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Original Article

Association of Inflammatory Markers with Mortality in Patients Hospitalized with Non-massive Pulmonary Embolism

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Abstract

OBJECTIVE: Pulmonary embolism (PE) is a serious pathology with high rates of morbidity and mortality. Studies regarding the efficacy of new inflammatory markers as a predictor of mortality in PE have thus far been limited. This study aimed to evaluate the predictive value of platelet/lymphocyte ratio (PLR), neutrophil/lymphocyte ratio (NLR), platelet/mean platelet volume (PLT/MPV), and C-reactive protein (CRP) on short-term and long-term mortality in patients with PE.

MATERIAL AND METHODS: A retrospective, observational cohort study was carried out in a tertiary teaching hospital. Patients with PE hospitalized in the pulmonology ward were enrolled. Their characteristics, hemogram parameters, PLR, NLR, CRP levels, PLT/MPV on admission, and mortality were recorded. The predictive accuracies of inflammatory markers were determined through receiver operating characteristic curves. The risk factors for mortality were further analyzed with Cox regression analysis.

RESULTS: A total of 828 patients with PE were included in the study. The 1-month mortality was 1%, and the 1-year mortality was 8.5%. An NLR value above 6 was associated with an almost 13-fold increase in short-term (30-day) mortality. We found that an NLR above 3.15 and age were independent risk factors for long-term (1-year) mortality. The other inflammatory markers, namely PLR and CRP, were not found to be associated with long-term mortality.

CONCLUSION: PE is a serious condition in the elderly. Elevated NLR values appear to be a good and feasible predictor of inflammation, which can be correlated with higher mortality over both the short-term and long-term periods.

KEYWORDS: Pulmonary embolism, mortality, inflammatory markers

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INTRODUCTION

Pulmonary embolism (PE) is a serious condition leading to high morbidity and mortality. Despite substantial progress in the diagnosis and treatment of acute PE, mortality remains high. The short-term, in-hospital, 30-day mortality varies from 2%-95% depending on the severity, although some recent studies have reported mortality to be 6%-18% [1-6]. There is relatively limited data on long-term mortality with PE, but these are reported to be between 12% and 19% [7-10]. Identifying prognostic markers for patients at greater risk of death is crucial for close monitoring and possible prevention of these deaths [1].

Inflammation and platelet activation play a major role in the pathophysiology and prognosis of PE. Platelet/lymphocyte ratio (PLR), neutrophil/lymphocyte ratio (NLR), and platelet/mean platelet volume (PLT/MPV) are new inflammatory markers that reflect systemic inflammation. High PLR and NLR are associated with a worse prognosis in some populations [11-14]. Studies regarding the utility of using these new inflammatory markers as a predictor of mortality in PE have thus far been limited and have been conducted with small population groups [10].

We hypothesized that elevated PLR and NLR levels are associated with a high mortality rate in PE. This study aimed to investigate the predictive ability of PLR, NLR, PLT/MPV, and C-reactive protein (CRP) on short-term and long-term mortality in patients with PE.

MATERIAL AND METHODS

This retrospective, observational cohort study was conducted at the Chest Diseases and Thoracic Surgery Training and Research Hospital, İstanbul, Turkey, between May 1, 2013, and August 1, 2015. The study protocol was approved by

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the local ethics committee (EC) of the institution (date of approval/No: 27.07.2015/6) and was conducted in full accordance with the ethical principles stated in the Declaration of Helsinki. All data were collected retrospectively from the hospital database. Owing to the retrospective nature of the study, informed consent was not obtained.

Patients diagnosed with PE by a pulmonology specialist, recorded according to the International Classification of Diseases (ICD) 10 with codes I26, and who were hospitalized in the pulmonology ward, were included in the study. All the patients had non-massive PE because patients with massive PE were not hospitalized in the pulmonology ward and were followed by cardiology or in the ICU. The diagnosis of PE was confirmed with computed tomography angiography in which intraluminal filling defect was visualized, showing the symptoms and signs suggestive of PE.

Patients without hemogram values on the first day of hospitalization were excluded from the study. Patients with abnormalities in the blood cell count (WBC>20x10^9/L or WBC<3x10^9/L, Hgb<80 g/L, platelets <80x10^9), active cancer, pneumonia, and renal or hepatic insufficiency were excluded. Patient enrollment is summarized in a flowchart in Figure 1.

