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Research Article

USABILITY OF SATURATION/RESPIRATORY RATE AS A PARAMETER IN PULMONARY THROMBOEMBOLISM RISK SCORING

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ABSTRACT

Objective: The first step of pulmonary thromboembolism (PTE) treatment management is the risk classification. The most commonly used scoring system for this purpose is the pulmonary embolism severity index (PESI). However, the large number of parameters it contains limits its usability. Therefore, the need for easily accessible, fast and accurate resulting parameters continues. This study was planned to evaluate the role of Saturation/Respiratory Rate (SPO2/RR) in determining the risk group.

Materials and Methods: This study was conducted retrospectively in patients diagnosed with PTE between 01.01.2020 and 01.11.2022 in Dışkapı Yıldırım Beyazıt Training and Research Hospital Emergency Department. Sociodemographic characteristics, vitals, laboratory results and radiological images of the patients were examined through the in-hospital information management system.

Results: 188 patients were included in the study. The average age of the patients was 64.97±16.64 years. 107(56.9%) of the patients in the study were women. When patients were divided into groups according to early mortality risk, 35 patients (18.6%) were high risk; 31 patients (16.4%) intermediate-high risk;65 patients (34.5%) were in the intermediate-low risk group and 57 patients (30.5%) were in the low-risk group. SpO2/RR was found 3.29±0.82;3.97±0.60;4.50±0.92;5.00±0.77 respectively($p<0.001$). It was determined that SpO2/RR was a guide in determining the risk group.

Conclusion: Saturation/respiratory rate can be used to determine risk groups in acute PTE and is also a guide in determining treatment management and mortality.

Keywords: Mortality, Pulmonary embolism, Saturation/respiratory rate

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INTRODUCTION

Pulmonary thromboembolism is an important cause of mortality, and its incidence increases every year (1). Therefore, PTE maintains its importance as a global burden of illness.

The presenting clinic in acute PTE is variable. It may be the cause of cardiac arrest, or it may be diagnosed incidentally in imaging taken for another reason in an asymptomatic situation. Therefore, treatment management is also variable. The first step in determining treatment is to determine the patient's mortality risk. The most used scoring system for this purpose is the pulmonary embolism severity index (PESI). PESI was designed by Aujesky D et al in 2005 and includes 11 clinical predictive variables (2). PESI is not a fast and easily applicable scoring system because it contains many parameters. Therefore, the need for easily accessible, fast and accurate resulting parameters continues.

Measurement of oxygen saturation in air (SpO_2) with pulse oximetry is one of the most important parameters to be evaluated at the time of admission. Low oxygen saturation is a poor prognostic factor in PTE (3). Respiratory rate is another clinical parameter that should be evaluated in every patient. In acute PTE, hypoxia due to occlusion in the pulmonary artery subsequently causes vasoconstriction. This may result in an increase in right heart pressure and decompensation of the patient (4). Therefore, respiratory rate and saturation are guiding parameters in critical diseases (5). In a study conducted on intensive care patients, Fuentes et al. defined the respiratory rate as a parameter that can predict weaning failure by proportioning it to the oxygen level (6). It was stated by Myers et al. that it could predict intubation in COVID-19-related respiratory failure (7). In the light of these studies, evaluation of saturation and respiratory rate may be an early warning prognostic factor in PTE. For this purpose, the role of SpO_2/RR in risk group classification and treatment management were evaluated.

MATERIALS AND METHODS

This study was designed retrospectively in patients diagnosed with PTE in the Emergency Department of Dışkapı Yıldırım Beyazıt Training and Research Hospital, as a single center. Because the study was designed retrospectively, no written informed consent form was obtained from patients. Artificial intelligence (AI) technology was not used in this study. Ethics committee approval was obtained with the decision of Ankara Etlik City Hospital Clinical Research Ethics Committee dated 16.08.2023 and numbered AEŞH-EK1-2023-431, and it was conducted by following the ethical principles determined by the Declaration of Helsinki.

Patients under 18 years of age and over 90 years of age, pregnant women, those who previously used long-term oxygen therapy due to respiratory failure, those with decompensated congestive heart failure, those with contraindications to thrombolytic therapy, and patients with missing data were excluded from the study. In addition, patients who developed acute respiratory failure due to pulmonary thromboembolism were included in the study, but patients who had previously used NIMV and LTOT due to chronic respiratory failure were excluded from the study.

