Original Article

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Evaluation of Pulmonary Embolism Risk Stratification Scores in Patients Admitted to the Internal Medicine Clinic

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Abstract

Aim: Pulmonary embolism (PE) is a common cardiovascular emergency, and a broad range of conditions must be included in the differential diagnosis because of the frequent and highly non-specific symptoms of PE. Risk stratification scores were created because unnecessary procedures are often performed during the diagnostic process. Modified Geneva and Wells scores are widely used scoring systems, but their reliability remains controversial. In our study, we evaluated these scoring systems according to the predictability of the diagnosis and its correlation with mortality in patients diagnosed with PE.

Methods: Our study was conducted in a single center with a retrospective, cross-sectional design. We included 108 patients diagnosed with PE and admitted to the internal medicine clinic between January 2016 and October 2019. The median follow-up period was 19 months. The patients' initial demographic, clinical, and radiological findings were recorded. The modified Wells, Wells, and Modified Geneva risk scores were calculated according to this information. The relationships among laboratory findings, risk scores, and mortality were evaluated.

Results: It was determined that 48 (44%) of the patients died, and 57 (53%) survived during the follow-up period. The death or survival information of three patients could not be obtained because of their foreign nationality. There was no significant difference between the mean ages of female and male patients (p=839). The relationship between patient evaluations according to the score systems and mortality was examined. The analysis determined that only the Modified Geneva score had a significant association with mortality (p=0.001). In contrast, the Wells and Modified Wells scores had no statistically significant relationship with mortality (p=0.396 and 0.391, respectively). Age, malignancy, and dyspnea at admission were independent factors affecting mortality (p=0.001, 0.026, and 0.023, respectively).

Conclusion: The risk stratification scoring systems' diagnosis and mortality predictability are insufficient. These scoring systems must be improved to prevent underdiagnosis and unnecessary testing.

Keywords: Pulmonary embolism, mortality, risk stratification

Introduction

Pulmonary embolism (PE) is a common cardiovascular emergency in which the pulmonary artery or its branches are blocked by substances originating from any body part (such as a thrombus, air, tumor, or fat). The most common cause is occlusion by a thrombus (1). Unnecessary tests performed during the diagnostic process lead to complications and financial losses. While PE mortality is 25-30% in untreated cases, this rate drops to 2-8% in treated patients (2,3). It is very often confused with other diseases at the admission clinic. Differential diagnoses are broad because PE findings are non-specific and are expected in different diseases (4-6). In addition, most cases do not present with the classic symptoms of PE, such as shortness of breath, chest pain, and hypoxia (7). All conditions included in this differential diagnosis (such as acute coronary syndrome, acute pericarditis, acute respiratory distress syndrome, and dilated cardiomyopathy)

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should be considered as alternative diagnoses in patients with suspected PE.

For this reason, risk scoring systems have been created. The widely accepted ones are the revised Geneva, Wells, and modified Wells scores (8). However, the reliability of these scoring systems in predicting both diagnosis and possible mortality risk remains controversial.

This study aimed to compare the predictive features of PE, evaluate their relationship with mortality in patients hospitalized with the suspicion or diagnosis of PE, and assess the factors affecting mortality in patients hospitalized with the diagnosis of PE during follow-up.

Materials and Methods

Compliance with Ethical Standards

The study protocol and subject matter were reviewed and approved by the Institutional Ethics Committee of the University of Health Sciences (ref no./date: 243/2019). The ethics committee anonymized and approved the database information without needing consent.

