

# Comparing CRP/Albumin Ratio and sPESI for Pulmonary Embolism Prognosis

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## Abstract

**Objective:** The aim of this study is to evaluate the prognostic value of the C-reactive protein (CRP)/albumin ratio (CAR) compared to the simplified pulmonary embolism severity index (sPESI) in predicting 30-day and 180-day mortality in patients with pulmonary embolism (PE).

**Materials and Methods:** This retrospective cross-sectional study included patients over 18 years of age, diagnosed with PE and admitted to the intensive care or pulmonary diseases departments. The study investigated the relationship between CRP/CAR, sPESI, and clinical outcomes such as 30-day and 180-day mortality, and hospital admissions.

**Results:** Among 111 patients, 17 died within 180 days and 7 within 30 days. While no significant association was found between 30-day mortality and the CRP/CAR or the sPESI the CRP/CAR was significantly higher in those with 180-day mortality ( $p < 0.001$ ). The area under the curve for the CRP/CAR in predicting 180-day mortality was 0.782 ( $p < 0.001$ ), compared to 0.593 for the sPESI ( $p = 0.224$ ). The DeLong test confirmed the superior predictive performance of the CRP/CAR.

**Conclusion:** This study shows that the CRP/CAR has greater prognostic value than the sPESI in predicting 180-day mortality in PE patients, though no significant association was found for 30-day mortality.

**Keywords:** CRP/albumin ratio, pulmonary embolism, simplified pulmonary embolism severity index, mortality

## Introduction

Pulmonary embolism (PE) is a prevalent condition encountered in emergency departments, resulting in significant morbidity and mortality [1,2]. To predict mortality in PE, various risk scoring systems have been developed. The pulmonary embolism severity index (PESI) and the simplified pulmonary embolism severity index (sPESI) are two such systems [3]. The prognostic strength of sPESI lies in its ability to identify patients with low 30-day mortality. However, sPESI may also categorize

low-risk patients as high-risk [4,5]. Although the sPESI score was originally developed to predict 30-day mortality in patients with PE, studies have demonstrated that it also holds significant prognostic value in predicting 90-day and 180-day mortality [6,7]. The sPESI score is more practical for use in emergency departments due to its ease of application and its comparable prognostic significance to the original PESI score [3,4].

Inflammation, by triggering thrombosis, constitutes the core pathological mechanism in patients with PE. Moreover, elevated



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levels of inflammation have been found not only to contribute to the development of PE but also to be closely associated with increased mortality [8]. C-reactive protein (CRP) is an acute phase reactant secreted by the liver, whereas albumin is a negative acute phase reactant. Elevated CRP and decreased albumin levels are recognized as key indicators of systemic inflammation. Due to their short half-lives, easy accessibility, and close association with disease prognosis, certain biomarkers are utilized in diagnosis, treatment, and mortality follow-up [9,10]. An increased CRP and decreased albumin ratio has recently been linked to mortality in PE patients [10]. The CRP/albumin ratio (CAR) is a novel indicator of systemic inflammation, calculated by dividing CRP by albumin [11]. Recent studies have suggested that CAR may be associated with mortality in PE patients [11,12]. One study concluded that CAR was more effective than PESI at predicting 180-day mortality in PE patients [12]. The sPESI is a scoring system that is simpler to apply in emergency departments for PE patients. A study evaluating the effectiveness of CAR in predicting 30-day and 180-day mortality in PE patients and comparing it with sPESI could enhance the ability to predict prognosis and manage PE patients in emergency departments.

The primary aim of this study is to evaluate the performance of CAR compared to sPESI in predicting 30-day and 180-day mortality in PE patients. The secondary aim is to assess the performance of CAR in predicting intensive care unit (ICU) admission.

