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The red cell distribution width to platelet ratio predicts 30−day mortality of acute pulmonary embolism patients

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ABSTRACT

Objective: To specify the clinical and sociodemographic characteristics, risk factors, factors affecting mortality including hematologic parameters, and red blood cell distribution width to platelet ratio (RPR) in patients with pulmonary thromboembolism, and to reduce the mortality. **Methods**: The archive records of patients diagnosed with pulmonary embolism were retrospectively examined. The histories, risk factors, physical examination findings, arterial blood gas analysis, X-rays, laboratory, and computed tomography reports of all cases were obtained *via* the hospital information system. Logistic regression analysis was performed to determine the independent variables affecting early mortality. **Results**: A total of 146 patients with a definitive diagnosis of pulmonary thromboembolism were included. Thirteen point seven percent (n=20) of the deceased patients died at early term. Ninety percent of patients with early mortality was 65 years or older. There were significantly differences in age, RPR, D-dimer, creatinine, lymphocyte, pH, and body temperature between patients with and without early mortality (P=0.017, P<0.001, P=0.019, P=0.025, P=0.042, P=0.013, P=0.017, respectively). Logistic regression analysis showed that RPR was a statistically significant and independent risk factors of mortality [P=0.026, OR: 0.254., 95% CI (0.326-5.056)]. In addition, there was a significant difference in pulmonary embolism severity index classification between patients with and without early mortality(P<0.034). **Conclusions**: RPR is an independent risk factor of mortality of pulmonary embolism patients and may help emergency physician to stratify mortality risks of pulmonary embolism patients.

1. Introduction

Acute pulmonary embolism has an essential role among emergency visits due to its morbidity and mortality[1]. Pulmonary embolism occurs due to deep venous thrombosis caused by venous stasis, hypercoagulability and vessel damage[2]. It is known that the clinical properties of the patients with acute pulmonary embolism are related to mortality[3]. It has been reported that acute pulmonary embolism has a higher mortality rate in the elderly than young patients[4]. Early diagnosis and treatment has shown to be the most critical components in reducing the mortality and morbidity of pulmonary embolism[5]. Previous studies showed immobility, tachycardia, hypotension, troponin T elevation, underlying coronary artery disease, cerebrovascular disease, massive-size pulmonary embolism, bilateral pulmonary embolism, possible pulmonary embolism in Wells scoring, and possible pulmonary embolism in Modified Geneva scoring to be related with early mortality[6]. Other

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studies on this subject showed that the most common symptom was dyspnea and the most critical risk factor was immobility[7].

It has been suggested that red blood cell distribution width to platelet ratio (RPR) is a new biomarker that can be used to demonstrate the severity and mortality of various diseases. For instance, Xie *et al*.[8] have reported that RPR can be used as a biomarker in describing the activity of systemic lupus erythematosus in their recently published studies. Cetinkaya *et al*. have also shown that RPR can be used to demonstrate mortality of acute pancreatitis[9]. Chen *et al*. found that RPR is a strong predictor of the degree of fibrosis and cirrhosis in patients with chronic hepatitis[10]. Pusuroglu *et al*. investigated the 1-year mortality of ST-segment elevation myocardial infarction. The authors showed that high RPR at admission was an independent predictor of this[11].

From these examples, RPR has been shown to be a useful biomarker in demonstrating inflammation in various diseases. However, according to our knowledge, there is currently no published article on the use of RPR to show the early mortality of pulmonary embolism. With this article, we intended to specify the clinical and sociodemographic characteristics, risk factors and the factors affecting mortality including hematologic parameters in patients with pulmonary thromboembolism. Our primary goal was to contribute to the reduction of mortality.

2. Materials and methods

We performed this study after obtaining the ethics committee approval from Baskent University Institutional Review Board for Medicine and Health Sciences (Project Number: KA15/301).

We retrospectively examined the archive records of patients diagnosed with pulmonary embolism between January 2011 and December 2015 in Baskent University Ankara Hospital's Adult Emergency Department. We obtained the histories, risk factors, physical examination findings, arterial blood gas analysis, conventional X-rays, hematologic & biochemical test results, and computed tomography reports of all cases *via* the hospital information system. We defined the deaths within the first 30 d after emergency visit as early mortality.

We analyzed the data with "SPSS 17.0 for Windows" program, and expressed the demographic data with the number of patients (n) and percentage (%). We used the χ^2 test to compare categorical groups; Kolmogorov-Smirnov test to check the normal distribution of continuous variables. We compared continuous variables by using the Mann-Whitney U test and Student's t-test. logistic regression analysis was did to investigate the factors affecting mortality. The value of $P<0.05$ was considered to be statistically significant.

