified by risk class. We report the agreement between PESI and sPESI in determining the dichotomous outcome of low risk vs higher risk using the kappa statistic.

We undertook two sensitivity analyses: one included only the first visits and the other included only the normotensive subgroup. All findings from both analyses were consistent with the results from our larger study cohort. All analyses were conducted using SAS statistical software, version 9.31 (SAS, Cary, North Carolina), and Stata, version 11.0 (StataCorp LP, College Station, Texas).

3. Results

Throughout the 28-month study period, 3813 patient encounters were electronically screened for eligibility, and 590 of these (15.5%) were manually excluded as ineligible (Fig. 1). Of the remaining 3223 patients, 217 non-health plan members (6.7%) were excluded for incomplete 30-day outcome data. The remaining 3006 cases were eligible for this study and constitute the study cohort. This includes 2948 individual patients, 58 of whom (2.0%) had two separate eligible episodes of acute PE during the study period.

We describe the clinical characteristics of our cohort in Table 2.

The number of missing ED vital signs were as follows: temperature, $n = 61$ (2.0%); respiratory rate, $n = 7$ (0.2%); systolic blood pressure, $n = 1$ (0.03%); oxygen saturation, $n = 1$ (0.03%); pulse, $n = 0$.

3.1. Risk classification and mortality outcomes

The rates of low-risk cases for the PESI and sPESI were 41.0% and 27.5%, respectively. The rates of higher-risk cases for the PESI and sPESI were 59.0% and 72.5%, respectively. We report class-specific 30-day adverse events in Table 3.

We report the time to death in Figs. 2 and 3, stratifying patients using the PESI and the sPESI, respectively.

The sPESI was as accurate as the PESI in predicting 30-day mortality: both indices had similar sensitivities, negative predictive values, and negative likelihood ratios (Table 4). Because both indices were designed to identify low-risk patients (i.e., to rule out short-term mortality), the specificity, positive predictive value, and positive likelihood ratio were expectedly low [13]. The specificity of the PESI, although relatively low, exceeded that of the sPESI (40.6% vs 28.8%). The discriminatory power of the PESI, as measured by the area under the receiver operating characteristic curve, was greater than its simplified counterpart, a finding consistent with other studies [13]. The slight difference in the positive likelihood ratios between the indices is clinically inconsequential.

Table 2
Clinical characteristics of emergency department cases with acute objectively confirmed pulmonary embolism.

	***N* = 3006 cases**	
Patient characteristics	**No**	%
Demographics		
Age median, years (IQR)	66	23 (54–77)
Sex male	1489	49.5
Race/ethnicity		
White	2149	71.5
African American	386	12.8
Hispanic or Latino	292	9.7
Asian or Pacific Islanders	137	4.6
Other	42	1.4
Comorbidities		
Body mass index (kg/m^2)		
Mean; median (IQR)	31.0; 29.2 (9.6)	
>30 (obesity)	1363	45.3
>40 (morbid obesity)	391	13.1
Cancer (active or history of)	872	29.0
Chronic lung disease	817	27.2
Prior venous thromboembolism	494	16.4
Coronary artery disease	436	14.5
Heart failure	304	10.1
Cerebrovascular disease	237	7.9
Smoking	178	5.9
Chronic severe renal failure	70	2.3
Charlson Comorbidity Index score		
Mean (SD)	1.9	2.4
Median	1.0	
No measure (no visits in prior year)	66	2.2
0	1190	39.6
1	575	19.1
≥2	1241	41.3
Mode of emergency department arrival		
Private vehicle	2361	78.5
Ambulance	645	21.5
Vital signs[a]		
Systolic blood pressure (mm Hg)		
≥90 and <100	327	10.9
<90 (at least one reading)	156	5.2
<90 over ≥15 min[b]	27	0.9
Pulse (beats/min)		
≥100 and <110	491	16.3
≥110	901	30.0
Respiratory rate (breaths/min)		
≥24 and <30	817	27.2
≥30	285	9.5
Oxygen saturation (%)		
<94 and ≥90	616	20.5
<90	523	17.4
Altered mental status[c]	155	5.2
Diagnostic imaging		
Spiral computed tomography (CT) alone	2096	69.7
Spiral CT and venous duplex Doppler/ compression ultrasound (US)	664	22.1
Ventilation-perfusion lung scan alone	95	3.2
Venous duplex Doppler/compression US alone	83	2.8
Ventilation-perfusion lung scan and venous duplex Doppler/compression US	57	1.9
Both spiral CT and ventilation-perfusion lung scan(with or without venous duplex Doppler/compression US)	11	0.4
Magnetic resonance angiogram	0	0.0
Pulmonary angiogram	0	0.0