## Materials and Methods

This study was designed as a retrospective observational, analytical, cross-sectional study conducted using data obtained from the emergency department of a tertiary care hospital. This hospital receives 300,000-400,000 adult patients annually and accepts numerous referrals from surrounding hospitals. Our study retrospectively analyzed patients who presented to the emergency department between July 1, 2017, and June 30, 2022, and were subsequently admitted to the pulmonary diseases department diagnosed with PE. This study was approved by the local Hitit University Faculty of Medicine Clinical Research Local Ethics Committee (decision number: 2023-05, date: 12.01.2023).

Patients over 18 years of age diagnosed with PE and admitted to the pulmonary diseases department or the ICU were included in the study. Exclusion criteria included a prior diagnosis of autoimmune disease, active infection, acute transient ischemic attack/stroke, albuminuria, or chronic liver disease. Patient selection and data collection were performed using the hospital's automation system. Demographic data, chronic diseases, and laboratory values, including CRP and albumin, were recorded for each case. Laboratory values obtained during the emergency department visit were used

for CRP and albumin. The CAR was calculated by dividing CRP by albumin, and the result was recorded. Additionally, sPESI scores were calculated based on patient records and system information. Patients with an sPESI score of 0 were classified as low risk, while those with a score of 1 or higher were classified as high-risk [3].

Measurements were taken from the computed tomographic pulmonary angiography images obtained during the patients' emergency department visits. Two axial sections perpendicular to the long axis of the heart showing the maximum distance between the ventricular endocardium and the interventricular septum were identified. The measurements of the right ventricle (RV) were then divided by the measurements of the left ventricle (LV) to calculate the RV/LV ratio [13]. Additionally, it was recorded whether the patients received thrombolytic therapy.

Subsequently, 30-day mortality, 180-day mortality, and ward-ICU admissions were identified and recorded through the hospital automation system. For patients whose 30-day and 180-day mortality data were not accessible through the system, mortality data were recorded by contacting their relatives via the phone numbers registered in the system. Following this, the relationship between patients' age, gender, chronic diseases, CRP, albumin, CAR, sPESI, RV/LV ratios, thrombolytic therapy administration, 30-day mortality, 180-day mortality, and ward-ICU admissions were statistically analyzed.

## Statistical Analysis

Statistical analyses were conducted using SPSS version 25 software. The normality of variable distributions was assessed using histograms and Shapiro-Wilk tests. Descriptive statistics for non-normally distributed variables were reported as median and interquartile range. The Mann-Whitney U test was utilized for non-normally distributed numerical variables, while chi-square or Fisher's exact tests (when chi-square test assumptions were not met) were employed for nominal variables. Diagnostic decision-making characteristics for predicting mortality and ICU admission were analyzed using receiver operating characteristic (ROC) curve analysis. For significant cut-off values, sensitivity, specificity, positive likelihood ratio (PLR), negative likelihood ratio (NLR), positive predictive value (PPV), and negative predictive value (NPV) were calculated. A p value of <0.005 was considered statistically significant.

## Results

A total of 256 patients were identified in the hospital database for this study. After excluding 145 patients who did not meet the study criteria, 111 patients were included in the analysis (Figure 1).

Among the included patients, 17 experienced deaths within 180 days, and 7 experienced deaths within 30 days. Of the

included patients, 43 were admitted to the ICU, while 68 were admitted to the ward. There was no difference in chronic diseases between patients admitted to the ward and those admitted to the ICU. In terms of 30-day mortality, there was no difference regarding additional diseases; however, a history of cancer was found to be a factor affecting 180-day mortality

( $p < 0.001$ ). Detailed information is presented in Table 1. Albumin levels were significantly lower in patients with 180-day mortality and those admitted to the ICU ( $p = 0.002$  and  $p < 0.001$ , respectively), while CRP levels were significantly higher in both groups ( $p < 0.001$  and  $p = 0.001$ , respectively). No difference was found in albumin, and CRP levels concerning 30-day mortality (Table 2).