Information about death and date of death was extracted from the Ministry of Health records. Death within 30 days of hospital admission was defined as short-term mortality, and death within 1 year was defined as long-term mortality.

Data were obtained from the hospital electronic database. Patient characteristics, comorbid diseases, hemogram parameters, PLR, NLR, PLT/MPV, and CRP levels were recorded. Coulter LH 780 Hematology Analyzer (Beckman Coulter Inc., Brea, CA, USA) was used for blood count (leukocyte, neutrophil, eosinophil, lymphocyte, platelet, and MPV) analysis. CRP was studied by nephelometry method with a BN II System (Siemens, Munich, Germany).

Statistical Analysis

Patient demographics and all clinical data were summarized by descriptive analysis. Patient groups were compared with the student's t-test for parametric continuous variables (that is, age, hemogram, and biochemistry values, NLR, PLR, PLT/MPV, and CRP), and values were defined as the mean±standard deviation. The Mann–Whitney U test was used for nonparametric continuous variables and shown as the median with interquartile range. The chi-squared test was used for dichotomous variables (that is, sex and comorbid diseases). Count and percentage were used when applicable.

Receiver operating characteristic (ROC) curves were generated to determine the best cut-off points of inflammatory markers for prediction of individual mortality within 30 days, 180 days, and 12 months. The area under the ROC curve (AUC) reflects how good the test is at discriminating between survivors and non-survivors. After determining the cut-off values for the inflammatory markers, they were converted into dichotomous variables. The risk factors for mortality in 30 days, 180 days, and 12 months were further analyzed separately using the Cox regression forward stepwise (likelihood) analysis.

Variables included in the Cox regression analysis were patient demographics, comorbid diseases, studied inflammatory markers, and the statistically significant parameters following univariate analyses of survival and non-survival of patients with PE within 30 days, 180 days, and 12 months of hospital discharge. The mortality risk ratio was showed as a hazard ratio (HR), and a p value below 0.05 was accepted as statistically significant.

RESULTS

A total of 828 patients who met the criteria were included in the study. Table 1 shows the demographics, comorbidities, and hemogram values for this population. The median age was 62 years, and 53% (n=437) were female.

The median values of inflammatory biomarkers on the first day of admission, length of hospitalization, and mortality rates are shown in Table 2. Median PLR was 150 (109–211), NLR was 2.85 (2.0–4.9), PLT/MPV was 30.9 (24–39), and CRP was 23.8 (5–72.1) mg/dL. The median length of hospitalization was found to be 4 (1-9) days. Following discharge from the hospital, all-cause mortality was 1% (n=8) within the first 30 days, 5.9% (n=49) within 180 days, and 8.5% (n=70) within 1 year.

Table 3 shows a comparison of age, sex, hospitalization days, and inflammatory markers between the survivor and non-survivor groups. Age was higher in the mortality group, that is, mean age was 80 years in the non-survivors and

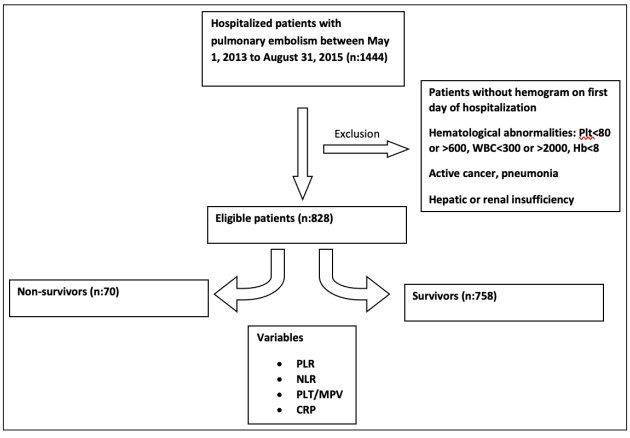

Figure 1. Flow chart of study on hospitalized patients with pulmonary embolism

MAIN POINTS

- Pulmonary embolism (PE) is a serious condition in the elderly.
- Elevated neutrophil/lymphocyte ratio (NLR) values appear to be correlated with higher mortality over both the short-term and long-term periods in PE.
- Physicians should follow up carefully elderly patients with PE and with NLR values of 6 and higher.