[a] The most abnormal vital signs in the direction of interest from the emergency department record are used.
[b] Sustained hypotension used to define massive pulmonary embolism.
[c] Altered mental status = acute or chronic disorientation, lethargy, stupor, and coma.

3.2. Misclassification by the sPESI

The sPESI classified a substantially lower proportion of patients as low risk than the PESI (27.5%, 95% confidence interval [CI]: 26.0%–29.1% vs. 41.0%, 95% CI: 39.2%–42.7%), but with similarly low mortality rates (0.1%, 95% CI: 0.0%–0.7% vs. 0.5%, 95% CI: 0.2%–1.1%). Using the PESI as the comparative standard, the sPESI misclassified 543 patients (18.1%): 443 low-risk patients (14.7%) were overclassified as higher-risk and 100 higher-risk patients (3.3%) were underclassified as low risk. The agreement between the two PE Severity Indices was fair (unweighted kappa 0.60). The risk classification rates and their respective 30-day all-cause mortality outcomes are reported in Table 5.

3.3. Risk classification and secondary outcomes

Regarding the secondary outcomes, the low-risk classes of both indices were associated with a low incidence (<2%) of major hemorrhage and recurrent venous thromboembolism (Table 3). The incidences of symptomatic recurrent DVT and PE were low for patients whatever their PESI or sPESI risk class, but this was not the case for major hemorrhage. The incidence of major hemorrhage divided along the risk classes of the PESI: low-risk PESI patients had a significantly lower incidence of major hemorrhage than their higher risk counterparts: 1.4% (95% CI, 0.8%–2.2%) vs 4.1% (95% CI, 3.2%–5.1%) (Table 3). The risk categories of the sPESI (low vs higher) did not distinguish as clearly two different rates of major hemorrhage.

3.4. Interrater reliability

The kappa values for interrater reliability by two independent abstractors ranged from 0.85 to 1.00 for the nine clinical variables of the PESI, as defined in Table 1. The kappa for the abstractor's PESI risk class (low vs higher) was 0.99. The kappas for the abstractor's three 30-day adverse outcomes ranged from 0.66 to 1.00 and percent agreement ranged from 97.8% to 100%, median 100% (IQR = 98.9% to 100%).

4. Discussion

In this retrospective cohort study, we found that both the PESI and the sPESI performed well in identifying a population of patients at low risk for 30-day adverse outcomes. The classification of low risk by both indices was associated with an incidence of 30-day recurrent venous thromboembolism and major hemorrhage <2% and an incidence of 30-day all-cause mortality <1%. The performance metrics of the two indices were similar: both had high sensitivities (>97%), high negative predictive values (>99%), and low negative likelihood ratios, although the PESI had slightly greater discriminatory power. Overall, our results strongly support the recommendations of the European Society of Cardiology and the American College of Chest Physicians: either prognostic tool could be safely employed to guide site-of-care decision making [16–18].