Demographic characteristics of the patients such as age and gender, additional diseases, symptoms at the time of admission, vital values, imaging tests (chest radiography, computed tomography pulmonary angiography), transthoracic echocardiography findings, laboratory values (complete blood count, biochemical tests, coagulation tests, D-dimer, Pro-BNP, troponin, blood gas values) and medical treatments were examined through HIMS and the Ministry of Health E-Pulse System. While evaluating the right ventricular dysfunction findings of the patients, right ventricular width and sPAP were examined. The sPAP values were divided into 4 separate groups as 24 and below, 25-35, 36-50 and over 50. The 30-day mortality of the patients was recorded.

PESI and sPESI (simplified PESI) indexes were used to determine risk groups by examining the comorbidities, vitals, blood tests, computed tomography images and echocardiography findings of the patients. Additionally, according to the current guideline of the European Society of Cardiology, patients were divided into risk classes as low risk, intermediate-low risk, intermediate-high risk and high risk in terms of early mortality. The saturation and respiratory rate which are the two criteria for the calculation of PESI and measured from the fingertip of these patients at the time of admission were evaluated. Patients' SpO_2/RR values, risk groups, vital signs were examined according to mortality status and treatment applied, and it was checked whether there was a statistically significant difference between the groups.

Statistical Analysis

The data were analyzed using Statistical Package for the Social Sciences (SPSS) 25.0 (IBM SPSS Statistics for Windows, Armonk, NY: IBM Corp.). The suitability of the variables to normal distribution was examined using visual (histogram and probability graphs) and analytical methods (Shapiro-Wilk test-Kolmogorov Smirrnov test), and parametric tests were used in normal distribution and non-parametric tests were used in non-normal distribution. Descriptive statistics were expressed as mean and standard deviation in normally distributed numerical data, median and minimum-maximum range in non-normally distributed data, and number and percentage in nominal data. Numerical variables that did not show normal distribution were analyzed using the "Mann Whitney U test" between two groups and the "Kruskal Wallis" between three groups. Nominal data were evaluated between the two groups using the “Pearson Chi-square test” or “Fisher's Exact test”. Spearman Correlation analysis was used to examine the relationship between numerical variables. In the analysis, a p-value < 0.05 was considered statistically significant. In ROC analysis, the area under the curve (AUC) was evaluated and the data were expressed with a 95% confidence interval.

Table 1. Distribution of patients according to socio-demographic characteristics and risk classifications

		All patients 188 (100%) ***N(%) Mean±sd***
Age, years		64.97±16.64
Gender	Women	107 (56.9%)
	Men	81 (43.1%)
Acquired risk factor		174 (92.6%)
	Immobilization	87(46.3%)
Comorbidity		128 (68.1%)
	Hypertension	73 (38.8%)
	Diabetes Mellitus	40 (21.3%)
	COPD*	30(15.9%)
Symptoms		185 (98.4%)
	Shortness Of Breath	149 (79.3%)
	Chest Pain	101 (53.7%)
PESI classification	Low risk	67 (35.6%)
	Medium risk	44 (23.4%)
	High risk	77 (41%)
sPESI classification	Low risk	58 (30.9%)
	High risk	130 (69.1%)
Evaluation of groups according to early mortality risk	Low risk	56 (29.7%)
	Medium-low risk	64 (34.0%)
	Medium-high risk	32 (17.0%)
	High risk	36 (19.1%)

* Chronic obstructive pulmonary disease

RESULTS

188 patients were included in the study. The average age of the patients was 64.97±16.64. The demographic characteristics and the risk group of the patients are given in Table 1. Table 2 shows the patients’ blood tests, vitals, transthoracic echocardiography (TTE) findings and SPO_2/RR values which are evaluated during emergency department admission.

The patients were grouped by measuring the sPAP values of the patients with echocardiography (Table 2). The sPAP values were divided into 4 separate groups as 24 and below, 25-35, 36-50 and over 50. Each of these subgroups was compared separately according to the risk groups to evaluate whether there was a significant difference.

According to the statistical analysis between the SPO_2/RR, PESI and Early Mortality Risk Classes sub-groups, each sub-group varied significantly with one other. As the risk classification progressed towards higher levels, SpO_2/RR decreased significantly (Table 3).

