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Original Article

Comparing the "simplified revised Geneva score", the "original PESI", and the "simplified PESI" for mortality prediction for pulmonary embolism. A 10 years follow-up study

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Abstract: Background: The purpose of this research was to investigate and compare the utilization of the revised Geneva score, original PESI, and simplified PESI in predicting the long-term mortality rate of patients with pulmonary embolism (PE). Methods: This retrospective investigation was conducted in Isfahan between June 2014 and July 2015 on patients with PE who were referred to our medical center. In this study, the revised Geneva score, the original PESI scales, and the simplified PESI scales were utilized. Additionally, diagnostic and treatment procedures were done in accordance with the standard protocol. We collected data of patients including gender, age, any risk factors for venous thromboembolism. After the primary data collection, contacts were made to the patients or their relatives for gathering information about patient's survival. The mortality rates of patients were determined within 10 years after the PE. Results: We analyzed data of 224 patients. Over a 131-month course of following up 224 patients, 105 deaths occurred that were related to PE. The initial PESI factor had a positive and negative predictive value of 83%. Patients with PE who scored extremely high on the PESI had a mortality and morbidity rate 42 times (9.22-87.32) greater than those with PE who scored very low. Furthermore, the death and morbidity rate of high-risk PE patients was 5% (0.67-1.70) in the Geneva score and 62% (0.30-2.31) in the simplified PESI score. Conclusion: The use of original PESI score could predict the long-term mortality of PE patients more accurately than other scores.

Keywords: Pulmonary embolism, mortality, long term

Introduction

Venous thromboembolism, which comprises deep vein thrombosis and pulmonary embolism (PE), is one of the main causes of death from coronary artery disease and stroke [1]. PE is a frequent multifactorial condition with substantial short- and long-term effects that can be deadly [1-4].

PE occurs in 1 to 3 cases per 1,000 adults in developed countries and is one of the three leading causes of cardiovascular death, along with myocardial infarction and stroke [5]. If there is no clinical suspicion, the mortality rate is 31 to 38% and in case of shock, 70% of patients with severe PE die [6].

According to PE registry systems, the in-hospital death rate for patients with acute right heart failure varies widely, from 8.1% in a population of stable patients to as high as 65% for those who require cardiopulmonary resuscitation and 25% for those who experience heart shock [7]. The existence and severity of comorbidities, on the other hand, greatly influence the long-term poor result. Acute PE has a correlation with a high mortality rate in the hospital or within 30 days (short-term) of 4% and 13%, respectively [8, 9].

Risk classification of patients with acute PE can identify low-risk individuals who can be treated on an outpatient basis and those who are at high risk and should benefit from intensive care

and thrombolytic treatment in a hospital [10]. In addition, accurate and targeted prognostic models may assist physicians in assessing whether early discharge or outpatient treatment of patients with low-risk acute pulmonary embolism is possible [11, 12].

Several tools are available to determine the short-term prognosis and appear to be beneficial in identifying individuals at low risk of mortality [13]. However, only a small number of studies have investigated the role of risk factors that may influence the long-term outcomes of these patients. There is a lack of standardized methods for classifying prognostic risk factors, and most data come from the patient's general history rather than the first three to six months after therapy has begun. Long-term follow-ups of patients with PE could indicate different results and be useful in the managements of patients [14, 15]. As a result, prognostic tools should be used to evaluate the long-lasting results for those with PE.

In the diagnostic investigation of patients with suspected PE, the updated Geneva score is a completely standardized clinical decision rule (CDR). Due to the fact that the variables comprising the decision rule each have their own relative importance, it is possible for there to be mistakes in the calculations performed in the event of an emergency [13]. The Pulmonary Embolism Severity Index (PESI) is a clinically established predictive model for individuals with PE [12]. This criterion predicts the thirty-day outcome of cases with pulmonary embolism and is shown to have satisfactory results in predicting the long-lasting death rate of PE patients [16]. PESI could be used as either original or simplified. These criteria could be useful in predicting the long-term data and have been used in previous studies [17]. However, no single and definite criteria is known to be useful in this regard.