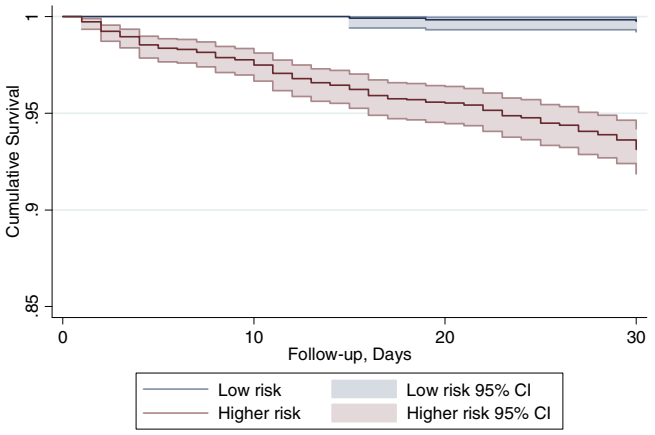

Fig. 2. Kaplan–Meier survival estimates for 30-day all-cause mortality stratified by risk using the original Pulmonary Embolism Severity Index.

The PESI and the sPESI differed, however, in their distribution of patients into low- and higher-risk categories, placing over 18% of patients in different binary risk groups. Using the PESI as the comparative standard, the sPESI overclassified 15% of patients and underclassified 3% of patients. The PESI low-risk patients who were overclassified by the sPESI as higher risk did not in fact carry a higher mortality risk. They had a 30-day all-cause mortality <1% (Table 5), thus confirming the designation of overclassification.

The PESI higher-risk patients who were underclassified by the sPESI as low risk also had a 30-day all-cause mortality of 1%. According to our definition above (Section 2.3), these patients were "underclassified," yet the designation does not correlate with 30-day all-cause mortality. This misclassification, although affecting few patients (3% of the study cohort), may actually be an improvement in classification. Higher-risk PESI patients who meet sPESI criteria for low-risk classification have similar outcomes to PESI low-risk patients.

Overall, the sPESI classified a lower net proportion of patients as low risk compared with the PESI: 27.5% vs 41.0%. Other studies have found similar disparities in the proportion of patients assigned to the low-risk group [13–15,21], now validated in this study among a large contemporary U.S. population. This difference could have implications for resource allocations if the sPESI were used to guide ED disposition decisions in which patients categorized as low risk were deemed eligible for outpatient management and higher-risk patients were admitted for inpatient care. For every 100 ED patients with an objectively confirmed diagnosis of acute PE, the sPESI would assign 15 "PESI low-risk/low-mortality" patients to inpatient care and 3 "PESI higher-risk/low-mortality" patients to home care consideration. We found that both of these re-assigned groups had low 30-day mortality rates

Table 3
Class-specific 30-day adverse events using both the original and the simplified Pulmonary Embolism Severity Indices.

Severity index			All-cause mortality			Major hemorrhage			Recurrent VTE		
	N	%	No.	%	95% CI	No.	%	95% CI	No.	%	95% CI
Full cohort	3006	100.0	132	4.4	3.7–5.2	91[a]	3.0	2.4–3.7	21[b]	0.7	0.4–1.1
PESI											
Low risk[c]	1171	41.0	3	0.3	0.1–0.8	16	1.4	0.8–2.2	11	0.9	0.5–1.7
Higher risk	1835	59.0	129	7.0	5.9–8.3	75	4.1	3.2–5.1	10	0.5	0.3–1.0
sPESI											
Low risk[c]	828	27.5	1	0.1	0.0–0.7	15	1.8	1.0–3.0	8	1.0	0.4–1.9
Higher risk	2178	72.5	131	6.0	5.1–7.1	76	3.5	2.8–4.4	13	0.6	0.3–1.0

PESI, Pulmonary Embolism Severity Index; sPESI, simplified PESI; CI, confidence interval; VTE, venous thromboembolism.
[a] Six of the major hemorrhages were fatal, leaving 85 non-fatal major hemorrhages.
[b] Two of these recurrent pulmonary emboli were fatal, leaving 19 non-fatal recurrent events.
[c] Low risk: PESI ≤85 points (Classes I and II); sPESI, 0 points (Table 1).