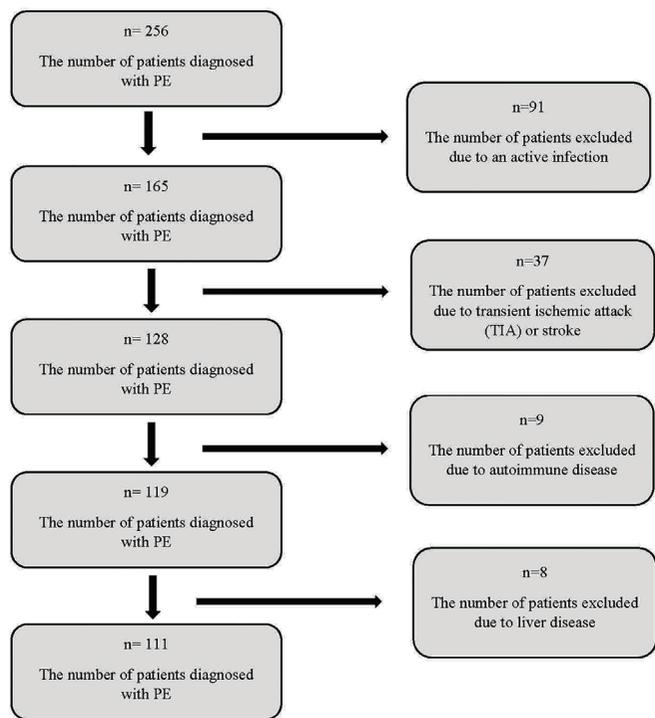


Figure 1. Flowcharts of study design

PE: Pulmonary embolism

When examining ICU and ward admissions, the CAR and RV/LV ratios were significantly higher in patients admitted to the ICU (both  $p < 0.001$ ). Additionally, all patients admitted to the ICU had an sPESI score of 1 or higher ( $p < 0.001$ ). Furthermore, all patients who received thrombolytic therapy were admitted to the ICU. In terms of 30-day mortality, there was no statistically significant difference regarding CAR, RV/LV ratio, sPESI, and thrombolytic therapy. However, for 180-day mortality, CAR was significantly higher in patients who experienced mortality within 180 days ( $p < 0.001$ ). No statistically significant differences were observed between sPESI, RV/LV ratio, and thrombolytic therapy for 180-day mortality. Detailed information is provided in Table 3.

The performance of CAR, sPESI, and the RV/LV ratio in predicting ICU admission, as well as the performance of CAR and sPESI in predicting 180-day mortality, were assessed using ROC curve analysis (Figure 2). For predicting ICU admission, the AUC value for CAR was 0.711 [95% confidence interval (CI) = 0.612, 0.809,  $p < 0.001$ ], for the RV/LV ratio was 0.777 (95% CI = 0.686, 0.868,  $p < 0.001$ ), and for sPESI was 0.676 (95% CI = 0.579, 0.774,  $p = 0.002$ ). When comparing the performance of CAR, RV/LV ratio, and sPESI in predicting ICU admission using the DeLong test, no statistically significant difference was found ( $p = 0.147$ ).

	ICU-ward admission status			30-day mortality			180-day mortality		
	Ward (n=68)	ICU (n=43)	p value	Survive (n=104)	Non-survive (n=7)	p value	Survive (n=94)	Non-survive (n=17)	p value
Age, median (IQR 25-75)	60 (43-72.25)	71 (62-82.5)	<0.001	65 (46.75-77)	63 (62-72)	0.653	62.5 (46-73)	77 (62-88)	0.003
Sex (n, %)									
Male	26 (38.2%)	21 (48.8%)	0.271	43 (41.3%)	4 (57.1%)	0.454*	39 (41.5%)	8 (47.1%)	0.669
Female	42 (61.8%)	22 (51.2%)		61 (58.7%)	3 (42.9%)		55 (58.5%)	9 (52.9%)	
Comorbidities (n, %)									
COPD	16 (23.5%)	12 (27.9%)	0.605	26 (25%)	2 (28.6%)	1.000*	22 (23.4%)	6 (35.3%)	0.363*
DM	17 (25%)	12 (27.9%)	0.734	29 (27.9%)	0 (0%)	0.187*	21 (22.3%)	8 (47.1%)	0.068*
HT	37 (54.4%)	30 (69.8%)	0.107	64 (61.5%)	3 (42.9%)	0.432*	54 (57.4%)	13 (76.5%)	0.182*
CHF	11 (16.7%)	5 (11.6%)	0.506	15 (14.4%)	1 (14.3%)	1.000*	13 (13.8%)	3 (17.6%)	0.709*
CAD	19 (27.6%)	17 (39.5%)	0.204	34 (32.7%)	2 (28.6%)	1.000*	30 (31.9%)	6 (35.3%)	0.784
Ca	12 (17.6%)	6 (14.0%)	0.607	16 (15.4%)	2 (28.6%)	0.317*	9 (9.6%)	9 (52.9%)	<0.001