Given that the PE is a serious condition and might require life-long observations and considering that the long-term results should be assessed in patients with PE, also regarding that no definite and accurate prognostic tool is identified yet, in the present study, we aimed to investigate and compare the use of the revised Geneva score, original PESI and simplified PESI in predicting the long-term mortality rate of PE patients. This study innovatively compares the revised Geneva score, original PESI, and simplified PESI in predicting long-term mortality (10 years) in PE patients. It provides insights into the effectiveness of these scoring systems, with the original PESI score found to be more accurate in long-term mortality prediction. Additionally, the study emphasizes the importance of extended follow-up for understanding ongoing risks and outcomes in PE patients.

Methods and material

Study design

This study is a retrospective cohort that was conducted at the Al-Zahra hospital, which is linked to the Isfahan University of Medical Sciences. The present investigation was carried out on 252 individuals with PE that referred to our medical center from June 2014 to July 2015 with the primary symptoms of PE. The protocol for the research was approved by the Research committee of the Isfahan University of Medical Sciences and confirmed by the Ethics committee (IR.MUI.MED.REC.1398.678).

Inclusion and exclusion criteria

The criteria for inclusion were admission to Al-Zahra Hospital between June 2014 to July 2015 with the following signs of PE: wheeze, dyspnea at rest, pleuritic pain, hemoptysis, chest pain, cough, unilateral swelling along with tenderness, orthopnea (≥2 pillows), and erythema with apparent size variation on the lower limbs. The patient presented with tachycardia, tachypnea, an increased P2 on cardiac auscultation, crackles/rales in the lungs, and classic evidence of deep venous thrombosis on physical exam. Other inclusion criteria included patients' availability for phone calls and their informed agreement to take part in this study. A chest CT-scan confirmed the diagnosis of PE. Patients who had already passed away before the PE was diagnosed, patients who skipped the follow-up appointments, patients who had a confirmed diagnosis of PE prior to visiting the emergency room and had already started treatment, and patients with any chronic illness who had less than one to two months to live were excluded due to incomplete data as well as a lack of access to the patient to complete the data.

Primary data gathering and scoring

At the start of the trial, the revised Geneva score, simplified PESI, and original PESI scales were used, and standard diagnostic and therapeutic methods were followed. For the patients who took part in this study, CT pulmonary angiography (multi-slice method, pulmonary thromboembolism protocol) was done. Checklists were used to record information about patients, and after a preliminary diagnosis was made and treatment was begun, patients were transferred to the intensive care unit or pulmonary-medical ward. A radiologist (who works at Al-Zahra Hospital) read and reported on the CT scans. However, in cases when CT angiography was not appropriate (such as severe kidney failure, intolerance to intravenous contrast, and pregnancy), a combination of nuclear V/Q scan, Doppler sonography of the lower limbs, and the D-dimer test (a negative test is useful) was employed.

Further data collection

We collected data of patients including gender, age, any risk factors for venous thromboembolism (VTE) such as trauma or surgery, presence of comorbidities such as ischemic heart disease (IHD), chronic heart failure (CHF), chronic obstructive pulmonary disease (COPD), hypertension, chronic kidney disease (CKD), diabetes mellitus (DM), hyperlipidemia (HLP), cancer and cerebrovascular accident (CVA). Clinical presentations of PE were also extracted from each patient's files. These presentations included: fever, tachypnea, tachycardia, circulatory collapse, orthopnea, cough etc.

After the primary data collection, contacts were made to the patients or their relatives for gathering information about patient's survival. In cases of patient deaths, accurate information was provided about the cause of death through questioning relatives or medical records, and then their deaths were documented as being correlated with PE, potentially correlated with PE, or unconnected to PE. The mortality rates of patients were determined within 10 years after the PE.

Means, standard deviations, and percentages were used to characterize the participants at baseline for continuous measurements and categorical variables, respectively.

Sensitivity and specificity analysis

To establish the sensitivity and specificity of the Geneva score, original PESI score, and simplified PESI score, the "receiver operating characteristic" (ROC) method was employed. For a set of diagnostic criteria, the ROC curve is constructed by plotting the sensitivity (y axis) as a function of [1-specificity] (x axis). The Chi-square test was used to investigate the independence hypothesis of these three factors and the response variable (death), and the Kruskal-Wallis test was used to assess the sensitivity and specificity of the aforementioned factors. Quantitative data was compared using the t-test.