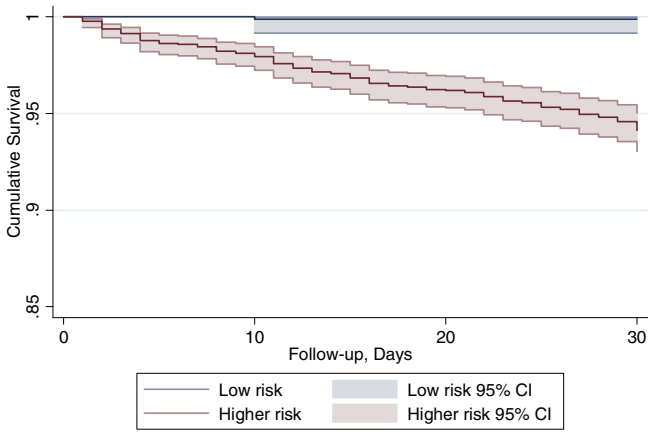

Fig. 3. Kaplan–Meier survival estimates for 30-day all-cause mortality stratified by risk using the simplified Pulmonary Embolism Severity Index.

(approximately 1%). Although reliance on the sPESI classification scheme might misallocate resources, it does not seem to pose a safety risk.

The PESI and sPESI were initially derived and validated in order to be applied to the full spectrum of outpatients with acute PE, regardless of systolic blood pressure [11,12]. This is why researchers on the comparative performance of the indices have not restricted their analyses to subgroups based on blood pressure measurements [13]. The European Cardiology Society guideline on pulmonary embolism, however, recommends that these two indices be used to risk stratify normotensive patients, not those with sustained hypotensive since the latter are a distinctly high-risk group requiring unique management considerations [16]. None of the hypotensive patients in our cohort, however, was misclassified as low risk by either index. Nevertheless, to replicate the clinical situation envisioned in the European guideline, we undertook a sensitivity analysis in the normotensive subgroup comparing the performance metrics of the indices and the sPESI misclassification rates. Our subgroup results reflect those we obtained in the entire cohort: the relative performance of the two indices was unchanged as was the sPESI's penchant to overclassification.

Given our findings that the patients deemed “low risk” by either index have a similarly low 30-day all-cause mortality rate, one could expand the pool of outpatient-eligible patients by using the PESI and sPESI in concert. Patients designated low risk by either index could be combined into one larger low-mortality cohort. Adding the “PESI higher-risk yet sPESI low-risk” patients to our “PESI low risk” group would have enlarged the low-risk population from 41.0% to 44.3%. This larger group of patients had a 30-day all-cause mortality rate of 0.3%.

In terms of matching a low-risk classification with a low-mortality outcome, the sPESI underperformed in comparison with the original PESI. The sPESI was designed to provide an alternative to the PESI that was easier to calculate and therefore easier to use [12]. However, in today's increasingly computerized world, clinicians do not need to rely on their faulty memories to accurately remember prognostic tools. For those with access to the internet, free electronic calculators like MDCalc (MD Aware, LLC, San Francisco, CA), which includes the PESI, are just one click away. Although obviating the need to remember the many prognostic variables of the PESI and their respective weight-based point scores, a web-based calculator nonetheless requires the clinician to enter the patient's data, which is a procedure susceptible to human error. In our healthcare system, we have sought to make the process easier still by designing a web-based electronic PESI that draws real-time patient-specific data from the electronic health record and presents it to the provider in the context of a clinical decision support system. The auto-populating of data helps reduce human error. We found this auto-populating PESI to be highly accurate [32] and have recently implemented it in the ED to aid in site-of-care decision making [37,38]. As healthcare systems improve their integration of patient-specific predictive analytics into the electronic health record, arguments that one prognostic tool is superior to another simply because it is easier to remember or to calculate may become obsolete [39]. Likewise, future studies deriving clinical decision rules need not be guided by the principle of structural simplicity [40].