The correlation analysis between saturation/respiratory rate and vital signs is shown in Table 4. A positive linear relationship was detected between SpO_2/RR and systolic and diastolic blood pressure. A moderate negative linear relationship was detected between SpO_2/RR and pulse.
Saturation/respiratory number was found to be lower in patients with reperfusion treatment, while higher in patients who did not need thrombolytic treatment (Table 5). There was a significant difference between the groups (p<0.001). With 80.6% sensitivity and 78.8% specificity, SpO_2/RR cut off value was determined as 3.7. SpO_2/RR was

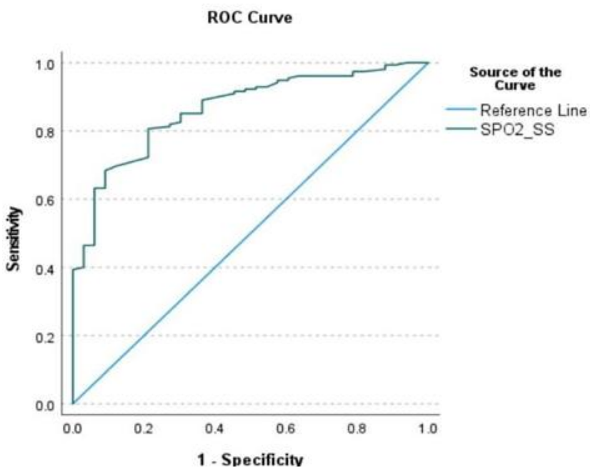

Figure 1. Roc analysis in mortality prediction of saturation/respiratory rate in pulmonary thromboembolism

Table 2. Evaluation of patients' admission vitals, laboratory tests and transthoracic echocardiography findings according to risk groups

	All patients (N=188) ***N(%)*** ***Mean±sd***	**High risk (N=36)** ***N(%)*** ***Mean±sd***	**Medium-high risk (N=32)** ***N(%)*** ***Mean±sd***	**Medium-low risk (N=64)** ***N(%)*** ***Mean±sd***	**Low risk (N=56)** ***N(%)*** ***Mean±sd***	**P value***
Systolic blood pressure (mmHg)	118±23	91±19	122±21	123±20	126±19	*<0.001*
Diastolic blood pressure (mmHg)	70±12	58±11	75±13	71±10	75±9	*<0.001*
Pulse (beats/min)	99±20	113±21	103±21	98±21	91±15	*<0.001*
Respiratory rate	21±4	25±4	22±3	20±3	19±2	*<0.001*
Saturation	87±8	79±10	86±6	87±6	93±3	*<0.001*
Saturation/ respiratory rate	4.34±1.01	3.29±0.82	3.97±0.60	4.51±0.95	5.00±0.77	*<0.001*
Lactate (mg/dL)	2.78±2.51	5.08±4.65	2.91±1.54	2.23±1.09	1.84±0.66	*<0.001*
D-Dimer (μg/mL)	7.75±6.79	10.75±7.04	10.54±6.73	7.93±6.98	4.17±4.56	*<0.001*
Right Spaces						
Normal	99(52.7%)	0	9	45	45	*<0.001*
Slightly wide	38(20.2%)	2	10	14	12	*<0.001*
Wide	51(27.1%)	33	12	6	0	*<0.001*
sPAP**						
<25 mmHg	46(24.5%)	0	0	14	31	*<0.001*
25-35 mmHg	60(31.9%)	3	7	31	23	*<0.001*
36-50 mmHg	41(21.8%)	9	13	16	3	*<0.001*
>50 mmHg	41(21.8%)	23	11	4	0	*<0.001*

** Kruskal Wallis-H Test was applied. **sPAP: Systolic pulmonary artery pressure*

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treatment (AUC: 0.863, 95 %CI 0.803-0.924, p <0.001). ROC analysis was given in Figure 1. 21 (11%) of the patients included in the study died within 30 days of follow-up. When the risk groups of the deceased patients were evaluated, 9 patients (25%) were in the high-risk group, 7 patients (21.8%) were in the intermediate-high risk group, and 5 patients (7.8%) were in the intermediate-low risk group. It was observed that there were no deceased patients in the low-risk group.

Table 3. Evaluation of saturation/respiratory rate according to risk groups

		Saturation/ respiratory rate (Min-Max)	p value
PESI risk classification	High risk	3.67 (1.43-6.64)	*0.004**
	Medium risk	4.50 (3.33-5.81)	
	Low risk	5.06 (3.46-7)	
sPESI risk classification	High risk	4.00 (1.43-6.64)	*<0.001**
	Low risk	5.08 (3.54-7)	
Classification according to early mortality risk	High risk	3.42 (1.43-5.28)	*<0.001**
	Medium high risk	3.91 (2.36-5.5)	
	Medium low risk	4.50 (2.11-6.64)	
	Low risk	5.11 (3.54-7)	

** Kruskal Wallis-H Test was applied. ** Mann-Whitney U analysis was applied.*

When the saturation/respiratory number was evaluated according to mortality, it was found to be lower in deceased patients. There was a significant difference between the groups (p=0.003) (Table 5). With 68.3% sensitivity and 71.4% specificity, SpO_2/RR cut off value was determined as 3.9. SpO_2/RR was found to be decisive in mortality estimation (AUC: 0.702, 95 %CI 0.593-0.812, p <0.001). ROC analysis was given in Figure 2.