\*According to Fisher's exact test results.  
 A p value of <0.05 was considered statistically significant.  
 ICU: Intensive care unit, IQR: Interquartile range, COPD: Chronic obstructive pulmonary disease, DM: Diabetes mellitus, HT: Hypertension, CHF: Congestive heart failure, CAD: Coroner arterial disease, Ca: Cancer

The AUC value for CAR in predicting 180-day mortality was 0.782 (95% CI =0.672, 0.892,  $p<0.001$ ), while the AUC value for sPESI was 0.593 (95% CI =0.460, 0.726,  $p=0.224$ ). When comparing the performance of CAR and sPESI in predicting 180-day mortality using the DeLong test the performance of CAR was found to be significantly superior (AUC difference =0.189, 95% CI =0.048, 0.330,  $p=0.008$ ).

The cut-off value of CAR for predicting 180-day mortality was calculated as 0.754 according to the Youden index. When the CAR ratio was  $\geq 0.754$ , the sensitivity for predicting 180-day mortality was 70.59%, specificity was 71.28%, PLR was 2.46, NLR was 0.41, PPV was 30.77%, and NPV was 93.06%. For high-risk patients (sPESI  $\geq 1$ ) in predicting 180-day mortality, the sensitivity of sPESI was 94.12%, specificity was 24.47%, PLR was 1.25, NLR was 0.24, PPV was 18.39%, and NPV was 95.83%.

## Discussion

This study is significant because it is the first to compare the performance of sPESI and CAR in predicting mortality in PE patients. It underscores the importance of an elevated CAR in predicting 180-day mortality in PE patients. Additionally, an increased CAR was associated with ICU admissions. However, no association was found with 30-day mortality. While an sPESI score above 1 was linked to ICU admission, no relationship was observed with 30-day and 180-day mortality.

Various scoring systems are utilized to predict mortality in PE patients, with PESI and sPESI being two such systems [14]. Although sPESI may categorize patients with a low mortality risk as higher risk, it is preferred in emergency departments due to having fewer parameters, ease of use, and efficacy in predicting