3. Results

3.1. General information

The universe of our study consisted of 147 719 patients who applied to the adult emergency department of Baskent University Ankara Hospital between January 1st 2011 and December 31th 2015. Preliminary diagnosis of 2 398 of these patients was pulmonary thromboembolism. We included 146 patients with a definitive diagnosis of pulmonary thromboembolism.

Of the participants, 59.6% were female (n=87). Sixty-five percent (n=95) of the patients were 65 years and over, and the remaining 35% (n=51) were in the 18-64 age group. Thirty-one point five percent (n=46) pulmonary embolism patients died. Accordingly, 13.7% (n=20) of the deceased patients died early term. Ninety percent of patients with early mortality was 65 years or older.

Fifty-five percent of the patients with early mortality were male, and the majority of the patients were female (61.9%) in the other group.

3.2. Risk factors of the patients

Immobility, malignancy, smoking and cardiovascular disease were the most common risk factors for pulmonary embolism. We also found significant difference in age and immobility between patients with and without early mortality (P=0.034 and P=0.003, respectively).

3.3. Co-morbidities

There was statistically significant difference in occurrence of arterial oxygen saturation below 90% between patients with and without early mortality (P=0.084) (Table 1).

The most common symptoms in patients with early mortality were dyspnea, change of consciousness and syncope. Hypertension, Alzheimer's and chronic obstructive pulmonary disease (COPD) were the most common concomitant diseases of pulmonary thromboembolism in this group (Table 2).

Concerning diseases associated with pulmonary embolism, there was statistically significant difference in morbidity of COPD and Alzheimer's disease between patients with and without early mortality (P=0.033 and P=0.017, respectively). Also, the occurrence of symptoms of chest pain, syncope, back pain and change of consciousness were also significant between patients with and without early mortality (P=0.016, P=0.002, P= 0.025, $P<0.001$, respectively) (Table 3).

Table 1

Hemodynamic-laboratory parameters and intensive care needs of patients regarding early mortality [*n*(%)].

Parameters	Early mortality (+) (*n*) (%)	Early mortality (-) (*n*) (%)	Total (*n*) (%)	*P*
Tachycardia (> 120/min)	8 (40.0)	41 (32.5)	49 (33.5)	0.172
SaO_2<90%	7 (35.0)	33 (26.2)	40 (27.3)	<0.001
Intensive Care Needs	16 (80.0)	28 (22.2)	44 (30.1)	0.649

Early mortality (+): The deaths within the first 30 d after emergency visit. Early mortality (-): No deaths within the first 30 d after emergency visit.

Table 2

Symptoms of patients regarding early mortality [*n*(%)].

Symptoms	Early mortality (+) (*n*) (%)	Early mortality (-) (*n*) (%)	Total (*n*) (%)	*P*
Dyspnea	13 (65.0)	87 (69.0)	100 (68.5)	0.714
Chest pain	1 (5.0)	39 (31.0)	40 (27.3)	0.016
Syncope	3 (15.0)	2 (1.6)	5 (3.4)	0.002
Back pain	-	26 (20.6)	26 (17.8)	0.025
Near syncope	1 (5.0)	4 (3.2)	5 (3.4)	0.677
Palpitation	2 (10.0)	7 (5.6)	9 (6.16)	0.443
Swelling of the leg	-	6 (4.8)	6 (4.10)	0.319
Consistency in arms	-	1 (0.8)	1 (0.06)	0.689
Weakness	-	2 (1.6)	2 (0.01)	0.570
Leg pain	-	6 (4.8)	6 (0.04)	0.319
Change of consciousness	6 (30)	4 (3.2)	10 (0.6)	<0.001
Hemoptysis	1 (5.0)	7 (5.6)	8 (0.05)	0.919

Early mortality (+): The deaths within the first 30 d after emergency visit. Early mortality (-): No deaths within the first 30 d after emergency visit.

Table 3

Comorbidities of patients regarding early mortality [*n*(%)].