62 years in the survivors. The length of hospital stay was longer in the non-survivors (5 days) than in the survivors (4 days). When the relationship between the inflammatory biomarkers and mortality was evaluated, PLR, NLR, PLT/MPV, and CRP all showed significant differences between the 2 groups for long-term (12-month) mortality. NLR was found to be significantly higher in the mortality group for both short-term and long-term mortality. The mean NLR was 7.5 in non-survivors for 30-day mortality and 2.8 in survivors. For the 1-year mortality, NLR was 4.3 in the non-survivors and 2.7 in the survivors. CRP was also significantly higher in the non-survivor group compared with that of the survivor group for both short-term and long-term follow-up, that is, 62 in non-survivors and 23 in survivors for the 30-day and 43 in the non-survivors and 23 in the survivors for the 1-year follow-up periods. PLR was significantly higher in non-survivors at the 1-year follow-up, that is, 194 in non-survivors and 148 in survivors. PLT/MPV showed no significant difference between survivors and non-survivors in the 30-day and the 1-year follow-up periods. The assessment of PLR, NLR, PLT/MPV, and CRP as mortality predictors are summarized in Table 4. In ROC analysis, a PLR value of 152.3 had a 64% sensitivity and 52% specificity for predicting 1-year mortality (AUC=0.64, p<0.001). The cutoff value of 6.1 for NLR had a 75% sensitivity and 75.6% specificity (AUC=0.75, p=0.017) for short-term mortality, and a NLR value of 3.1 had a 68.6% sensitivity and 59.8% specificity (AUC=0.67, p<0.001) for long-term mortality (1 year).

Table 1. Patient characteristics and laboratory findings

Variables	n=828	Values
Age, years median (IQR)	828	62 (51-73)
Female, %	437	53
Comorbidities		
• COPD, %	233	28.1
• Hypertension, %	39	4.7
• Asthma, %	39	4.7
• Deep vein thrombosis, %	21	2.5
• Diabetes mellitus, %	17	2.1
• Chronic respiratory failure, %	16	1.9
• Congestive heart failure, %	13	1.6
• Coronary artery disease, %	12	1.4
• Pulmonary arterial hypertension, %	11	3
• Interstitial lung disease, %	5	0.6
Hemogram values, median (IQR)		
• Leukocyte count, 109 L	828	8.22 (6.43-10.39)
• Neutrophil count	828	5.27 (3.93-7.31)
• Monocyte count	828	0.56 (0.40-0.77)
• Lymphocyte count	828	1.79 (1.33-2.25)
• Eosinophil count	215	0.11 (0.02-.22)
• Basophil count	215	0.04 (0.02-0.06)
• Erythrocyte count, 1012L	828	4.42 (4.04-4.76)
• Hemoglobin, g/dL	828	12.53 (11.25-13.70)
• Hematocrit, %	828	38.1 (34.46-41.33)
• MCV, FL	828	87 (83-91)
• Platelet count, 109 L	828	264.7 (213.8-320)
• Mean platelet volume	828	8.45 (7.8-9.13)

Table 2. Descriptive values of inflammatory markers and mortality rates in the follow-up period

Variables	n	Values
Inflammatory markers, median (IQR)		
• Platelet to lymphocyte ratio	828	150.1 (109.4-211.5)
• Neutrophil to lymphocyte ratio	828	2.85(2.02-4.97)
• Platelet to mean platelet volume ratio	828	30.9 (24-39.5)
• C-reactive protein, mg/dL	557	23.8 (7.5-72.1)
Days of hospitalization, median (IQR)	828	4(1-9)
Mortality		
• 30-day mortality, %	8	1.0
• 180-day mortality, %	49	5.9
• 12 month mortality, %	70	8.5

IQR: inter quartile range

Using the data shown in Table 4, we included age, sex, NLR, CRP, PLR, PLT/MPV, hypertension, congestive heart failure, COPD, and pulmonary arterial hypertension as parameters in the Cox regression model for short and long-term mortality (Table 5). The association between NLR and short-term mortality is shown in Figure 2. An NLR value above 6.1 was found to be associated with a 13-fold higher short-term mortality rate. Table 5 shows independent mortality predictors of HR for 180 days and 1 year. An NLR value above 3.25 was associated with an almost 3-fold increase in mortality over 180 days. Advanced age and NLR were found to be independent predictors of long-term mortality. An NLR value above 3.14 was associated with a 2.2-fold increase in mortality over 1 year. In terms of age, every increased year was associated with a 1.07-fold increase in mortality for long-term mortality.

