

Original Article

Evaluation of the Association Between Pulmonary Embolism, Laboratory and Clinical Parameters, and Pulmonary Involvement in COVID-19 Patients More Than 60 Years: A Single-Center Retrospective Study

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Abstract

Introduction: Coronavirus disease 2019 (COVID-19) is a viral infection that emerged in 2019. This infection causes a wide range of clinical manifestations, including pulmonary embolism (PE), which has been frequently reported in affected patients. Although numerous studies have investigated PE in patients with COVID-19, the relationship between PE, laboratory indices, and patient mortality has not been fully examined. Therefore, the present study aimed to address this issue.

Methods: In this retrospective study, patients were selected from those who were admitted to Hajar Hospital, Shahrekord, Iran, between 2020 and 2023. COVID-19 and PE were diagnosed based on laboratory tests and clinical symptoms by an infectious disease specialist. Following confirmation of the diagnosis, clinical records were retrieved from the hospital archives.

Results: Based on the results, the mean age, oxygen saturation, and pulmonary pressure were lower in patients with PE; however, the differences were not statistically significant ($P > 0.05$). Furthermore, pulmonary involvement was slightly higher in patients with PE ($P = 0.37$) than in those without PE. Moreover, the mean mortality rate was higher in patients with PE compared to those without PE, but the difference was not significant ($P = 0.70$). The mean levels of lactate dehydrogenase (LDH), red blood cells (RBCs), hemoglobin (Hb), and ejection fraction (EF) were higher in individuals with PE, but these differences were not significant ($P > 0.05$). By contrast, the mean levels of C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), ferritin, white blood cell (WBC) count, and platelet count were higher in patients without PE ($P > 0.05$).

Conclusion: Overall, the results demonstrated no significant relationship between clinical and laboratory parameters and the incidence of PE in COVID-19 patients.

Keywords: COVID-19, Pulmonary embolism, Laboratory parameters



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Introduction

Coronavirus disease 2019 (COVID-19) was first identified in China in 2019 (1, 2). The disease gradually spread worldwide and affected a large number of patients. In addition, healthy individuals were also exposed to the virus (3, 4). The spread of COVID-19 was so extensive that it led to the death of both patients and healthy individuals (5, 6). Although the causative agent of COVID-19 belongs to the family of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), it was a novel strain, and only limited information was initially available about it

(7). This lack of knowledge contributed to increased death rates. Although COVID-19 mainly affects the respiratory system, other organs may also be involved. The most crucial clinical manifestations associated with COVID-19 include inflammation, coagulation disorders, respiratory involvement, and lung dysfunction (8).

Pulmonary embolism (PE) is one of the complications observed in these patients. Despite the reduction in arterial SpO_2 , PE can cause respiratory disorders in patients (9-11). In addition, PE leads to changes in laboratory parameters, clinical findings, and CT scan images. The severity of PE



and its impact on patient mortality vary depending on each patient's clinical condition and underlying diseases (12-14).

Although numerous studies have investigated PE in patients with COVID-19, the relationship between PE, laboratory indices, and patient mortality has not been fully examined. Therefore, the present study was designed to address this issue.

Materials and Methods

This retrospective study included patients admitted to Hajar Hospital, Shahrekord, Iran, between 2020 and 2023. The ethical approval code for this study was IR. SKUMS. MED.REC.1400.019.

Inclusion and Exclusion Criteria

The inclusion criteria were hospitalization with a diagnosis of COVID-19, an age of at least 18 years, and no previous history of severe chronic obstructive pulmonary disease (COPD), valvular diseases, or congenital disorders. The exclusion criteria encompassed a history of lung diseases such as asthma, COPD, or pulmonary artery hypertension, as well as a history of valvular diseases, heart failure, or embolism.

Data Collection

COVID-19 and PE were diagnosed in patients based on laboratory tests, clinical symptoms, and imaging findings by an infectious disease specialist. Following diagnostic confirmation, patients' clinical records were retrieved from the hospital archives. Pulmonary involvement was assessed using a semiquantitative scoring system (15). Using a visual assessment process, each of the five lung lobes was visually scored from 0 to 5: score 0 (no involvement), score 1 (< 5% involvement), score 2 (5%-25% involvement), score 3 (26%-49% involvement), score 4 (50%-75% involvement), score 5 (> 75% involvement).

