### Utility of original and simplified pulmonary embolism severity indices in risk stratification of patients with pulmonary embolism: a study from Saudi Arabia

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Received: 02-Nov-2023 Revised: 09-Nov-2023 Accepted: 23-Dec-2023 Published: 23-Apr-2024

The Egyptian Journal of Chest Diseases and

Tuberculosis 2024, 73:193-198

#### **Background**

We aimed to report our experience using both the pulmonary embolism severity index (PESI) and its simplified form (s-PESI) score in evaluating patients with PE admitted at a large Saudi Arabian Hospital.

#### Patients and methods

This was a retrospective analysis where the adult (≥14 years old) patients admitted to the hospital of the Armed Forces Hospital Southern Region with the diagnosis of acute PE through 1 year were enrolled. The accuracy of both PESI and s-PESI was evaluated for mortality.

#### Results

Two hundred and twelve patients were enrolled. We encountered a significant relation only with the 90, 180 days, 1 year, and overall in-hospital mortality for low versus high-risk classification by the s-PESI score. There was neither a significant correlation between any-period mortality and classes of PESI score nor between low versus high-risk s-PESI score and 30-day mortality. The sensitivity of PESI and s-PESI in predicting mortality were 66.7 and 97.0%, respectively. The area under the curve of PESI and s-PESI were 0.611 (P=0.043), and 0.629 (P=0.005), respectively.

#### Conclusion

Besides being an easier tool for stratifying the risk of patients with PE, our data show that the s-PESI score is utilizable in Saudi Arabian patients with PE admitted at a large tertiary hospital. s-PESI and PESI have good potential to predict the prognosis of PE in terms of in-hospital mortality, with higher sensitivity, negative predictive value, and area under the curve for s-PESI versus PESI. There was a significant correlation between the s-PESI and the 90, 180 days, 1 year, and the overall in-hospital mortality. Further prospective multicenter studies are needed.

#### **Keywords:**

Index, mortality, predictive, pulmonary embolism, Saudi Arabia, severity, simplified, utility

Egypt J Chest Dis Tuberc 2024, 73:193-198 © 2024 The Egyptian Journal of Chest Diseases and Tuberculosis 2090-9950

#### Introduction

The clinical presentations of pulmonary embolism (PE) vary from completely asymptomatic to catastrophic events [1]. Acute PE has a considerable short-term mortalities ( $\geq 13\%$ ) [2]. Moreover, it was observed that patients with PE had increased rates of 1-year mortality (25%) [3]. Risk stratification is of crucial importance and has been used in the management of acute PE, and it aims to discriminate between low-risk and highrisk categories, for whom in-hospital management will differ [4]. Therefore, the international guidelines on managing acute pulmonary thromboembolism (PTE) [4] recommend using prognostic scores, following hemodynamic assessment.

The proposed pulmonary embolism severity index (PESI), which is composed of 11 items and five risk classes, and its simplified PESI (s-PESI), which comprises six items and two risk classes, are the commonest addressed and validated scores for acute PE [5,6]. In their meta-analysis which included 71 studies (44 300 patients), Elias et al. [7] provided evidence-based data about the utility and validity of both scores in acute PE that may help identify

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low-risk patients. The overall 1-month mortality rate was 2.3 and 11.4% in the low-risk and high-risk groups for PESI, whereas it was 1.5 and 10.7% in the low-risk and high-risk groups for s-PESI, respectively [7].

However, to the best of our knowledge, neither the original nor the s-PESI scores were tested before in the assessment of risk among Saudi patients with PE.

Therefore, the current study aimed to report our experience with using PESI and s-PESI scores in evaluating patients with PE admitted at a large tertiary-referral Saudi Arabian Hospital.