Survival graph and further statistical models

The Kaplan-Meier survival graph and cox regression were applied to compare survival in the 131-month (approximately 10 years) follow-up and factor-analyze mortality.

The present study used multivariate-adjusted Cox proportional hazards model for estimating hazard ratios (HRs) and 95% confidence intervals (CIs) of incidence of mortality for increase in mentioned factors.

We used three models to look at the relationship between the revised Geneva score, the original PESI score, the simplified PESI score, and incident mortality, considering baseline factors that were progressively changed over time.

In unadjusted model 1, we included as simplified revised Geneva score, original PESI score and simplified PESI score.

We added individual factors (age and gender) in model 2.

Model 3 is further adjusted in terms of recent trauma, recent surgery, VTE in history, cancer, heart failure, COPD, CAD, stroke, altered mental status, dyspnea, chest pain, circulatory collapse, heart rate, systolic blood pressure, arterial oxygen saturation, respiratory rate, temperature, echo-pap median and ECG-S1.Q3.T3 pattern.

The Doppler ultrasound, CT angiography, perhaps a nuclear scan, and D-dimer results were used to complete the checklist without interfer-

Table 1. Pulmonary embolism severity index and simplified version of the Geneva score

Simplified Geneva prognostic score				
Cancer	+2	Low		≤2
Heart Failure	+1	High		>2
Previous DVT	+1			
SBP<100 mmHg	+2			
PaO_2<8 kPa (60 mmHg)	+1			
DVT shown by Doppler sonography	+1			
Variables	PESI: Original Score	PESI: Simplified Score	PESI Original Score: Risk stratified	
Age	Age, in year	1	I: Very Low	≤65
Male Gender	+10		II: Low	66-68
Cancer	+30	1	III: Intermediate	86-105
Heart Failure	+10	1	IV: High	106-125
Chronic lung disease	+10		V: Very High	≥126
SBP<100 mmHg	+30	1		
Respiratory rate ≥30/min	+20			
Temperature <30°C	+20			
			PESI Simplified Score: Risk stratified	
Altered mental status	+60		Low	<0
Arterial blood oxygen saturation <90%	+20	1	High	≥1

PESI: Pulmonary embolism severity index, DVT: Deep venous thrombosis, SBP: Systolic blood pressure.

ing in any manner with the patients' treatment plan. Morbidity and death were tracked for the patients.

During data collection, the following variables were also considered: The following factors were also considered during data collection: Patient demographics, comorbid conditions, admission diagnoses, symptoms, frequency of recurrent thromboembolic and hemorrhagic events, date of death, and cause of death.

Data source

The information was gathered from patient charts at the emergency room, hospitalization records, and notes taken during visits to the therapeutic unit. The checklist was used to determine the Geneva and PESI scores on the same day or the day after admission. In the event of recurring respiratory or lower extremity problems, patients were given instructions to visit the follow-up clinic. After 131 months following their original diagnosis, patients were contacted by phone or in person at Al-Zahra Hospital to inquire about their rates of mortality and survival, as well as any morbidity attributed to their disease. Any time a patient went back to the hospital or passed away, their medical records were reviewed as part of the follow-up process. The deaths were documented as being correlated with PE, potentially correlated with PE, or unconnected to PE.

Statistical analysis

SPSS (Chicago, Illinois, USA) version 22.0 was utilized for the statistical analysis. Receiver Operating Characteristic (ROC) curve was drawn to compare the performance of Geneva prognostic score and original PESI score in predicting PE. Data were presented as mean and standard deviation. We used Cox proportional hazards regression and Kaplan-Meier graph to evaluate the scoring systems. The level of significance was determined to be $P<0.05$.

Results

Study population

In this study, 252 individuals with PE symptoms attending the Emergency Department of Al-Zahra Hospital were chosen, with 224 meeting the inclusion criteria. There were 28 patients who were not included because of various factors, including a lack of informed consent (5), a history of pulmonary embolism (PE) (4), the use of warfarin (4), a lack of contact (8), pregnancy (3), kidney disease (3), and an allergy to contrast material (1).