Table 4. Correlation analysis results between saturation/respiratory rate and vital signs

	Systolic blood pressure	Diastolic blood pressure	Pulse	Respiratory rate
SpO2/RR*	r 0.262	r 0.177 p<0.001	r -0.346 p<0.001	r -0.954 p<0.001

* SpO2/RR: Saturation/respiratory rate. Spearmen correlation analysis was performed.

DISCUSSION

Pulmonary thromboembolism is a cardiovascular emergency that develops as a result of varying degrees of obstruction of the pulmonary arteries. The clinical picture varies depending on the degree of obstruction in the vascular bed. It may result in sudden death, or it may be encountered incidentally during imaging taken for another reason in an asymptomatic condition. The risk of 30-day mortality should be evaluated to make the treatment approach correctly. The most commonly used scoring systems in this prognostic assessment are the PESI and sPESI. The fact that these risk classification systems contain multiple parameters restricts the use of physicians. Therefore, the need for easily accessible, fast and accurate resulting parameters continues. This study was designed to evaluate the usability of SpO_2/RR in risk classification.

Acute PTE is often considered a disease of old age (8). In our study, the average age of the patients was 64.9 years. Although the clinical picture in acute PTE is variable, the most common symptoms are shortness of breath and chest pain (9). In our study, the most common symptoms were shortness of breath and chest pain.

Table 5. Evaluation of saturation/respiratory rate according to reperfusion therapy and mortality status

		SpO_2/RR* Median (Min-Max)	p value**
Treatment	Reperfusion therapy *N=33 (%17.6)*	3.42 (2.80-3.75)	***<0.001***
	Absence of reperfusion *N=155 (%82.4)*	4.50 (3.91-5.28)	
Mortality Status	Ongoing survival *N=167 (%89)*	4.50 (3.71-5.22)	***0.003***
	Mortality recorded *N=21 (%11)*	3.73 (3.29-4.15)	

**SpO_2/RR: Saturation/respiratory rate ** Mann-Whitney U analysis was applied.*

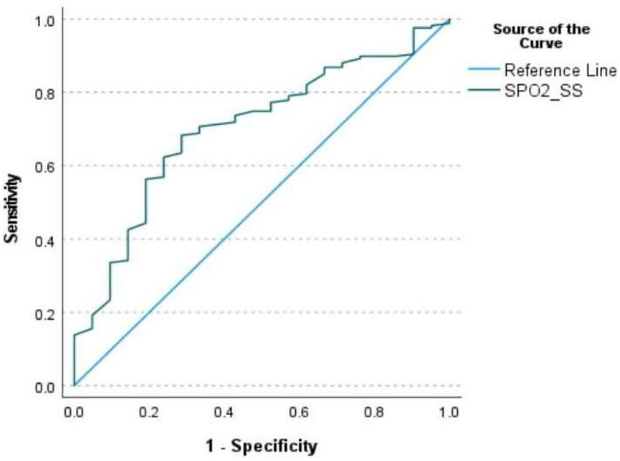

Figure 2 ROC Analysis in Mortality Prediction of Saturation/Respiratory Rate in Pulmonary Thromboembolism

The development of right ventricular dysfunction in intermediate and high-risk PTE may cause a decrease in cardiac output. This may disrupt renal perfusion and cause an increase in urea. In the study conducted by Gök et al., right ventricular dysfunction was associated with intra -hospital mortality (10). Our study also showed that high-risk patients had renal dysfunction. This condition was associated with right ventricular dysfunction.

In the meta-analysis conducted by Wang et al., it was stated that lactate level was associated with short- and long-term mortality, but it was stated that more studies were needed to evaluate it according to risk groups (11). In our study, lactate was observed to be significantly higher in the high-risk group. Hypoxia due to vascular obstruction in PTE is associated with increased lactate and may be a guide in determining the risk groups of patients.

D-dimer is one of the fibrin degradation products which is formed as a result of the endogenous fibrinolytic system breaking down the thrombus. It is frequently used in the diagnosis and exclusion of PTE along with clinical probability scores. However, it has been reported that d-dimer is higher in patients with high thrombus burden and reported to be predictive of right ventricular dysfunction (12). In our study, when patients were separated according to risk groups, it was observed that d-dimer levels were lower in low-risk PTE, where thrombus burden was less.