This study is subject to the limitations inherent in retrospective cohort studies, although we tried to temper this by following recommended principles for chart review studies [41,42]. Moreover, some of these shortcomings are mitigated by the comprehensive inpatient-outpatient electronic health record used in the study setting, our complete capture of outcomes among patients who were all members of an integrated delivery system, and the study's high interrater reliability. In our discussion of the variables influencing physician site-of-care decisions for ED patients with acute PE, we include only 30-day adverse outcomes; other PE factors (like evidence of right ventricular strain), comorbidities, and social variables bear on the disposition decision [35] but are not included in this study. Also, we did not characterize the size or location of the emboli. Although the study was conducted in 21 community hospitals, the results we found reflect the study population and treatment they received and may not be generalizable to other locations and practice settings. For example, our study patients were heavier than those in large European registries, but lighter than those in other multicenter U.S. registries [43,44].

In conclusion, the results of this study serve to validate the PESI and the sPESI in a large U.S. community-based population. Both indices perform well in identifying patients at low risk for 30-day all-cause mortality. If used as a guide to identify ED patients with acute PE who might be eligible for outpatient management, the PESI is preferable to the sPESI as it includes a larger pool of low-mortality patients in its low-risk category and thus might benefit more patients while conserving limited resources.

Table 4
Performance of original and simplified Pulmonary Embolism Severity Indices in predicting 30-day all-cause mortality (low risk[a] vs. higher risk).

	Pulmonary Embolism Severity Indices			
	Original		Simplified	
Performance	**Estimate**	95% CI	**Estimate**	95% CI
Sensitivity (%)	97.7	93.5–99.5	99.2	95.9–100.0
Specificity (%)	40.6	38.8–42.5	28.8	27.1–30.5
Positive predictive value (%)	7.0	5.9–8.3	6.0	5.1–7.1
Negative predictive value (%)	99.7	99.3–100.0	99.9	99.3–100.0
Positive likelihood ratio	1.65	1.58–1.71	1.39	1.35–1.43
Negative likelihood ratio	0.06	0.00–0.12	0.03	0.00–0.08
Area under the ROC curve	0.77	0.75–0.79	0.73	0.71–0.75

ROC, receiver operating characteristic.
[a] Low risk: original ≤85 points (Classes I and II); simplified, 0 points (Table 1).

Conflict of interest

The authors have no conflicts of interest in relation to this work.

Author contributions

- Conception and design: Vinson DR, Ballard DW, Mark DG, Reed ME, and Aujesky D
- Procurement of funding: Vinson DR, Ballard DW, Mark DG, Reed ME, and Rauchwerger AS
- Collection of data: Huang J, Vinson DR, Ballard DW, Mark DG, Wang DH, Lin JS, Kene MV, Pleshakov TS, Sax DK, Sax JM, McLachlan DI, Yamin CK, Swap CJ, Rauchwerger AS, Iskin HR, Vemula R, Fleming BS, and Elms AR
- Statistical analysis: Huang J
- Interpretation of data: Vinson DR, Ballard DW, Mark DG, Reed ME, and Aujesky D

Table 5
Classification agreement between the original and simplified Pulmonary Embolism Severity Indices with associated 30-day all-cause mortality.

Pulmonary Embolism Severity Indices (PESIs)		Cases $N = 3006$	Misclassification of original PESI risk by the simplified PESI	30-day all-cause mortality rate
Original	**Simplified**	*n* (%)		%
Low risk[a]	Low risk	728 (24.2)	–	0.0
	Higher risk	443 (14.7)	Overclassified	0.7
Higher risk	Low risk	100 (3.3)	Underclassified	1.0
	Higher risk	1735 (57.7)	–	7.4

[a] Low risk: original ≤85 points (Classes I and II); simplified, 0 points (Table 1).

- Composition of the manuscript: Vinson DR
- Revision of the manuscript for important intellectual content and approval of the final draft: all authors
- Taking responsibility for the paper as a whole: Vinson DR

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