Table 2. Primary demographic and clinical data of participants (frequencies and percentages)

Variable	Geneva		Original PESI		Simplified PESI	
	Low risk	High risk	Low risk	High risk	Low risk	High risk
Gender, Male, n (%)	50 (64)	82 (56)	49 (66)	83 (55)	26 (67)	106 (57)
Age, mean years (SD)	55 (19)	58 (19)	40 (16)	65 (14)	47 (18)	59 (18)
Risk factors for VTE, n (%)						
Recent Trauma	6 (8)	24 (16)	13 (18)	17 (11)	5 (13)	25 (14)
Recent Surgery	11 (14)	49 (34)	23 (31)	37 (25)	9 (23)	51 (28)
VTE in history	1 (1)	24 (16)	4 (5)	21 (14)	1 (3)	24 (13)
Co-morbidity, n (%)						
Cancer	3 (4)	36 (25)	1 (1)	38 (25)	1 (3)	38 (21)
Heart Failure	7 (9)	16 (11)	0	23 (15)	0	23 (12)
COPD	17 (22)	33 (23)	6 (8)	44 (29)	4 (10)	46 (25)
CAD	16 (21)	23 (16)	5 (7)	34 (23)	4 (10)	35 (19)
Stroke	4 (5)	6 (4)	0	10 (7)	0	10 (5)
Altered mental status	11 (8)	9 (10)	0	20 (13)	2 (5)	18 (10)
Clinical presentations, n (%)						
Dyspnea	72 (92)	133 (91)	68 (92)	137 (91)	33 (85)	172 (93)
Chest Pain	61 (45)	26 (29)	42 (57)	45 (30)	24 (61)	63 (34)
Circulatory collapse	1 (1)	14 (10)	0	15 (10)	0	15 (8)
Heart rate ≥110 b/min	45 (33)	43 (49)	25 (34)	63 (42)	0	88 (48)
SBP<100 mmHg	11 (8)	35 (39)	11 (15)	35 (23)	8 (20)	38 (20)
Arterial oxygen saturation <90%	85 (63)	73 (81)	31 (42)	127 (85)	5 (13)	153 (83)
Respiratory rate ≥30/min	26 (19)	16 (18)	10 (13)	32 (21)	4 (10)	38 (30)
Temperature <30°C	0	0	0	0	0	0
Echo-pap median, mean (SD)	51 (20)	50 (17)	49 (21)	51 (18)	49 (25)	51 (18)
ECG-S 1.Q3.T3 pattern, n (%)	29 (22)	16 (18)	14 (19)	31 (20)	7 (18)	38 (21)

Table 3. Statistical characteristics of ROC curves of the factors used in the study

Factors	Sensitivity	Specificity	AUC	*P*-value
Geneva				0.015
High risk	73%	42%	42%	
Original PESI			83%	<0.001
≥I	98%	30%		
≥II	89%	55%		
≥III	70%	78%		
≥IV	45%	95%		
V	2%	100%		

Over a 131-month course of following up 224 patients, 105 deaths occurred that were related to PE. The participants were retrospectively divided into two "low risk" and "high risk" categories based on the three "Simplified PESI, Original PESI, and Geneva" variables based on the existing data in the files (**Table 1**).

Follow-up data

Patients were contacted via phone or in the order of their arrival at the clinic for up to 131 months after admission. **Table 2** displays the patients' primary data. For example, 132 (59%) of the study participants were male gender, among whom 49 people (66%) were in the low-risk Original PESI group and 83 people (55%) were in the high-risk Original PESI group. As can be observed in **Table 2**, there was also significant heterogeneity in various individual and clinical characteristics across three levels.

The result of Chi-square test showed that the three factors mentioned and the death variable are not independent.

Area under curve and survival rates

The area under the curve (AUC) indices were employed in this study to compare the predic-