#### Patients and methods

#### Study population and design

Those study participants were all adult (≥14 years old) patients admitted to the inpatient units of the Armed Forces Hospital Southern Region (AFHSR) with the diagnosis of acute PE between June 2021 and June 2022 and their data were retrospectively retrieved from the inpatients' electronic records. The enrolment criterion was acute PE diagnosis as per the criteria defined by computed tomography with intravenous contrast (CTPA). Patients who were aged less than 14 years, those with chronic PE, or chronic thromboembolic pulmonary hypertension with the absence of an acute thromboembolic event during the study period, and those with incomplete or deficient follow-up data, were excluded.

#### **Outcomes and variables**

The primary study outcome was to study the predictive rules for the in-hospital mortality after establishing the diagnosis of acute PE. The overall mortality was defined as death due to any cause. The data related to mortality were obtained from hospital records for patients with in-hospital mortality and by follow-up (up to 1 year) using patient ID numbers for those who were discharged from the hospital.

A review of the hospital's electronic records was carried out to obtain the baseline features, including those variables utilized to estimate the original and s-PESI scores. Other items, like the type of malignancy, other risk factors rather than that of cancer (i.e. history of immobilization or surgery for ≥72 h, and use of hormone replacement or oral contraceptive therapy), concomitant deep venous thrombosis, type of diagnostic test, treatment for acute PE, history of previous PE, previous deep venous thrombosis, as well as the absence or presence of medical conditions/comorbidities were also recorded.

## Pulmonary embolism severity index and simplified pulmonary embolism severity index scores

For the calculation of PESI, a total score is got by adding the age of the patient (in years) to the points for each item (if present) of these items: gender, systolic blood pressure, body temperature, heart rate, respiratory rate, presence of oxygen desaturation, change in the conscious level, history of malignancy, chronic pulmonary disease, and cardiac failure [5].

Thereafter, each study participant was assigned to her/his risk class as follows: class V for a score more than 125, class IV for a score between 106 and 125, class III for that between 86 and 105, class II for that between 66 and 85, and finally class I for those with a score less than or equal to 65. Low-risk patients were those in classes I and II risk classes, while high-risk patients with those in classes III–V risk groups [5].

For the s-PESI calculation, the later excludes some of the parameters of the PESI, namely gender, and body temperature, and makes a combination between lung disease and heart failure to constitute a single item named 'chronic cardiopulmonary disease' [6].

Each item was assigned one point with a score between 0 and 6. Patients who matched any of those score variables were assigned high-risk, whereas they were assigned low-risk if they did not match any of these variables [6].

The predictive accuracy of both PESI and s-PESI was assessed for deaths/mortality within consecutive timeperiods (i.e. 1 month, 3 months, 6 months, and 1 year).

#### **Ethical aspects**

The review board of the AFHSR had approved the current study (approval number; AFHSRMREC/2022/PULMONOLOGY-INTERANL MEDICINE/565) and a written consent was obtained from the study participants.

#### Statistical analysis

The test of Pearson  $\chi^2$  or the Fisher's exact test were utilized for comparison of categorical variables. The comparison of mortality at the subperiods was carried out both among the risk classes and between low-risk and high-risk groups. The characteristic features like specificity, sensitivity, predictive values, and likelihood ratios for the two major groups (low-risk vs. high-risk patients) according to PESI and s-PESI, were estimated [8]. The area under the curve (AUC) was used to determine the discriminatory power of both PESI and specified PESI to predict mortality. The overall mortality of low-risk versus high-risk patients was compared using the characteristic Kaplan–Meier

Table 1 Baseline patients' characteristics (*N*=212) and predictors of pulmonary embolism severity index and simplified pulmonary embolism severity index scores

	N=212 [n (%)]
Age (years)	
Mean±SD	58.11 ± 21.3
Median (range)	59 (17–105)
Sex (males)	88 (41.5)
History of chronic pulmonary disease	7 (3.3)
History of cancer	7 (3.3)
History of cardiac failure	12 (5.6)
Temperature <36°C	39 (18.4)
RR ≥30 min	6 (2.8)
PR ≥110 BPM	76 (36.8)
SBP <100 mmHg	34 (16)
Altered conscious level	10 (4.7)
PaO <sub>2</sub> <90%	142 (67)
Other characteristics	
Essential hypertension	97 (45.8)
Coronary artery disease	19 (9)
DM	88 (41.5)
CKD	34 (16)
Charlson Comorbidity Index	
Mean±SD	$3.23 \pm 2.8$
Median (range)	3 (0–10)
PESI score	
Class I	61 (28.8)
Class II	37 (17.5)
Class III	52 (24.5)
Class IV	26 (12.3)
Class V	36 (17.0)
Simplified PESI score	
Low risk	40 (18.9)
High risk	172 (81.1)