Comorbidities	Early mortality (+) (*n*) (%)	Early mortality (-) (*n*) (%)	Total (*n*) (%)	*P*
Diabetes mellitus	3 (15.0)	28 (22.2)	31 (0.21)	0.514
Hypertension	13 (65.0)	56 (44.4)	68 (0.46)	0.087
Congestive heart failure	3 (15.8)	8 (6.4)	11 (0.07)	0.151
Asthma	2 (10.5)	9 (7.3)	11 (0.07)	0.619
COPD	5 (25.0)	11 (8.7)	16 (0.10)	0.033
Coronary artery disease	4 (20.0)	17 (13.5)	21 (0.14)	0.450
Chronic kidney disease	-	3 (2.4)	3 (0.02)	0.495
Cerebrovascular event	-	6 (4.8)	6 (0.04)	0.329
Alzheimer's disease	6 (30.0)	14 (11.1)	20 (0.13)	0.017

Early mortality (+): The deaths within the first 30 d after emergency visit. Early mortality (-): No deaths within the first 30 d after emergency visit.

3.4. Laboratory results

Table 4 showed vital signs, laboratory, and blood gas analysis results of pulmonary embolism patients according to early mortality status. According to this table, there was a significant difference in age, RPR, D-dimer, creatinine, lymphocyte, pH, body temperature between patients with and without early mortality (*P*=0.017, *P*<0.001, *P*=0.019, *P*=0.025, *P*=0.042, *P*=0.013, *P*=0.017, respectively).

We performed logistic regression analysis (age, RPR, D-dimer, creatinine, lymphocyte, body temperature) to determine the independent variables affecting early mortality. We found that none of them independently affected mortality, except RPR. We found RPR to be an independent predictor of mortality (*P*=0.022)(Table 5).

We compared Wells Scores (low, medium, high-risk groups) of pulmonary embolism patients with early mortality. There was no statistically significant difference between Wells scores of patients (*P*=0.111) in terms of early mortality.

Table 6 showed pulmonary embolism severity index (PESI) and the simplified PESI (sPESI) classifications of pulmonary embolism patients according to early mortality status. There was a statistically significant difference in risk of PESI classification between patients with and without early mortality (*P*=0.034). There was no statistically significant difference in sPESI classification (*P*=0.088).

Table 4

Vital signs, laboratory, and blood gas analysis results of pulmonary embolism patients according to early mortality status.

Parameters	Early mortality (+)	Early mortality (-)	*P*
Systole (mmHg)	146.5 ± 35.97	132.62 ± 25.08	0.036
Diastole (mmHg)	88.66 ± 27.00	70.74 ± 15.85	0.379
Leucocyte (10^3/μL)	13.07 ± 3.52	10.56 ± 3.44	0.966
PO_2 (mmHg)	63.14 ± 21.75	58.19 ± 19.69	0.244
PCO_2(mmHg)	33.46 ± 11.90	33.34 ± 9.23	0.740
Age (years)	82.50 ± 18.00	72.50 ± 28.00	0.017
RPR	0.11±0.10	0.07±0.30	<0.001
D-dimer (μg/mL)	13.29 (15.30)	2.81 (7.60)	0.019
Creatinine (mg/dL)	1.23 (0.94)	0.88 (0.36)	0.025
Platelet (10^3/μL)	258.0 (214.0)	228.5 (115.5)	0.162
Lymphocyte (10^3/μL)	2.04 (3.83)	1.56 (0.87)	0.042
PLR	132.52 (126.30)	135.58 (126.07)	0.532
Lactate (mmol/L)	1.60 (1.40)	1.35 (1.08)	0.481
pH	7.44 (0.05)	7.45 (0.06)	0.013
Body temperature (℃)	36.00 (2)	36.50 (1)	0.017

Early mortality (+): The deaths within the first 30 d after emergency visit. Early mortality (-): No deaths within the first 30 d after emergency visit. PO_2: Partial oxygen pressure; PCO_2: Partial carbon dioxide pressure; PLR: Platelet to lymphocyte ratio. Data not normally distributed were given as Median (IQR). Normally distributed data were given as mean ± standard deviation.

Table 5

Logistic regression analysis of variables affecting early mortality.

Variables	*P* value	*OR*	95% CI
Age	0.52	0.075	-0.075-0.146
Creatinine	0.72	-0.044	-0.120-0.084
RPR	0.02	0.254	0.326-5.056
Lymphocyte	0.98	-0.003	-0.071-0.069
D-dimer	0.10	0.204	-0.002-0.023
pH	0.31	-0.130	-1.420-0.459
Body temperature	0.07	-0.226	-0.206-0.008

Table 6

PESI and sPESI classifications of pulmonary embolism patients according to early mortality status [*n*(%)].