Demographic Data

Demographic data collected included age, sex, smoking status, duration of hospitalization, intensive care unit (ICU) admission status, mortality, SpO_2 , pulmonary pressure, and the degree of pulmonary involvement.

Laboratory data

Hematological parameters analyzed included lactate dehydrogenase (LDH), C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), ferritin, white blood cell (WBC) count, red blood cell (RBC) count, hemoglobin (Hb), platelet count, and ejection fraction (EF).

Statistical Analysis

The normality of continuous variables was assessed using the Shapiro-Wilk test. The chi-square test was applied to compare categorical variables, while the Mann-Whitney U test was employed to compare continuous variables between groups. Additionally, the Pearson correlation coefficient was used to analyze the correlation between quantitative variables, and the Kaplan-Meier method was used for survival analysis. Statistical analyses were

performed using SPSS software (version 25). A P -value of < 0.05 was considered statistically significant.

Using the following formula and considering a 10% margin of error and $P = q = 0.5$, the sample size was calculated to be 110 patients using simple random sampling:

$$n = \frac{z^2 pq}{d^2} = 110$$

$$N = z^2 \cdot p \cdot q / d^2 = 110$$

Results

Descriptive Information of Patients

Table 1 presents the demographic and clinical characteristics of the patients based on the presence or absence of PE. The results indicated that the mean age, SpO_2 , and pulmonary pressure were lower in patients with PE ($P > 0.05$). Moreover, pulmonary involvement was higher in patients with PE, but this difference was not significant ($P = 0.37$). In addition, the mean mortality rate was higher in patients with PE compared to those without PE ($P = 0.70$). The findings for other variables are presented in Table 1.

Laboratory Indices

The mean levels of LDH, RBCs, Hb, and EF were higher in patients with PE compared to those without PE ($P > 0.05$). Conversely, the mean values of CRP, ESR, ferritin, WBC count, and platelet count were higher in patients without PE, but these differences were not statistically significant ($P > 0.05$), as illustrated in Table 2.

Table 1. Descriptive Characteristics of Patients

Variables		Pulmonary Embolism		P-value
		Yes	No	
Age (years), mean $\pm$ SD		69.69 $\pm$ 18.28	69.75 $\pm$ 13.18	0.66*
Sex, n (%)	Female	55 (58.5)	0.26**	0.26**
	Male	39 (41.5)		
Smoking, n (%)	Yes	21 (22.3)	0.39**	0.39**
	No	73 (77.7)	8 (66.7)	
ICU Admission, n (%)	Yes	15 (16)	1 (8.3)	0.48**
	No	79 (84)	11 (91.7)	
Hospitalization Time (days), mean $\pm$ SD		9.01 $\pm$ 7.72	10.83 $\pm$ 10.65	0.98*
Mortality, n (%)	Yes	19 (20.2)	3 (25)	0.70**
	No	75 (79.8)	9 (75)	
SpO_2 (%), mean $\pm$ SD		81.47 $\pm$ 12.19	87.00 $\pm$ 11.60	0.07*
Pulmonary Pressure (mm Hg), mean $\pm$ SD		40.00 $\pm$ 12.10	44.81 $\pm$ 18.12	0.51**
Pulmonary Involvement, n (%)	5	26 (29.2)	2 (16.7)	0.37*
	25	32 (36)	3 (25)	
	50	14 (15.7)	3 (25)	
	75	13 (14.6)	4 (33.3)	
	100	4 (4.5)	0 (0)	

Note. SD: Standard deviation; ICU: Intensive care unit; SpO_2 : oxygen saturation; mmHg: Millimeters of mercury. *Chi-square test; ** Mann-Whitney U test

Univariate and Multivariate Logistic Regression

Based on the results, none of the demographic or laboratory variables was statistically significant using logistic regression ($P > 0.05$), as depicted in Table 3.