**Table 2. Laboratory parameters of patients based on mortality and admission status**

Laboratory parameters, median (IQR 25-75)	ICU-ward admission status			30-day mortality			180-day mortality		
	Ward (n=68)	ICU (n=43)	p-value	Survive (n=104)	Non-survive (n=7)	p-value	Survive (n=94)	Non-survive (n=17)	p-value
Hemoglobin (g/dL)	12.75 (11.55-14.32)	13.1 (12.15-14.25)	0.517	12.9 (11.7-14.3)	11.2 (10.15-14.6)	0.524	12.95 (11.9-14.37)	12.3 (10.7-13.6)	0.126
Hematocrit (%)	38.2 (36.17-41.97)	40.7 (36.3-43.25)	0.333	39.3 (36.37-24.5)	36.3 (32.7-44.65)	0.743	39.6 (36.42-42.72)	39 (33-40.7)	0.142
MCV (fL)	85.3 (79.87-89.17)	87.3 (81.7-91.15)	0.230	86.5 (81.32-90.5)	74.8 (71.85-86.05)	0.030	86.75 (81.4-90.7)	84.8 (77.4-88.1)	0.161
Neutrophil ( $10^9/L$ )	6.06 (4.59-7.64)	7.14 (4.93-8.77)	0.042	6.36 (4.59-7.88)	9.34 (5.92-10.84)	0.089	6.06 (4.49-7.84)	7.87 (6.42-9.34)	0.010
Lymphocyte ( $10^9/L$ )	1.9 (1.5-2.7)	1.6 (1.18-2.27)	0.181	1.76 (1.35-2.46)	1.37 (1.31-2.12)	0.369	1.87 (1.47-2.72)	1.13 (0.66-1.9)	0.004
Platelet ( $10^9/L$ )	234.5 (197-294.75)	218 (177.5-278)	0.254	229.5 (193.75-282.5)	242 (216.5-302)	0.430	223.5 (193.25-279.5)	250 (227-320)	0.152
Glucose (mg/dL)	110 (100-137.25)	129 (112-167.5)	0.029	115.5 (101-153.25)	140 (122-162)	0.267	114 (100.25-137.75)	165 (140-200)	<0.001
Creatinine (mg/dL)	0.8 (0.6-0.92)	0.9 (0.75-1.1)	0.003	0.8 (0.7-1)	0.8 (0.7-0.95)	0.888	0.8 (0.7-1)	0.8 (0.7-1)	0.729
GFR (mL/min./1.7)	95.5 (75.5-109.5)	73 (55.5-97)	<0.001	90 (67-107.25)	94 (67-98)	0.889	91.5 (70-107.75)	78 (56-96)	0.151
Sodium (mmol/L)	138 (136.75-140)	137 (135.5-138)	0.014	138 (136-139)	137 (134-137.5)	0.206	138 (136-139.75)	137 (136-138)	0.233
Potassium (mmol/L)	4.25 (4-4.4)	4.31 (3.8-4.56)	0.552	4.3 (4-4.5)	3.87 (3.6-4.45)	0.269	4.26 (4-4.5)	4.3 (3.87-4.43)	0.679
Albumin (g/L)	40 (38-42)	37 (33-40)	0.002	40 (36-42)	36 (34.5-40)	0.401	40 (37-42)	33 (31-37)	<0.001
CRP (mg/L)	14.7 (6.64-29.47)	28.5 (18.25-46.1)	<0.001	21 (8.2-36.3)	25.7 (16.95-54.55)	0.294	18.25 (7.18-32.22)	37 (25.7-56.9)	0.001
Troponin-I (ng/L)	100 (100-107)	327 (100-1025)	<0.001	100 (100-324.25)	227.5 (100-364)	0.636	100 (100-333)	107 (100-258)	0.895

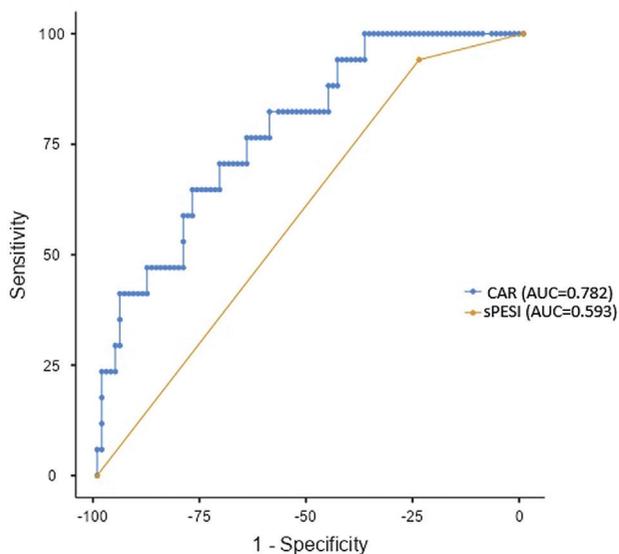
A p-value of <0.05 was considered statistically significant.