Study Design

Our study was conducted in a single center with a retrospective, cross-sectional design. A total of 108 patients, 60 (55.6%) women and 48 (44.4%) men, hospitalized with a diagnosis of PE in the Internal Medicine Clinic of University of Health Sciences Turkey, Istanbul Haseki Training and Research Hospital between January 2016 and October 2019, were included in our study. PE was diagnosed or excluded by evaluating the patients' anamnesis, physical examination findings and biochemistry, echocardiography, and pulmonary computed tomography (CT) angiography examinations. Patients hospitalized with a preliminary diagnosis of PE and diagnosed with a different condition during hospitalization and those under the age of 18 were excluded from the study. According to the data obtained from the hospital information operating system, the patient's age, gender, family history, and existing comorbidities (such as hypertension, diabetes mellitus, ischemic heart disease, cerebrovascular disease, inflammatory bowel disease, cirrhosis, viral hepatitis, malignancy, venous thromboembolism, rheumatological diseases, and autoimmune diseases) were recorded. The patients' complaints, past medical history, vital signs at admission, and imaging results (Doppler ultrasonography, pulmonary CT angiography, echocardiography) were recorded. Serum urea, creatinine, uric acid, alanine aminotransferase, aspartate aminotransferase, total cholesterol, low-density lipoprotein (LDL)-cholesterol, high-density lipoprotein (HDL)-cholesterol, triglyceride, sodium, potassium, calcium, total protein, albumin, blood gas parameters, C-reactive protein (CRP), procalcitonin levels, and hemogram results of the patients were recorded. The Wells Score, Modified Wells Score, and Modified Geneva Score were calculated based on the information recorded when the patients first applied to the emergency department. The predictive properties of these scoring systems were evaluated. Patients were followed for a median of 19 months to determine whether mortality occurred after discharge and, if so, why. Mortality information was obtained using the national death notification system and the hospital information operating system. Mortality data could not be obtained for the three patients because they were not Turkish citizens. Therefore, analyses regarding mortality were performed on 105 patients (Figure 1).

Statistical Analysis

All data obtained in the study were recorded on a computer and evaluated using the Statistical Package for Social Sciences for Windows 20.0. In descriptive statistics, continuous variables are expressed as means. Standard deviations and categorical variables are expressed as percentages. Their distribution was evaluated using the Kolmogorov-Smirnov test. To compare the two groups, numerical data with a normal distribution were evaluated using the Student's t-test. If the distribution was abnormal, the Mann-Whitney U test was used for pairwise

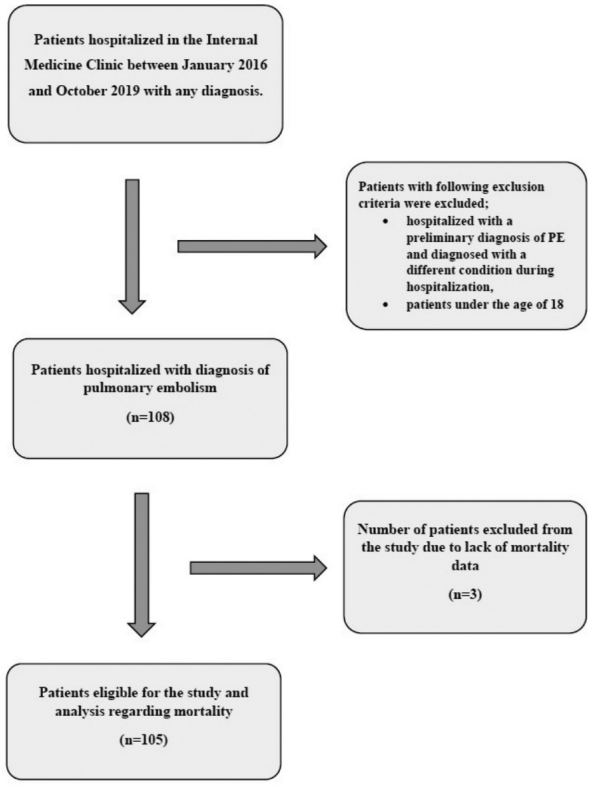


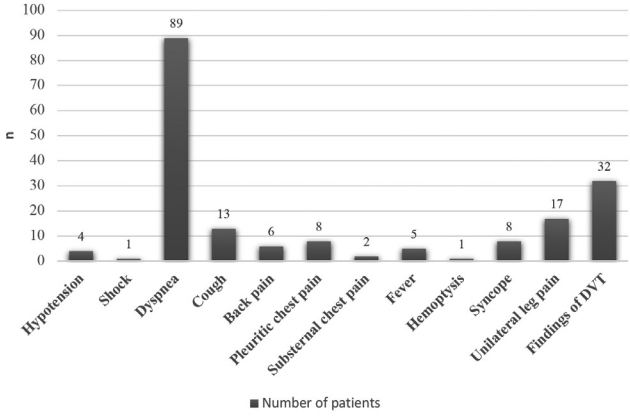
Figure 1. Flow diagram of patient selection
PE: Pulmonary embolism

comparisons of numerical data. Categorical variables were assessed using the chi-square test. P<0.05, or 95% confidence interval, was considered statistically significant.