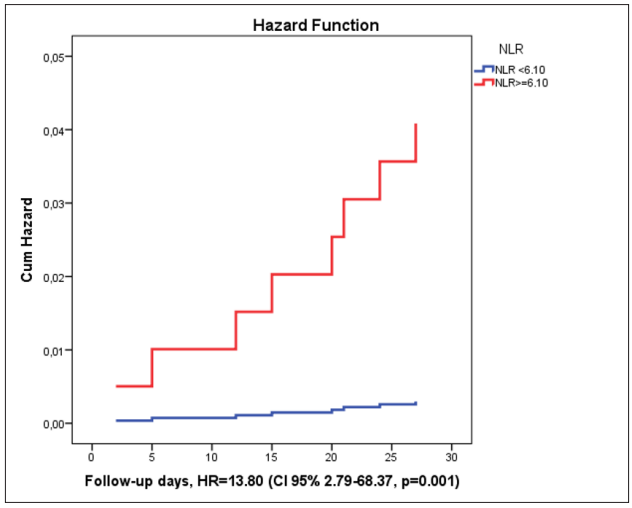

Figure 2. Neutrophil/lymphocyte ratio above 6.1 is associated with a 13.8 fold increase in 30 days mortality

Table 3. Inflammatory markers and other patient characteristics associated with 30-day, 180-day, and 12-month mortality

Variables	Survivors	Non-survivors	p
30-day mortality	n=820	n=8	
Female %	56.5	45.8	0.003
Age, years	62 (51-73)	80 (61-89)	0.02
PLT/MPV	30.9 (24.17-39,54)	23.2 (20.73-33.16)	0.18
PLR	149.8 (109.1-211.2)	245.9 (127.8-376.7)	0.13
NLR	2.84 (2.01-4.91)	7.50 (4.9-12,1)	0.04
CRP	23.6 (7.3-71.8)	62.4 (37.8-104.5)	0.02
Days of hospitalization	4 (1-9)	5 (4-10)	0.19
180-day mortality	n=779	n=49	
Female %	58.1	45.8	<0.001
Age, years	61 (50-73)	77 (67-82)	<0.001
PLT/MPV	30.9 (24.25-39.49)	29.1 (20.96-42.63)	0.73
PLR	148.3 (107.9-207.7)	201.1 (126.7-333.2)	<0.001
NLR	2.79 (1.98-4.80)	4.85 (3.15-9.84)	<0.001
CRP	22.8 (6.9-71.0)	43.5 (20.4-104.5)	0.003
Days of hospitalization	4 (1-8)	7 (4-11)	<0.001
12-month mortality	n=758	n=70	
Female %	57.3	47.2	0.004
Age (years)	61 (49-73)	77 (66-82)	<0.001
PLT/MPV	31 (24.18-39.52)	29.5 (21.55-41.27)	0.64
PLR	148 (107.6-206.4)	194.1 (125.5-329.1)	<0.01
NLR	2.77 (1.97-4.75)	4.31 (2.87-7.71)	<0.001
CRP	22.8 (6.8-71)	42.9 (15.7-93.2)	0.005
Days of hospitalization	4 (1-8)	7 (72-10)	0.001

Table 4. Cut-off values of inflammatory markers for short and long-term follow-up of pulmonary embolism patients

Variables	AUC	CI-95% lower-upper	Cut-off	Sensitivity	Specificity	p
30 days						
NLR	0.75	0.57-0.92	6.10	75.0%	75.6%	0.017
PLR	0.62	0.39-0.84	158.38	62.5%	47.9%	0.26
PLT/MPV	0.36	0.17-0.56	21.5	75.0%	18.8%	0.18
CRP	0.73	0.62-0.83	41.5	75.0%	62.8%	0.027
180 days						
NLR	0.71	0.64-0.78	3.25	71.4%	60.7%	<0.001
PLR	0.65	0.57-0.74	156.38	65.3%	54.8%	<0.001
PLT/MPV	0.48	0.39-0.58	29.1	51.0%	42.2%	0.73
CRP	0.63	0.56-0.71	33.7	63.6%	59.1%	0.003
12 m						
NLR	0.67	0.61-0.74	3.14	68.6%	59.8%	<0.001
PLR	0.64	0.57-0.71	152.38	64.3%	52.2%	<0.001
PLT/MPV	0.48	0.40-0.56	29.1	52.9%	42.2%	0.64
CRP	0.61	0.54-0.68	32.9	61.4%	58.6%	0.005