Brain natriuretic peptide and NT-proBNP are released as a result of increased ventricular filling pressure or in cases of myocardial ischemia. Elevated natriuretic peptide levels in acute PTE are associated with right ventricular (RV) dysfunction. Chen et al. stated that NT-proBNP is a very sensitive marker in determining RV dysfunction and mortality, and if it is detected low, mortality is significantly reduced (13). In the study conducted by Chen et al., it was stated that proBNP was higher in high-risk PTE patients and could be used in treatment management (13). In our study, NT-proBNP levels were found to be lower in the intermediate-low and low-risk groups. Because it is associated with right ventricular dysfunction, it can be used in treatment management in intermediate-high and intermediate-low risk groups.

In acute PTE, perfusion decreases because of occlusion of the vascular bed. This results in hypoxemia and reduced oxygen supply to tissues (14). Additionally, mechanical occlusion of the vascular bed by thrombus causes hypoxic vasoconstriction of the pulmonary arterial system. This results in an increase in pulmonary vascular resistance (PVD) and pulmonary artery pressure (PAP). A sudden increase in PAP may cause dilation and dysfunction in the RV, resulting in hypotensive shock (15). Therefore, hypoxia is a poor prognostic factor in acute PTE (16). In our study, saturation was observed to be lower in the high-risk group, while it was higher in the low-risk group. Respiratory rate is the first parameter that should be evaluated in every patient presenting with shortness of breath. It is also included as a component in PESI. Tachypnea is associated with adverse outcomes in patients with PTE (2). In the study conducted by Becattini et al., it was stated that respiratory rate was a guide in grouping intermediate-risk PTE patients as intermediate-low and intermediate-high (4). In our study, it was shown that the respiratory rate was lower in low-risk patients.

In 2019, Roca et al evaluated saturation and respiratory rate in determining the need for intubation in patients with acute hypoxemic respiratory failure due to pneumonia and monitored with high-flow nasal oxygen. They defined the ratio of these two parameters as the ROX index and described it as a parameter that can be easily used at the bedside to determine the need for intubation (17). It was later defined as an important parameter that should be evaluated in critical diseases (6,7). In his study, Jolobe pointed out that respiratory rate is a guiding parameter and its accurate measurement in patients with suspected pulmonary embolism (18). In our study, when patients were divided into groups according to risk groups, the increase in SpO_2/RR was associated with low-risk disease. There was a significant difference between the groups when evaluated according to both PESI and early mortality risk. SpO_2/RR is a simple, easily applicable parameter that should be evaluated in each patient and can be used to determine risk classification.

In high-risk PTE associated with hemodynamic instability, deaths usually occur within the first hours. There is still a need for parameters that can be applied quickly and provide accurate results in the detection of these patients. In the study conducted by Vedovati et al., the ratio of oxygen saturation to respiratory rate was called respiratory index and was shown to be an independent determinant of mortality in hemodynamically stable PTE patients (19). When the patients who received reperfusion therapy were examined, it was seen that SpO_2/RR was lower. In addition, SpO_2/RR was lower in mortal patients and higher in surviving patients and was a guide for mortality evaluation.

Our study has some limitations. Although we excluded patients with previously known heart failure, previous TTE findings of the patients included in the study were mostly unknown, so it is not clear whether right ventricular dysfunction is associated with acute pulmonary thromboembolism. In addition, due to its retrospective design, the respiratory rate was obtained by scanning the files and it was not known for how many seconds it was evaluated. An evaluation could not be made between the rate at which the respiratory rate returned to normal and mortality. The fact that it was performed in a single center is another situation that causes limitations. Supporting it with multicenter studies will increase the value of our study.

CONCLUSION

As a result, SpO_2/RR, which includes the first parameters that should be evaluated in every patient presenting with respiratory distress, can be an important early warning risk factor both in determining the risk group and management of treatment and in determining mortality in acute PTE patients. This parameter, which is easily and quickly applied with the advantage of being evaluated at the bedside, can be used in emergency departments.

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Authorship contributions
The study was conceived by M.A., F.Y., and E.U. The design was developed by M.A., E.A., and E.U. Data collection and processing were carried out by E.A., M.A., and A.T.Ç. Analysis and interpretation were performed by A.T.Ç., E.A., and Ö.F.T. The literature review was conducted by F.Y., E.U., and A.T.Ç. The manuscript was written by M.A., F.Y., and Ö.F.T. All authors provided feedback on earlier drafts of the manuscript and approved the final version.

Data availibity statement
Data available on request.

Declaration of competing interest
The authors declare that there is no conflict of interest.

Ethics
Ethics committee approval was obtained with the decision of Ankara Etlik City Hospital Clinical Research Ethics Committee dated 16.08.2023 and numbered AEŞH-EK1-2023-431.

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