Results

A total of 108 patients, 60 women (55.6%) and 48 men (44.4%), were included in the study. The average age was calculated as 66.34±16.5 [minimum (min.) 24, maximum (max.) 91]. Patients admitted with a diagnosis of PE were followed for a median of 19 months after discharge from the hospital (min.: 0, max.: 51 months). Forty-three of the patients (39.8%) were under 65 years of age, and 65 (60.2%) were over 65 years of age. A patient was pregnant. Thirteen patients had an operation history within the last six months. There were bone fractures in the lower extremities in four patients. Eight had a hip or knee prosthesis history. Eighteen patients had solid malignancies, and two patients had hematological malignancies. Five patients had a history of trauma within the last six months. Two patients had a history of laparoscopic surgery within the previous three months. There was immobilization in the history of 22 patients (20.4%). Concomitant infections were detected in 63 patients (52.3%). Respiratory failure was detected in 16 patients (14.8%) at admission or during hospitalization. Atrial fibrillation was present in 10 patients (9.3%). A provoking cause was detected in 16 patients (14.8%). Four patients presented with hypotension, and one patient presented with shock. Eighty-nine patients (82.4%) had shortness of breath at admission. Cough was present in 13 patients (12%), and 6 had back-chest pain (5.6%). Fever was detected in 5 patients (4.6%). Unilateral leg pain was observed in 17 patients (15.7%), and ultrasound imaging revealed deep vein thrombosis in 32 patients (29.6%) (Graphic 1).

It was determined that 48 patients died and 57 survived. Ten patients died within the first month after the diagnosis of PE. Four patients died during hospitalization.



Graphic 1. Symptoms and findings at admission

The average age of the non-survived patients was 74.9±10.8 years. The average age of surviving patients was found to be 60.04±17.2 years (p<0.001). White blood cell, neutrophil, CRP, and lactate values were higher in the patient group who did not survive during follow-up (p=0.008, 0.004, 0.023, and 0.039, respectively). Triglyceride and HDL cholesterol values were elevated in patients who survived (p=0.020 and 0.014, respectively), as shown in Table 1.

The Cox regression analysis performed to evaluate the risk factors affecting mortality showed that for those over 65 years of age, mortality risk increased by 3.78 times (p=0.001). We also observed that having malignancy increased mortality by 2.03 times (p=0.26), and having respiratory failure when the patient first came to the hospital increased mortality by 2.23 times (p=0.023) (Table 2).

According to the Modified Geneva Score, 14 patients were classified as low-risk. There were no deaths among

Table 1. Relationship between demographic data and initial laboratory parameters and mortality

Demographic data and laboratory values	Survivor (n=57)	Non-survivor (n=48)	p-value
Age	60.04±17.22	74.90±10.84	**<0.001**
Age >65 [n (%)]	24 (42.1%)	40 (83.3%)	**<0.001**
Sex (F/M)	32/25	26/22	0.839
Hemoglobin (g/dL)	12.01±1.83	11.75±2.3	0.534
WBC (10^3 uL)	8.99±3.15	11.6±5.96	**0.008**
Neutrophils (10^3 uL)	6.41±3.11	9.18±5.71	**0.004**
Lymphocyte (10^3 uL)	1.71±0.68	1.46±0.72	0.070
Glucose (mg/dL)	130.81±70.57	141.18±76.2	0.471
Urea (mg/dL)	40.05±20.26	61.8±30.59	**<0.001**
Creatinine (mg/dL)	0.86±0.34	1.02±0.55	0.067
Uric acid (mg/dL)	6.07±1.87	6.89±2.69	0.112
CRP (mg/L)	56.85±62.65	89±79.38	**0.023**
Glucose (mg/dL)	130.81±70.57	141.18±76.2	0.471
Total cholesterol (mg/dL)	179.7±47.27	160.33±42.65	**0.050**
Triglyceride (mg/dL)	156.42±82.34	121.49±46.09	**0.020**
HDL (mg/dL)	38.76±10.88	33.02±10.15	**0.014**
LDL (mg/dL)	112.56±37.35	101.74±36.45	0.181
PaO_2 (mmHg)	85.23±31.1	80.44±36.5	0.525
$PaCO_2$ (mmHg)	38.72±35.52	33.27±7.5	0.298
SpO_2 (%)	93.9±5.5	93.06±5.1	0.478
Lactate (mmol/L)	1.39±0.7	2.12±1.88	**0.039**
pH	7.43±0.05	7.43±0.1	0.885
Homosistein	15.06±3.9	5.35±7.56	**0.008**