CKD, chronic kidney disease; DM, diabetes mellitus; PESI, pulmonary embolism severity index; PR, pulse rate; RR, respiratory rate; SBP, systolic blood pressure.

analyses and the log/rank testing. All statistical tests were carried out using the software IBM Statistical Package for Social Sciences (SPSS) for Windows, version 24.0. The level of statistical significance was considered at *P* value less than 0.05.

#### Results

#### Clinical and demographic characteristics

Two hundred and twelve patients were enrolled in the current analysis, the median age of whom was 59 years. Fifty-eight percent of the participants were females. The participants' characteristics used to estimate the studied scores are shown Table 1. The distribution of patients according to the PESI and s-PESI classes are detailed in Table 1.

# The pulmonary embolism severity index and simplified pulmonary embolism severity index scores and mortality

Mortality follow-up data for 1 year were completed for all enrolled patients (*n*=212). The reported mortality rates were 10.4, 13.7, 15.6, and 15.6%, at 30, 90, 180 days, and 1 year, respectively. The overall in-hospital mortality was 15.6%. Table 2 shows the analysis of mortality according to the PESI and s-PESI risk classes at 30, 90, 180 days, and 1 year. The risk stratification according to the PESI and s-PESI scores revealed a significant correlation only with the 90, 180 days, 1 year, and the overall in-hospital mortality for low-risk versus high-risk classification by the s-PESI score. There was neither a significant relation between any-period mortality and the classes of PESI score nor between low-risk versus high-risk s-PESI score and 30-day mortality. Table 2 details these results.

Table 2 Pulmonary embolism severity index and simplified pulmonary embolism severity index scores in relation to the risk/ class-specific mortality

	30 days deaths	90 days deaths	180 days deaths	1 year deaths	Overall in-hospital deaths
Overall	22/212 (10.4)	29/212 (13.7)	33/212 (15.6)	33/212 (15.6)	33/212 (15.6)
PESI	22/212 (10.4)				
Low risk	6/98 (6.0)	11/98 (11.2)	11/98 (11.2)	11/98 (11.2)	11/98 (11.2)
Class I	3/61 (4.9)	6/61 (9.8)	6/61 (9.8)	6/61 (9.8)	6/61 (9.8)
Class II	3/37 (8.0)	5/37 (13.5)	5/37 (13.5)	5/37 (13.5)	5/37 (13.5)
High risk	16/114 (14.0)	18/114 (15.8)	22/114 (19.3)	22/114 (19.3)	22/114 (19.3)
Class III	6/52 (11.5)	7/52 (13.4)	7/52 (13.4)	7/52 (13.4)	7/52 (13.4)
Class IV	6/26 (23.0)	6/26 (23.0)	7/26 (27.0)	7/26 (27.0)	7/26 (27.0)
Class V	4/36 (11.1)	5/36 (13.8)	8/36 (22.2)	8/36 (22.2)	8/36 (22.2)
P for trend*	0.890	0.847	1.000	1.000	1.000
P for low versus high-risk	0.072	0.062	0.129	0.129	0.129
Simplified PESI	22/212 (10.4)	29/212 (13.7)	33/212 (15.6)	33/212 (15.6)	33/212 (15.6)
Low-risk	1/40 (2.5)	1/40 (2.5)	1/40 (2.5)	1/40 (2.5)	1/40 (2.5)
High-risk	21/172(12.2)	28/172 (16.3)	32/172 (18.6)	32/172 (18.6)	32/172 (18.6)
P for low versus high-risk	0.085	0.021	0.008	0.008	0.008

PESI, pulmonary embolism severity index.