ICU: Intensive care unit, IQR: Interquartile range, CRP: C-reactive protein, GFR: Glomerular filtration rate, MCV: Mean corpuscular volume, min.: Minimum

**Table 3. The relationship between CAR, RV/LV ratio, sPESI, and thrombolytic therapy with patient hospitalization and mortality**

Indices	ICU-ward admission status			
	Ward (n=68)	ICU (n=43)	95% CI	p value
CAR, median (IQR 25-75)	0.38 (0.16-0.74)	0.77 (0.47-1.47)	-0.539, -0.164	<0.001
RV/LV, median (IQR 25-75)	0.91 (0.8-1.04)	1.19 (1.06-1.51)	-0.423, -0.201	<0.001
sPESI (>0, high-risk) (n,%)	44 (64.7%)	43 (100%)	0.378, 0.588 <sup>b</sup>	<0.001 <sup>a</sup>
Thrombolytic therapy (n,%)	0 (0%)	19 (44.2%)	0.649, 0.829 <sup>b</sup>	<0.001
	30-day mortality			
	Survive (n=104)	Non-survive (n=7)	95% CI	p value
CAR, median (IQR 25-75)	0.54 (0.21-1.01)	0.65 (0.49-1.39)	-0.841, 0.224	0.300
RV/LV, median (IQR 25-75)	1.03 (0.85-1.28)	0.90 (0.86-0.91)	-0.037, 0.339	0.147
sPESI (>0, high-risk) (n,%)	81 (77.9%)	6 (85.7%)	-0.068, 0.123 <sup>b</sup>	1.000 <sup>a</sup>
Thrombolytic therapy (n,%)	17 (16.3%)	2 (28.6%)	-0.094, 0.196 <sup>b</sup>	0.406
	180-day mortality			
	Survive (n=94)	Non-survive (n=17)	95% CI	p value
CAR, median (IQR 25-75)	0.47 (0.17-0.84)	1.05 (0.65-1.87)	-1.05, -0.427	<0.001
RV/LV, median (IQR 25-75)	0.99 (0.83-1.22)	1.07 (0.91-1.34)	-0.292, 0.80	0.304
sPESI (>0, high-risk) (n,%)	71 (75.5%)	16 (94.1%)	0.028, 0.256 <sup>b</sup>	0.114 <sup>a</sup>
Thrombolytic therapy (n,%)	18 (19.1%)	1 (5.9%)	-0.248, 0.005 <sup>b</sup>	0.181

<sup>a</sup>According to Fisher's exact test results.  
<sup>b</sup>Difference in proportions.  
 A p-value of <0.05 was considered statistically significant.  
 ICU: Intensive care unit, CAR: C-reactive protein/albumin ratio, RV/LV: The ratio of the right ventricle to the left ventricle, sPESI: Simplified pulmonary embolism severity index, IQR: Interquartile range, CI: Confidence intervals



**Figure 2.** Receiver operating characteristic curve analysis; the performance of CAR and sPESI in predicting 180-day mortality

sPESI: Simplified pulmonary embolism severity index, CAR: C-reactive protein/albumin ratio, AUC: Area under the curve

30-day mortality [4]. Alongside these scoring systems, various laboratory parameters are also being investigated to predict mortality risk in PE patients [15]. The CAR is a novel indicator

of inflammation being studied in PE patients [11,12]. CAR includes both CRP and albumin; increased CRP or decreased albumin correlates with an elevated CAR [10]. A recent study concluded that an elevated CAR is closely associated with venous thromboembolism, particularly in middle-aged and older adults. This association was attributed to the increased risk of thrombosis resulting from heightened inflammation, with the CAR being recognized as a reliable marker of systemic inflammatory response [16].

In a study by Norton et al. [10], increased CRP and decreased albumin levels were associated with 180-day mortality in PE patients. Another study suggested that an elevated CAR could be used to determine the prognosis of PE patients [11]. Similarly, in a study conducted by Artac et al. [17], the CAR was found to be closely associated with both early- and late-term mortality in patients with PE. In another study, Özcan et al. [12] found that an increased CAR was associated with 180-day mortality in PE patients. They compared CAR with PESI and concluded that an elevated CAR was superior to PESI in predicting 180-day mortality [12]. In our study, considering the applicability in emergency departments, we used sPESI instead of PESI. We examined the performance of the CAR ratio and sPESI in predicting 180-day mortality and found CAR to be superior to sPESI. Additionally, in our study, the CAR ratio was

higher in patients admitted to the ICU, indicating that CAR may be effective in identifying high-risk patients.