Classification		Early mortality (+)	Early mortality (-)	*P*
PESI	Class 1	-	26 (20.6)	0.034
	Class 2	5 (25.0)	25 (19.8)	
	Class 3	3 (15.0)	26 (20.6)	
	Class 4	5 (25.0)	24 (19.0)	
	Class 5	7 (35.0)	25 (19.8)	
sPESI	Low risk	3 (15.0)	43 (34.1)	0.088
	High risk	17 (85.0)	83 (65.9)	

Early mortality (+): The deaths within the first 30 d after emergency visit. Early mortality (-): No deaths within the first 30 d after emergency visit.

4. Discussion

The results of our study revealed that 90% of patients with early mortality were 65 years or older. Male gender was higher in patients with early mortality and women in the other group. Cugno *et al*. reported that the number of male patients (M/F=15/12) was higher in the mortality group. In the same study, the average age of the patients in the early mortality group [73.0 (13.5)] was higher than the other group [69.2 (15.5)][12]. The results of our study are consistent with the literature in terms of more upper mean age in the group with early mortality, and more frequently observed in the male gender.

In our study, the most common comorbidities in patients with pulmonary thromboembolism were hypertension, Alzheimer's disease, and COPD. Ciftci *et al*. also showed that 38.9% of patients with pulmonary embolism had hypertension and 8.5% had COPD[13]. Likewise, the most common comorbidities in the study of Aydogdu *et al*. are hypertension, COPD, Alzheimer's disease, diabetes mellitus, coronary artery disease, malignancy, cerebrovascular disease, and congestive heart failure[14]. Similar to our study, Friz *et al*. found a relationship between chronic cardiopulmonary disease and 30-day mortality[4]. In the light of this information, the results of our study were compatible with the literature regarding comorbidities.

Altinsoy *et al*. reported no significant association between 30-day mortality and syncope in patients diagnosed with pulmonary embolism[15]. In our study, 15% of the group with early mortality had syncope, and 30% of them had consciousness changes. We think that this difference may be due to the inadequacy of the clinically more serious patient to express the symptoms.

Akgullu *et al*. found that D-dimer and creatinine levels were significantly higher in the mortality group compared to the survival group[16]. Similarly, in our study, these two values were high in the mortality group. In the study of Labyk *et al*., systolic blood pressure was lower in the mortality group[17]. Conversely, in our study, systolic blood pressure was higher in the early mortality group. We think that this difference is due to the investigation of 30-day mortality rather than instant mortality in our study.

In our study, there was a statistically significant difference in risk of PESI classification between patients with and without early mortality (*P*=0.034). Similarly, in the study of Batt *et al*., The PESI risk classes (I to V) were significantly correlated with mortality rates of 3, 7, 30 and 90 d. Besides, sPESI has no less predictive features compared to PESI. Based on this, the authors concluded that the simplified version of the PESI might be of high benefit in daily clinical use[18]. In this study, early mortality was not observed in the sPESI low-risk group, whereas in our study, in the group with early mortality, the sPESI classification of 3 patients was low risk. We think that this difference is due to the underlying comorbidities of the patient.

Red cell distribution width has been shown as a biomarker in Zorlu *et al*.'s study to show early mortality and hemodynamic deterioration in acute pulmonary thromboembolism[19]. Mirdania *et al*. found that the degree of chronic liver fibrosis was significantly related to the RPR found by dividing red cell distribution width into platelets[20]. Bekmez *et al*. showed that RPR could be used in the diagnosis and follow-up of patent ductus arteriosus[21]. Besides, Hira *et al*. found no significant difference in RPR values in osteoarthritis patients compared to the control group[22].

Qiu *et al*. found that elevated levels of RPR on Day 3 and Day 7 were associated with 90-day mortality in burn patients. They also showed that RPR is an independent risk factor on mortality[23]. Bilgin *et al*. showed that RPR could be used as a biomarker for

colorectal cancers, especially right-sided[24].

Based on the results of our study, we suggest that RPR can be used safely in demonstrating early mortality in patients with pulmonary embolism without any additional cost. The emergency physicians always need rapid laboratory tests, which do not cause patient discomfort. Since RPR has these characteristics, it can provide the emergency physicians with the idea of predicting the mortality of pulmonary embolism. Considering that the most critical step in preventing the mortality and morbidity of pulmonary embolism is early diagnosis and treatment, this idea will lead to significant contributions.

In conclusion, pulmonary embolism is a preventable disease with early diagnosis and appropriate treatment. The results of our study showed that RPR is an independent risk factor for predicting mortality due to pulmonary embolism. We believe that this rate measured in the complete blood count within minutes can provide essential clues to the emergency physicians.

Conflict of interest statement

The authors report no conflict of interest.

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