Survival Analysis

Cox regression analysis was used to assess the average survival time. The results indicated that a longer duration of hospitalization was associated with a lower survival rate (Figure 1 and Table 4).

Table 2. Laboratory Parameters in the Groups

Variables	Pulmonary Embolism		P-value
	Yes	No	
LDH (U/L)	505.95 ± 306.27	356.75 ± 216.31	0.06*
CRP (mg/L)	66.34 ± 9.08	71.33 ± 58.96	0.27*
ESR (mm/hr)	28.42 ± 24.29	38.00 ± 40.72	0.87*
Ferritin (µg/L)	365.57 ± 385.96	439.16 ± 517.95	0.93*
WBC count (× 10 ³ /µL)	8919.14 ± 4250.14	10575.00 ± 4035.10	0.11*
RBC count (× 10 ⁶ /µL)	5.64 ± 9.14	4.46 ± 1.31	0.21*
Hb (g/dL)	13.75 ± 7.24	12.35 ± 2.20	0.32*
Platelet Counts (× 10 ³ /µL)	188638.29 ± 67686.00	189833.33 ± 78999.23	0.96*
EF (%)	52.04 ± 7.30	51.66 ± 4.43	0.24*

Note. Data are presented as mean ± SD. SD: Standard deviation; LDH: Lactate dehydrogenase; CRP: C-reactive protein; ESR: Erythrocyte sedimentation rate; WBC: White blood cell; RBC: Red blood cell; Hb: Hemoglobin; EF: Ejection fraction. * Mann-Whitney test

Table 3. Univariate and Multivariate Logistic Regression Analysis

Parameters	Univariate Logistic Regression		Multivariate Logistic Regression	
	OR (95% CI)	P-value*	OR (95% CI)	P-value**
Age (years)	1 (0.96 to 1.03)	0.99	1.08 (0.83 to 1.42)	0.538
Gender, n (%)	1.97 (0.58 to 6.67)	0.27	0.000 (0.00 to 35794)	0.272
Smoking, n (%)	0.57 (0.15 to 2.10)	0.40	30.95 (0.00 to 2294405.96)	0.549
ICU, n (%)	2.08 (0.25 to 17.40)	0.49	13015191910485068.00 (0.00 to 1.16)	0.308
Hospitalization Time (days)	1.02 (0.96 to 1.08)	0.46	4.10 (0.22 to 76.38)	0.344
Mortality, n (%)	0.76 (0.18 to 3.08)	0.70	0.17 (0.00 to 686708.23)	0.819
SpO ₂ (%)	1.05 (0.98 to 1.13)	0.15	7.04 (0.13 to 378.93)	0.337
Pulmonary Pressure (mm Hg)	1.02 (0.98 to 1.07)	0.24	2.62 (0.41 to 16.44)	0.303
LDH (U/L)	0.99 (0.99 to 1.00)	0.07	0.94 (0.84 to 1.05)	0.326
CRP (mg/L)	1.00 (0.99 to 1.00)	0.86	0.87 (0.66 to 1.15)	0.349
ESR (mm/h)	1.01 (0.99 to 1.03)	0.24	1.83 (0.57 to 5.89)	0.309
Ferritin (µg/L)	1.00 (0.99 to 1.00)	0.55	1.00 (0.98 to 1.01)	0.851
WBC (× 10 ³)	1.00 (1.00 to 1.00)	0.21	1.00 (0.99 to 1.00)	0.272
RBC (× 10 ⁶)	0.85 (0.42 to 1.70)	0.65	2.56 (0.36 to 18.18)	0.347
Hb (g/dL)	0.91 (0.74 to 1.12)	0.39	0.366 (0.03 to 3.59)	0.389
Platelet (× 10 ³)	1.00 (1.00 to 1.00)	0.95	1.00 (1.00 to 1.00)	0.392
EF (%)	0.99 (0.91 to 1.07)	0.86	0.427 (0.08 to 2.10)	0.296
Pulmonary Involvement	1.37 (0.83 to 2.27)	0.20	0.18 (0.002 to 21.43)	0.487
Constant			0.000	0.336