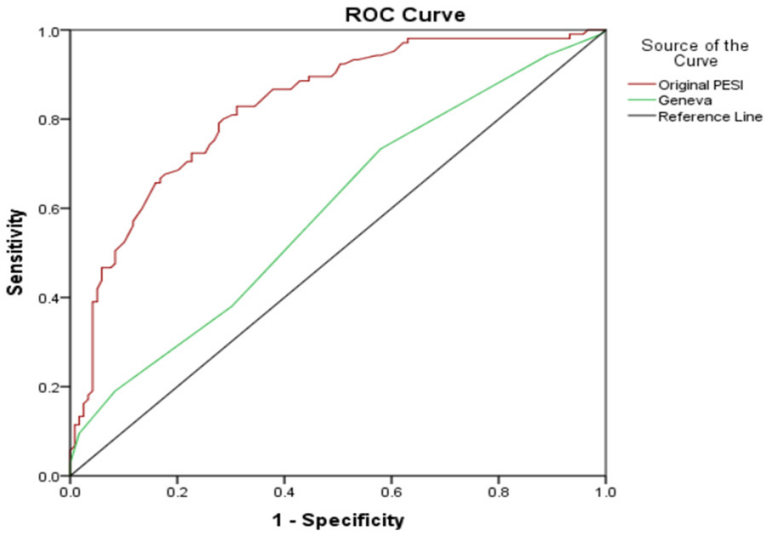

Figure 1. ROC curves of the Geneva prognostic score and original PESI score.

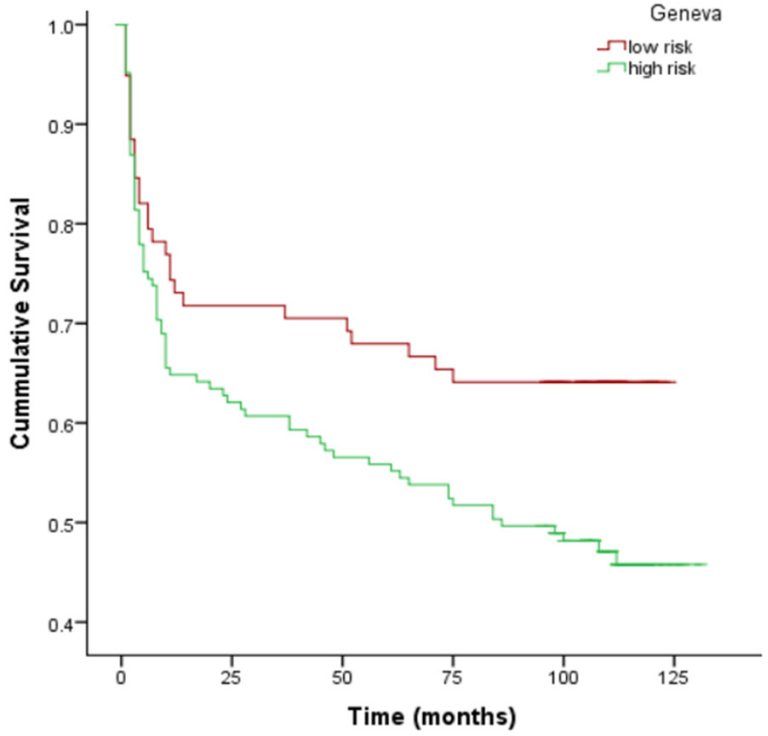

Figure 2. Survival rate on the basis of the simplified Geneva prognostic score (Kaplan-Meier gragh).

tive value of the variables in PE patients. The original PESI factor was shown to have a specificity as well as a sensitivity of 0.83 (positive) and 0.83 (negative) at the optimal cutoff point. When predicting morbidity and death in patients with PE, an AUC closer to one is preferred (**Table 3** and **Figure 1**).

Patient survival rates at 131 months are shown in **Figures 2-4** according to the Geneva score, the original PESI score, and the simplified PESI score, each of which indicates a decreasing probability of survival with an increasing slope at higher risk levels.

Model results

Table 4 shows the mortality model results. Patients with PE who were categorized as very high risk in the PESI score had 42 times (9.22-87.40) higher risk of morbidity and mortality than those categorized as very low risk. The highest significant link was reported in the fully adjusted model (Model 3) for an extremely high risk PESI score, with a hazard ratio (HR) of 6.02 (1.03-35.17).

Discussion

Based on our findings, we discovered a 46.8% death rate within 10 years. The initial PESI factor had a positive and negative predicting value of 83%, and patients with PE who were categorized as very high risk had a higher rate of death and morbidity than those who were categorized as very low risk. According to additional analyses, the rates of death and morbidity of PE patients categorized as being at high risk were 5% in the Geneva score and 62% in the modified PESI score. These data show that original PESI could be an acceptable criterion for prediction of death in PE patients.