DISCUSSION

We showed the prognostic value of the new inflammatory markers in hospitalized patients with non-massive PE for both short-term (30 days) and long-term (12 months) mortality. We revealed that NLR was a significant predictor of mortality, both in the short-term and long-term. An NLR value above 6 was associated with an almost 13-fold increase in the 30-day mortality. The 1-year mortality was 8.5% in all patients

Table 5. Cox regression analysis for mortality hazard ratio during long-term follow-up of hospitalized PE patients

		CI 95%		
	HR	lower	upper	p*
180 days				
NLR => 3.25	2.77	1.48	5.18	0.001
Age, for every increased year	1.07	1.04	1.09	<0.001
12 months				
NLR => 3.14	2.20	1.32	3.66	0.003
Age, for every increased year	1.07	1.04	1.09	<0.001

* Cox regression forward stepwise (likelihood ratio) analysis. The cox regression model included: age, sex, hypertension, congestive heart failure, pulmonary arterial hypertension (PAH), COPD, NLR, PLR, PLT/MPV, and CRP

with PE. We found that an NLR above 3.15 and age were independent risk factors for mortality. The other inflammatory markers, namely PLR and CRP, were not found to be associated with long-term mortality.

Short-Term and Long-Term Mortality in PE

Although the number of patients diagnosed with PE has increased over the years, mortality rates have not changed. The mortality rate in patients with PE in Turkey has been reported as 13% [2], whereas in Canada, mortality was reported at 3.9% 30 days post discharge and 12.9 % for 1 year [9]. Short-term mortality rates have varied between 6%–18% in recent studies [3-6]. We demonstrated rather lower 30-day mortality rates (1%) compared with other studies on patients hospitalized with PE. The lower short-term mortality rate we observed may be attributed to the lower severity of non-massive PE. Previous studies reported long-term mortality rates of between 12%–19 % for 1 and 2-year follow-up periods [7-10]. Our 1-year mortality was 8.5%, and, as with the short-term mortality rate, this lower rate may be because of the fact that we did not include patients with massive PE. Almost one-third of the patients with PE have COPD, and mortality was all-cause mortality in this study. COPD and other variables were included in the Cox regression model to find independent risk factors for mortality, and NLR was found to be an independent risk factor for mortality in PE.

Inflammatory Markers in PE: NLR, PLR, PLT/MPV, and CRP

Meta-analyses reveal that high levels of NLR are associated with a nearly 9-fold increased risk for short-term mortality in patients with PE [10, 15]. The prognostic value of NLR was evaluated by Karatas et al. [7] with 241 patients with PE, and they have reported that an NLR above 5.93 is associated with a higher risk of long-term mortality. Further, 4 studies, which also evaluated the 30-day mortality, all showed NLR values between 5.47 and 9.2 [1, 6, 7, 16] and demonstrated that the mortality risk increased nearly 9-fold when the NLR was above 5 [1, 6, 7, 16]. Although the NLR levels we reported were nearly half of the NLR values reported by Karatas et al. [7], we showed a similar association of NLR and mortality and observed an even greater fold increase (13-fold) when the NLR was above 6.1. The sample size of previous studies varied between 241-359 [1, 6, 7, 16], whereas our sample size was nearly 2–4 times more. With the support of previous studies, our findings may be crucial for physician alertness where there is a high risk of 30-day mortality in patients with PE whose NLR is above 6. Similar meta-analyses that also studied the prognostic value of PLR reported that a high PLR value was associated with an almost 7-fold increase in short-term mortality [1, 7, 8, 10, 17]. Karataş et al. [7] have reported that a PLR value above 191 is associated with long-term mortality with a mean of 20-month follow-up. Cetin et al. [8] showed that a PLR value above 149 is associated with mortality over a 28-month follow-up. Our results support those of Cetin et al. [8] as the PLR cutoff values over 30 days, 6 months, and 12 months were between 150 and 160. An association of long-term (2 or 3 years) mortality with PLR and NLR does not appear to be clear cut; however, over the short-term (30 days), these inflammatory markers should be seriously considered for predicting mortality. Gunay et al. [18] proposed that MPV can be used to determine the severity of PE as a negative correlation was found between MPV values and platelet numbers; however, MPV was not found to be a reliable indicator for diagnosing PE in another study [19]. We also studied the association of PLT/MPV values with short-term and long-term mortality in patients with PE and found the values to be similar between non-survivors and survivors, and there was no association with mortality. A study conducted in Turkey that evaluated CRP for its prognostic value in patients hospitalized with PE and during their long-term follow-up (36 months) showed that CRP values over 48 mg/dL were a prognostic risk factor [20]. We found that CRP values were significantly higher in the non-survivor group, but was not found to be a predictor of mortality, both in the short and long-term. This could be owing to the lower number of fatal cases we observed.