Several studies have evaluated the association between the CAR and short-term mortality in patients with PE [11,17,18]. In a study by Hocalı and Tanrıverdi [11], CAR was identified as an independent predictor of in-hospital mortality among PE patients. Similarly, Artac et al. [17] reported that CAR was closely associated with early mortality in this patient population. Another study found a significant relationship between CAR and mortality [18]. In our study, we aimed to investigate the prognostic value of CAR in predicting 30-day mortality in patients with PE. However, unlike the aforementioned studies, our findings did not demonstrate a statistically significant association. This discrepancy may be attributed to the retrospective, single-center design of our study and the relatively small sample size. Additionally, the number of patients who experienced mortality within 30-days was notably low, which may have limited the statistical power of our analysis. Further large-scale, multicenter prospective studies are needed to clarify this issue. Moreover, in our study, we did not identify a significant association between the sPESI score and 30-day mortality.

### Study Limitations

Our study has several limitations. Firstly, it was designed retrospectively. In our study, data from the hospital database were inaccessible or incomplete for nearly 60% of the patients, which led to a reduced study population. Additionally, the number of patients who experienced 30-day mortality was less than 10% of the total population, which may have resulted in insufficient data regarding 30-day mortality. Furthermore, these data are based on a single measurement, and repeated measurements may not accurately reflect the relationship between changes in CAR over time and mortality. Another limitation of our study is that the number of patients initially evaluated was higher than the final study population due to the application of detailed exclusion criteria. This may have led to selection bias in our study. Moreover, in our study, mortality was defined as death due to any non-traumatic cause. However, the causes of death were not specified in our dataset, which may have influenced the overall mortality outcomes by including deaths from unrelated causes. Nonetheless, in patients who have experienced a major risk factor such as PE, the contribution of PE to mortality cannot be entirely ruled out.

Additionally, due to the retrospective nature of our study, complete data for all parameters were not available, and therefore, an assessment based on the PESI score could not be performed. Although this represents a significant limitation, the sPESI score remains valuable due to its greater practicality in emergency settings. Our study is the first to evaluate this aspect. Future research may enhance the literature by comparing sPESI and PESI scores concurrently. Lastly, we only

included hospitalized patients; therefore, our study results do not include information about low-risk PE patients who were deemed suitable for outpatient treatment.

### Conclusion

In conclusion, this study demonstrates that an increased CAR is associated with 180-day mortality and ICU admissions in PE patients. Furthermore, we found that CAR had a higher prognostic value than the sPESI score in predicting 180-day mortality. These findings suggest that CAR may serve as a valuable prognostic marker for late-term mortality in PE patients. However, similar results were not observed for predicting 30-day mortality. Nevertheless, the current study is of particular value as it is the first to compare CAR with the sPESI score in this context. Future research should focus on reevaluating these findings in prospective, large-scale, multicenter cohorts and further investigating the prognostic utility of CAR in this patient population.

### Ethics

**Ethics Committee Approval:** This study was approved by the local Hitit University Faculty of Medicine Clinical Research Local Ethics Committee (decision number: 2023-05, date: 12.01.2023).

**Informed Consent:** Retrospective study.

### Footnotes

#### Authorship Contributions

Surgical and Medical Practices: S.G., S.Y., Y.Y., G.M., İ.H.T., Concept: S.G., A.Ö., S.K., A.K.E., Design: S.G., A.K.E., Data Collection or Processing: S.Y., A.Ö., G.M., Y.A.Y., S.K., Analysis or Interpretation: S.G., İ.H.T., Literature Search: S.G., Y.Y., Writing: S.G., S.Y., Y.Y., S.K.

**Conflict of Interest:** No conflict of interest was declared by the authors.

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