These findings were consistent with prior research that validated the original and simplified PESI [18]. In the present study we observed that original PESI score has high predictive

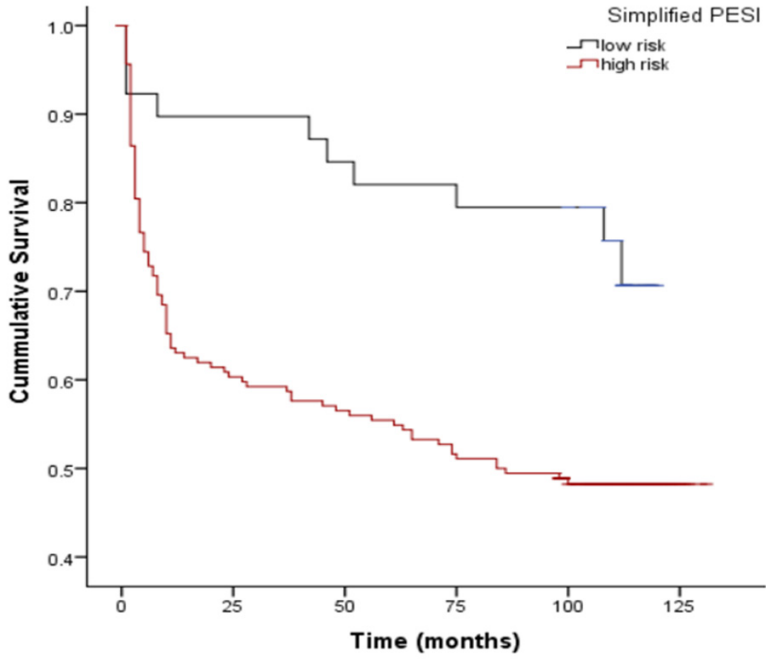

Figure 3. Patients' survival rate on the basis of the simplified PESI score (Kaplan-Meier graph). PESI: Pulmonary Embolism Severity Index.

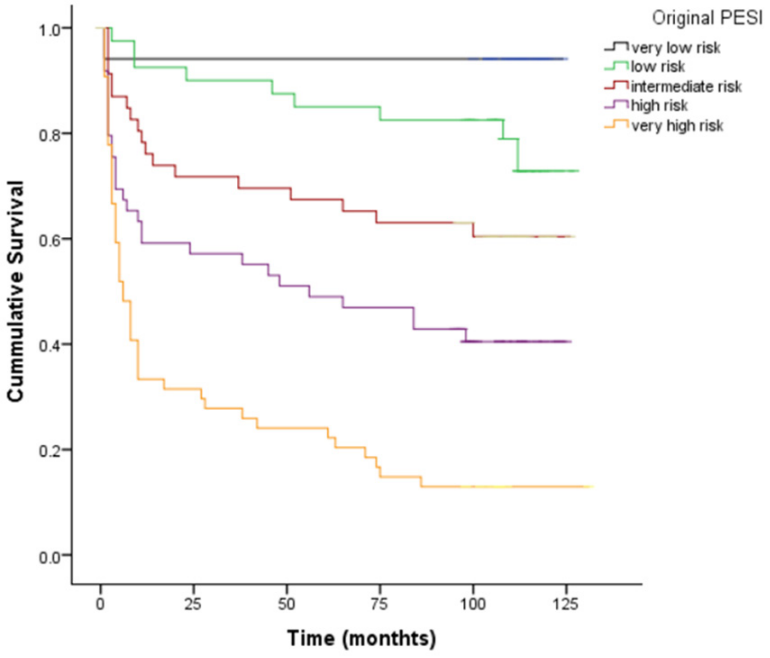

Figure 4. Patients' survival rate on the basis of the original PESI score (Kaplan-Meier graph). PESI: Pulmonary Embolism Severity Index.

value for mortality of patients compared to other scores.

We also observed 46.8% mortality rate within 10 years after the PE diagnosis and treatment. Investigations of morality rates in different previous research have reported almost similar results. In 2011, Ng and colleagues showed that the 5-year mortality rate of PE parents was 31.6% and in 2020, a study by Barco and others showed that the long-term mortality rate of PE patients could increase over time mostly because of cardiovascular malfunctioning [19]. On the other hand, different studies have evaluated the mentioned scores for predicting the mortality of the patients.