\*Five PESI classes were compared.

## Predictive powers of original and simplified pulmonary embolism severity index scores

The sensitivity of PESI and s-PESI in predicting mortality were 66.7 and 97.0%, respectively. The AUC of PESI and s-PESI were 0.611 (*P*=0.043) and 0.629 (*P*=0.005), respectively. Table 3 and Fig. 1 detail these results.

#### **Discussion**

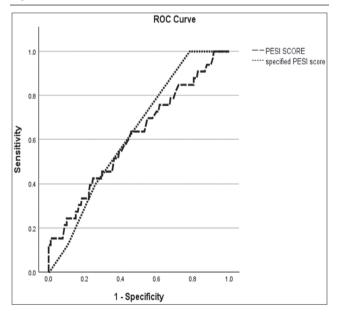
Despite that, both PESI and s-PESI scores were used for a long time for stratifying patients with PE before, however, the current study is the first one that evaluates the utility of both scores among patients with PE admitted at a large tertiary-referral Saudi Arabian

Table 3 Predictive powers of pulmonary embolism severity index and simplified pulmonary embolism severity index scores for in-patient mortality

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Diagnostic criteria	PESI score	Specified PESI score			
AUC	0.611	0.629			
95% CI	0.504-0.718	0.539-0.719			
SE	0.055	0.046			
P value	0.043	0.005			
Cut-off	60	0.5			
Accuracy%	51.4	33.5			
Sensitivity%	66.7	97.0			
Specificity%	48.6	21.8			
NPV%	88.8	97.5			
PPV%	19.3	18.6			

AUC, area under the operating curve; CI, confidence interval; NPV, negative predictive value; PESI, pulmonary embolism severity index; PPV, positive predictive value.

Figure 1



Predictive powers of original and simplified PESI scores. PESI, pulmonary embolism severity index.

Hospital. The ideal scoring model for risk assessment of patients with acute PE should be validated in a different population and has its clinical impact [7,9].

It is noteworthy that, the original PESI, which comprises 11 variables (five risk classes), and the s-PESI, with six variables (two risk classes) were frequently studied as well as validated prognostic scores for acute PTE [5–7].

Our results showed that 46.3 and 53.7% of our patients were categorized as low-risk and high-risk classes, while 18.9 and 81.1% were classified so, using the PESI and s-PESI scores, respectively.

We observed that the mortality rates for our enrolled patients were 10.4, 13.7, 15.6, and 15.6%, at 30, 90, 180 days, and 1 year, respectively. In their study of 1025 patients with the diagnosis of acute PE, Ng *et al.* [10] reported mortality rates of 8.3, 11.1, 16.3, 26.7, and 31.6%, at 3, 6 months, 1, 3, and 5 years of follow-up, respectively. Recently, Sandal *et al.* [8], reported higher mortality rates (13.3% at 1 month, 21.8% at 3 months, 32.6% at 1 year, and 51.0% at 5 years) and justified that by the higher prevalence of malignancy (31.9%) among their cohorts.

Our results showed that the stratification revealed a significant correlation only with the 180 days, 1 year, and the overall in-hospital mortality for low-risk versus high-risk classification by the s-PESI score. These results differ from those obtained by previous studies [8,11]. Dentali *et al.* [11] have observed that, according to PESI, long-term mortality had a significant relationship to risk classes (*P*<0.001) for mortality at 3, 6, and 12 months, respectively. On the other hand, Sandal *et al.* [8], observed that both risk stratification of the PESI and s-PESI were significantly related to short-term and long-term mortality.

These disagreements with previous studies could be explained by the differences in patients' characteristics (e.g. higher prevalence of patients with cancer in the study by Sandal and colleagues), enrolled patients' numbers, and the follow-up periods.