Age and PE

Friz et al. [21] studied the mortality (30–90 days) and prognosis of 470 elderly patients, 106 of whom had confirmed PE. The elderly patients (over 80 years) had an 18.9% mortality in those with confirmed PE versus 12.6% in those who did not have PE. Alottaibi et al. [9] studied 31,656 patients with deep venous thromboembolism and found that 30-day mortality in PE was 3.9%, and mortality increased with increased age. Jo et al. [22] found that age was not a factor between survivors and non-survivors within the 30 days of follow-up in PE. This study indicated that age was a predictor of mortality within 6 months and 1 year in patients with PE.

Our study did have some limitations. First, it was a retrospective and single-centered design study. However, the results from a large sample size and specific patient group provided valuable clinical information for assessing inflammatory biomarkers for predicting mortality in patients with PE. Second, although the study population comprised 828 patients with PE, the short-term 30-day mortality was 1% (n=8), and the predictor for mortality was thus limited. Nonetheless, the prognostic risk factor defined in this study may be valuable for future studies. Third, study mortality was defined as all-causes mortality. The study results may be difficult to associate with PE and inflammatory markers for long-term mortality. However, other studies have also assessed all-cause mortality and for long-term mortality, this may be acceptable. Finally, the patients included in this study were only hospitalized pa-

tients with non-massive PE. If we had included patients with massive PE, the short and long-term mortality may have been higher with increased number of prognostic predictors. However, the patients with massive PE were referred to another center specialized in cardiac diseases.

The strengths of this study lie in the large study population and in that the data was recorded electronically from the hospital database, reducing human error.

In conclusion, this study indicates that NLR and age were associated with mortality in hospitalized patients with PE. Elevated NLR values appear to be a good and feasible predictor of inflammation, which is correlated with higher mortality over both the short and long-term. PE is a serious condition in the elderly, and increased age is related to higher mortality during the follow-up period. Physicians should follow up carefully elderly patients with PE and with NLR values of 6 and higher after discharge from the hospital. Close monitoring of these patients can lead to the early diagnosis, possible prevention, and timely treatment of undesirable events.

Ethics Committee Approval: Ethics Committee approval for the study was obtained from the Local Ethics Committee of the University of Health Sciences, Süreyyapaşa Chest Diseases and Thoracic Surgery Training and Research Hospital (Date of approval/No: 27.07.2015/6) and was conducted in full accordance with the ethical principles stated in the Declaration of Helsinki.

Informed Consent: Owing to the retrospective nature of the study, informed consent was not obtained.

Peer-review: Externally peer-reviewed.