Previous studies have emphasized the use of difference criteria and scores in prediction of patient's mortality [16, 17]. As indicated, original PESI had the highest prognostic value than Geneva and simplified PESI. In 2016, an investigation was conducted by Tamizifar et al. that evaluated and compared the values of Geneva, original, and simplified PESI scores within a 1-month follow-up. Based on this data, the Geneva and original PESI had acceptable predictive value for mortality of PE patients [20].

An interesting aspect of our research was that we compared the long-term prediction qualities of these scores, which could have high clinical values. While the majority of studies have been undertaken in the short term and have investigated the utilization of these ratings in individuals with acute PE [21].

Although it is difficult to provide an accurate assessment of models due to the subjectivity of interpretation, we must acknowledge that PESI currently has the most extensive public data. Another study concluded that retaking or

Table 4. Estimated hazard ratios and 95% confidence intervals by Cox proportional hazards regression models for mortality

	Model 1		Model 2		Model 3	
	HR (95% CI)	*P*-value	HR (95% CI)	*P*-value	HR (95% CI)	*P*-value
Geneva						
Low risk	Ref.		Ref.		Ref.	
High risk	1.05 (0.67-1.70)	0.837	1.07 (0.67-1.71)	0.781	1.92 (0.56-2.51)	0.728
Original PESI						
Very low risk	Ref.		Ref.		Ref.	
Low risk	4.46 (0.95-20.88)	0.058	1.86 (0.38-9.10)	0.445	1.83 (0.37-9.09)	0.463
Intermediate risk	10.71 (2.30-49.81)	0.002	2.97 (0.56-15.69)	0.200	2.02 (0.37-11.17)	0.419
High risk	19.88 (4.36-90.55)	<0.001	4.93 (0.92-26.40)	0.062	3.70 (0.66-20.75)	0.138
Very high risk	41.57 (9.22-87.40)	<0.001	7.96 (1.46-43.32)	0.016	6.02 (1.03-35.17)	0.046
Simplified PESI						
Low risk	Ref.		Ref.		Ref.	
High risk	1.62 (0.30-2.31)	0.214	1.78 (0.34-2.81)	0.564	1.90 (0.38-2.11)	0.806

Model 1: Geneva, Original PESI and Simplified PESI. Model 2: Adjusted by Geneva, Original PESI, Simplified PESI, Age and Gender. Model 3: Adjusted by Geneva, Original PESI, Simplified PESI, Age, Gender, Recent Trauma, Recent Surgery, VTE in history, Cancer, Heart Failure, COPD, CAD, Stroke, Altered mental status, Dyspnea, Chest Pain, Circulatory collapse, Heart rate, Systolic Blood Pressure, Arterial oxygen saturation, Respiratory rate, Temperature, Echo-pap median and ECG-S 1.Q3.T3 pattern. Significance level = 0.05.

simplifying PESI scores after 24 to 48 hours can be considered a safe, comprehensive risk classification method [21].

A meta-analysis showed original PESI has a significant prognostics value in patients with PE but also suggested that further studies should be conducted on the long-term results [20]. These findings were also consistent with those of our investigation.

In 2021, Roy and colleagues conducted a randomized trial on cases with acute PE and evaluated the 30-day complication of these patients. Following the findings of this research, original and simplified PESI had significant predictive values for evaluating these complications in patients. They also discussed if these criteria could predict long-term therapeutic results regarding the importance of this issue [22].

The results of these previous studies were also somehow in line with our findings but the important issue was that none of these surveys has compared the three useful criteria in a long-term setting. As a result, these data could have high importance.

We reviewed the patient's documents retrospectively. The drawbacks of this study included the possibility of unidentified potential confounders, the use of data collected for these purposes but not all pertinent information, and had a lower level of evidence than prospective research. We also had a smaller sample size than in some previous studies, so we recommend that more research be conducted on larger populations. A larger study is necessary to complement our research. Studies that were carried out in tertiary care hospitals, which are facilities that serve patients who have many conditions at the same time, showed increased mortality and morbidity rates. However, these findings were essentially irrelevant when attempting to determine the risk for the patients who were the focus of the study.

Conclusion

The use of original PESI score could predict the long-term mortality of PE patients more accurately than other scores. These data could have high clinical values.

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Disclosure of conflict of interest

None.

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