F: Female, M: Male, CRP: C-reactive protein, HDL: High-density lipoprotein, LDL: Low-density lipoprotein, PaO_2: Partial pressure of oxygen, $PaCO_2$: Partial pressure of carbon dioxide, SpO_2: Oxygen saturation

them. While 33 of 72 patients (47.1%) who were considered medium risk were alive, 37 (52.9%) died. According to this scoring system, 77.1% of the total mortality consisted of patients evaluated as medium risk. Twenty-two patients were assessed as high-risk. Mortality information was obtained for 21 patients. It was determined that ten patients (47.6%) survived and 11 patients (52.4%) died (p=0.001) (Tables 3 and 4).

Table 2. Cox regression analysis of factors affecting mortality

	Sig.	Exp(B)	95% CI for Exp(B)	
			Lower	Upper
Age >65	**0.001**	3.78	1.76	8.11
Presence of malignancy	**0.026**	2.03	1.08	3.80
Admission with dyspnea	**0.023**	2.23	1.11	4.45

CI: Confidence interval

Table 3. Distribution of patients according to the clinical scoring systems

Clinical Scoring Systems	Number of patients n (%)
Modified Geneva Score	
Low probability	14 (13%)
Intermediate	72 (66.7%)
High probability	22 (20.3%)
Wells Score	
Low probability	44 (40.7%)
Intermediate	62 (57.4%)
High probability	2 (1.9%)
Modified Wells Score for PE	
PE unlikely	87 (80.6%)
PE likely	21 (19.4%)

PE: Pulmonary embolism

Table 4. Association between clinical scoring systems and mortality rates

		Survivor (n=57)	Non-survivor (n=48)	p-value
Modified Geneva Score	Low probability	14	0	**0.001**
	Intermediate	33	37	
	High probability	10	11	
Wells Score	Low probability	20	23	0.396
	Intermediate	36	24	
	High probability	1	1	
Modified Wells Score	PE unlikely	45	41	0.391
	PE likely	12	7	

PE: Pulmonary embolism

According to the Wells Score, out of 44 low-risk patients for whom mortality information was available, 20 were found to be alive and 23 were found to be dead. Patients determined to have low risk constituted 21.9% of the total deaths. Sixty-two patients were considered to have medium risk. It was determined that 36 (60%) of the patients who were considered to have medium risk survived, and 24 (40%) had died. In total, 50% of those who died were patients whose Wells score was determined to be at medium risk. Two patients were evaluated to have high risk, and one survived (p=0.396) (Tables 3 and 4).

According to the Modified Wells Score, 87 patients (80.6%) were evaluated as PE unlikely and 21 (19.4%) as PE likely. It was determined that 45 (52.3%) patients survived and 41 (47.7%) patients died among the patients who were considered PE unlikely. Mortality information for one of them could not be obtained. Deaths accounted for 85.4% of the total mortality among patients with unlikely PE. It was determined that 12 (63.2%) of the patients evaluated as having possible PE survived, and 7 (36.8%) died. 14.6% of the total mortality consisted of patients considered PE likely (p=0.391) (Tables 3 and 4).

Discussion

Pulmonary embolism is a cardiovascular emergency that is difficult to diagnose unless suspected. It is also a disease for which primary prevention can be provided and treated.

In our study, no statistically significant difference was found regarding the gender distribution of patients. In a study by Santosa et al. (9) with PE patients in Germany, PE incidence was not different between both genders.

In the regression analysis, we found that patients over 65 years of age had a significant relationship with mortality. In addition, when we did not use 65 as the cut-off age, mortality increased with age. Studies have shown that mortality in patients with PE is generally associated with malignancy, accompanying chronic cardiopulmonary comorbidities, and advanced age (10,11). We found that concomitant malignancies were also associated with mortality. This condition may be caused by malignancies, and sometimes chemotherapeutic agents increase the risk of thromboembolism.