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REFERENCES

1. Ma Y, Mao Y, He X, et al. The values of neutrophil to lymphocyte ratio and platelet to lymphocyte ratio in predicting 30 day mortality in patients with acute pulmonary embolism. BMC Cardiovasc Disord 2016;16:123. doi: 10.1186/s12872-016-0304-5. [Crossref]
2. Özsu SS, Gürel Durmuş Z, Coşkuner MB, et al. Does the incidence and mortality of pulmonary thromboembolism change over the years? Turk Thorac J 2017;18:78-81. [Crossref]
3. Yazıcı S, Kırış T, Ceylan US, et al. The accuracy of combined use of troponin and red cell distribution width in predicting mortality of patients with acute pulmonary embolism. Wien Klin Wochenschr 2016;128 (Suppl 8):596-603. doi: 10.1007/s00508-016-1081-y. Epub 2016 Sep 19. [Crossref]
4. Zhou XY, Chen HL, Ni SS. Red cell distribution width in predicting 30-day mortality in patients with pulmonary embolism. J Crit Care 2017;37:197-01. doi: 10.1016/j.jcrc.2016.09.024. Epub 2016 Oct 6. [Crossref]
5. Akgüllü Ç, Ömürlü İK, Eryılmaz U, et al. Predictors of early death in patients with acute pulmonary embolism. Am J Emerg Med 2015;33:214-21. [Crossref]
6. Çavuş UY, Yıldırım S, Sönmez E, et al. Prognostic value of neutrophil/lymphocyte ratio in patients with pulmonary embolism. Turk J Med Sci 2014;44:50-5. [Crossref]
7. Karatas MB, Ipek G, Onuk T, et al. Assessment of Prognostic Value of Neutrophil to Lymphocyte Ratio and Platelet to Lymphocyte Ratio in Patients with Pulmonary Embolism. Acta Cardiol Sin 2016;32:313-20.
8. Ozcan Cetin EH, Cetin MS, Canpolat U, et al. Platelet-to-lymphocyte ratio as a novel marker of in-hospital and long-term adverse outcomes among patients with acute pulmonary embolism. A single center large-scale study. Thromb Res 2017;150:33-40. [Crossref]
9. Alotaibi GS, Wu C, Senthilselvan A, McMurty MS. Secular Trends in Incidence and Mortality of Acute Venous Thromboembolism: The AB-VTE Population-Based Study. Am J Med 2016;129:879e19-25. [Crossref]
10. Wang Q, Ma JU, Jiang Z, Ming L. Prognostic value of neutrophil-to-lymphocyte ratio and platelet-to-lymphocyte ratio in acute pulmonary embolism: A systemic review and meta-analysis. Int Angiol 2018;37:4-11.
11. Li W, Liu Q, Tang Y. Platelet to lymphocyte ratio in the prediction of adverse outcomes after acute coronary syndrome: A meta-analysis Sci Rep 2017;7:40426. doi: 10.1038/srep40426. [Crossref]
12. Kurtipek E, Bekci TT, Kesli R, et al. The role of neutrophil-lymphocyte ratio and platelet-lymphocyte ratio in exacerbation of chronic obstructive pulmonary disease. J Pak Med Assoc 2015;65:1283-7.
13. Jagadesham VP, Lagarde SM, Immanuel A, Griffin SM. Systemic inflammatory markers and outcome in patients with locally advanced adenocarcinoma of the oesophagus and gastro-oesophageal junction. Br J Surg 2017;104:401-7. doi: 10.1002/bjs.10425. [Crossref]
14. Duman D, Aksoy E, Coban Agca M, et al. The utility of inflammatory markers to predict readmissions and mortality in COPD cases with or without eosinophilia. Int J Chron Obstruct Pulmon Dis 2015;10:2469-78. doi: 10.2147/COPD.S90330. Erratum in: Int J Chron Obstruct Pulmon Dis 2016;11:417. [Crossref]
15. Soylu K, Gedikli Ö, Ekşi A, et al. Neutrophil-to-lymphocyte ratio for the assessment of hospital mortality in patients with acute pulmonary embolism. Arch Med Sci 2016;12:95-100. [Crossref]
16. Kayrak M, Erdogan HI, Solak Y, et al. Prognostic value of neutrophil to lymphocyte ratio in patients with acute pulmonary embolism: a retrospective study. Heart Lung Circ 2014;23:56-62. [Crossref]
17. Kundi H, Balun A, Cicekcioglu H, et al. The relation between platelet-to-lymphocyte ratio and Pulmonary embolism severity index in acute pulmonary embolism. Heart Lung 2015;44:340-3. [Crossref]
18. Günay E, Ulaslı SS, Kacar E, et al. Can platelet indices predict obstruction level of pulmonary vascular bed in patients with acute pulmonary embolism? Clin Respir J 2014;8:33-40. [Crossref]
19. Sunnetçioğlu A, Karadaş S. Mean platelet volume as an indicator of disease in patients with acute pulmonary embolisms. East J Med 2014;19:107-11.

20. Abul Y, Karakurt S, Ozben B, et al. T. C-reactive protein in acute pulmonary embolism. J Invest Med 2011;59:8-14. [Crossref]
21. Friz P, Corno V, Orenti A, et al. Comorbidity assessment as predictor of short and long term mortality in elderly patients with hemodynamically stable acute pulmonary embolism. J Thromb Thrombolysis 2017;44:316-23. [Crossref]
22. Jo JY, Lee MY, Lee JW, et al. Leukocytes and systemic inflammatory response syndrome as prognostic factors in pulmonary embolism patients. BMC Pulm Med 2013;13:74. [Crossref]