On the other hand, the finding of a significant correlation between in-hospital mortality and s-PESI, not PESI, could be explained by the fact that different parameters and points as well as low-risk versus highrisk classes are used for the calculation of PESI and s-PESI, respectively [5,6].

The frequencies of in-hospital deaths among patients categorized by the s-PESI as having low clinical hazards were inferior to their matching values in the

low-risk PESI group (2.5 vs. 11.2%), without the need for an imaging tool or complex laboratory assay. Moreover, there were significant differences between the low-risk versus high-risk classes stratified by the s-PESI with regards to the 180 days, 1 year, and the overall in-hospital mortality. Utilizing s-PESI, only 1/40 of patients in the low-risk group died during the 1-year follow-up. Our results confirm those obtained by previous reports [5-8,12] and support the importance of using s-PESI in stratifying Saudi patients with acute PE.

The s-PESI score was adopted by Jiménez et al. [6] to overcome the weaknesses in PESI. Our data prove that the sensitivity and negative predictive value of s-PESI are more than those of PESI, which was observed in previous reports, as well [6,12,13]. We had reported a sensitivity and negative predictive value of 97.0 and 97.5% for s-PESI compared with 66.7 and 88.8% for PESI (P=0.005 and 0.043, respectively). This study showed that both s-PESI and PESI have considerable accuracy in predicting PE prognosis in terms of in-hospital mortality, with a higher AUC for s-PESI. This is in agreement with the findings of the meta-analysis by Zhou et al. [14], who found that, in the s-PESI subgroup, the AUC was 0.792 ± 0.012,  $0.832 \pm 0.0547$ , and  $0.645 \pm 0.0197$ , for predicting allcause deaths, PTE-related deaths, and serious adverse effects, respectively [14].

According to the recent meta-analysis by Elias *et al.* [7], the agreement between the s-PESI and PESI was fair. Because of their importance in the risk classification of patients with PE, both PESI and s-PESI models are now involved in the risk stratification of patients with PTE in the recent ESC guidelines [7].

We agree with Yousif and Hussein [12], that certain observations support the superiority of the s-PESI over other prognostic scores: s-PESI is obtained from simple, yet objective clinical data that are regularly encountered at patient admission; second, it does not need expensive or time-consuming laboratory assays, such as cardiac troponin, or echocardiographic maneuvers that cost time and expertise [13]; third, s-PESI takes into consideration both clinical PE impact and comorbid disease burden; and lastly, it does not require an invasive procedure such as arterial blood gases but rather the simple noninvasive O2 saturation [12]. In daily clinical practice, and for these advantages, we recommend the use of s-PESI in risk assessment of patients with PE in Saudi Arabia.

Despite the limitations inherent to retrospective studies conducted at highly specialized centers, the current study results are robust and provide initial national data that can bridge the existing gap between the daily practice of respiratory medicine and clinical/academic studies in Saudi Arabia. In patients with the diagnosis of acute PE, it is important to predict those with poor outcomes, clinical prognostic scores being useful for that context. They are also useful in selecting/tailoring the most appropriate therapy for almost every patient. However, prospective multicenter studies focusing on risk stratification-guided management are needed for a better level of evidence to strengthen the given recommendations for the management of acute PTE in Saudi Arabia.

#### Conclusion

Besides being an easier tool for risk stratification of patients with PE, our data show that the s-PESI score is utilizable in Saudi Arabian patients with PE admitted at a large tertiary hospital. Both s-PESI and PESI have good accuracy in predicting PE prognosis in the context of in-hospital mortality, with higher sensitivity, negative predictive value, and AUC for s-PESI versus PESI. There was a significant correlation between the s-PESI and the 90, 180 days, 1 year, and the overall in-hospital mortality. Further prospective multicenter studies are needed.

#### **Acknowledgements**

The authors thank Mr Omar Abdelwahab, Al-Fasial University, Riyadh, Saudi Arabia (omaromar44666@ gmail.com) for his great help with this research.

#### Financial support and sponsorship Nil.

#### **Conflicts of interest**

The authors do not have any conflicts of interest.

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