In different studies, it has been observed that short-term mortality in treated patients diagnosed with PE can decrease below 8% (3,12). The mortality rate among those treated was 45.7% in our study. This may be because of the high average age of our patients, multiple comorbidities, and the fact that our study examined long-term mortality in addition to the short period after diagnosis.

Triglyceride, HDL, and LDL cholesterol levels were higher in the surviving patient group. It was thought

that this was because patients who developed mortality had worse nutritional status due to accompanying comorbidities, increasing age, and, therefore, lower lipid levels. In some studies conducted with different patient groups, triglyceride and LDL cholesterol levels were lower in patients who developed mortality, supporting the results of our research (13,14).

In our study, 82.4% had shortness of breath at admission. This was followed by tachycardia, cough, pleuritic chest pain, and hemoptysis. Similarly, in the article in which Dalen JE interpreted the results of the Prospective Investigation of PE Diagnosis study, it was stated that dyspnea was the most common disease in patients with PE, followed by tachypnea, tachycardia, chest pain, cough, and hemoptysis (15). Compared with the aforementioned large-scale study, the proportionally lower incidence of symptoms and findings other than shortness of breath may be because our patients were hospitalized in the internal medicine clinic and did not require intensive care. As mentioned before, the spectrum of clinical findings is highly variable depending on the severity of the disease (12). Although some studies found that symptoms were not associated with mortality, a study conducted by Zuin et al. (16) showed that acute onset dyspnea and chest pain were associated with mortality. Omar et al. (17) found that hospital admission for syncope was associated with the severity of pulmonary embolism.

Because the symptoms and clinical findings used in calculating these risk scores can be seen in many other diseases, and PE may present with different presentations, we believe that these scoring systems are not sufficiently effective in diagnosis and treatment decisions. Other studies have also reached the same results (18,19). Despite the diagnosis of PE in all our patients, the predictive features of these scoring systems are not up to the mark.

According to the modified Wells score, the diagnosis of PE was considered unlikely in 80.6% of the patients, and the diagnosis of PE was deemed unlikely in 40.7% of the patients. According to the modified Geneva score, PE diagnosis was highly likely in only 20.3% of the patients. In contrast to our study, Naderi et al.'s (20) study from 2023 found that the Geneva score used to assess the risk of PE was insufficient to predict mortality in patients diagnosed with PE. In the study conducted by Girardi et al. (18) with patients hospitalized in intensive care with a diagnosis of PE, these scoring systems were found to be unreliable in predicting the diagnosis. Ishimaru et al. (21) found that these clinical scores had low sensitivity in the diagnosis of PE and had limited prognostic values.

Our study found that the Modified Geneva score had a statistically significant relationship with long-term mortality. According to this score, no deaths among patients were considered low-risk. It was determined that the modified Wells and Wells scores did not have a significant relationship with mortality, consistent with previous studies. This can be attributed to the fact that there is no age in the Wells scoring system, and age is among the criteria in the Modified Geneva system.

Study Limitations

There are some limitations to our study. Because this was a retrospective study, the data were based on hospital information and operating system records. The study only reflects patients admitted to the internal medicine clinic; therefore, it excludes patients who are followed up in the intensive care unit with a more severe course. In addition, the small number of patients may reflect something other than the general population.

Conclusion

Pulmonary embolism is a disease that may have high mortality, and the possibility of missing a diagnosis is increased. However, risk stratification scores cannot provide the desired level of prediction when making a diagnosis. Novel scoring systems, or biomarkers, should be developed to prevent missed diagnoses and unnecessary examinations.

Ethics

Ethics Committee Approval: The study protocol and subject matter were reviewed and approved by the Institutional Ethics Committee of the University of Health Sciences (ref no./date: 243/2019).

Informed Consent: The ethics committee anonymized and approved the database information without needing consent.

Authorship Contributions

Concept: E.E., Design: E.H., Data Collection or Processing: E.E., E.H., Analysis or Interpretation: E.E., Literature Search: E.E., E.H., Writing: E.E., E.H.

Conflict of Interest: No conflicts of interest were declared by the authors.

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