Note. OR: Odds ratio; CI: Confidence interval; ICU: Intensive care unit; SpO₂: oxygen saturation; LDH: Lactate dehydrogenase; CRP: C-reactive protein; ESR: Erythrocyte sedimentation rate; WBC: White blood cell; RBC: Red blood cell; EF: Ejection fraction. **Multivariate logistic regression; *Univariate logistic regression

Discussion

COVID-19 emerged as a global pandemic in 2019, primarily affecting the respiratory system of patients and leading to a variety of pulmonary complications. It has been demonstrated that COVID-19 can disrupt the structure and function of lung cells (10, 16, 17). This study evaluated the association of laboratory and clinical parameters with PE in patients with COVID-19.

The results indicated that mean age, SpO₂, and pulmonary pressure were lower in patients with PE ($P > 0.05$). Moreover, pulmonary involvement was higher in patients with PE, but this difference was also not statistically significant compared to the other group ($P = 0.37$). Furthermore, the mortality rate was higher in patients with PE, E, although this difference was not statistically significant ($P = 0.70$).

A systematic study revealed that the rate of ICU hospitalization was higher in patients with PE, which is consistent with the findings of the present study (18). In addition, Scudiero et al showed that mortality was higher in patients with PE. They also reported no associations between age, sex, medical history, ICU admission, or other demographic variables and PE in COVID-19 patients (19). Moreover, Miro et al demonstrated that mortality was higher in COVID-19 patients with PE. They also reported that PE in COVID-19 patients was rare and occurred mainly in CU-admitted patients. Furthermore, variables such as age, sex, clinical condition, and previous medical history were significantly different between COVID-19 patients with PE and healthy individuals (20). Another study indicated that PE incidence in COVID-19 patients

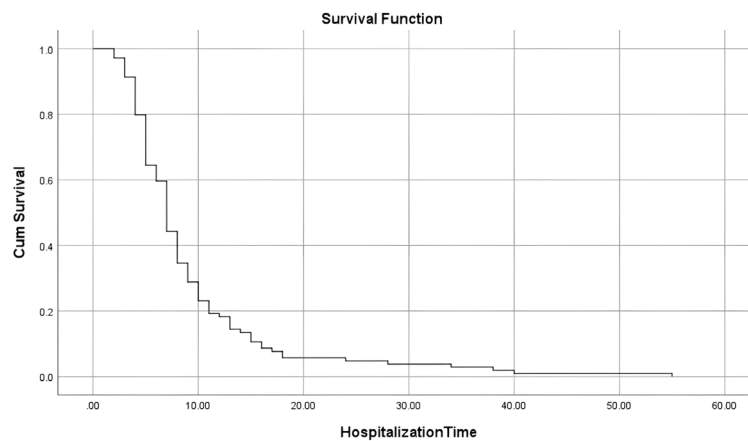


Figure 1. Survival Analysis Associated With Hospitalization Time

Table 4. Mean and Median for Survival Time Estimates

Mean ^a				Median			
Estimate	Std. Error	95% CI		Estimate	Std. Error	95% CI	
		Lower bound	Upper bound			Lower bound	Upper bound
9.221	0.792	7.669	10.773	7.000	0.317	6.380	7.620

Note. Std. Error: Standard error; CI: Confidence interval. a. Estimation is limited to the largest survival time if it is censored

was higher in males and was associated with a longer duration of ICU hospitalization (21).

We also found that the mean levels of LDH, RBCs, Hb, and EF were higher in patients with PE ($P > 0.05$). Conversely, the mean levels of CRP, ESR, ferritin, WBCs, and platelets were higher in patients without PE ($P > 0.05$).

Radkhah et al reported no relationship between platelet count, CRP, ferritin, Hb, and the percentages of neutrophils and lymphocytes with the incidence of PE in COVID-19 patients, which is consistent with findings of the present study (22). In another study, significant differences were reported in Hb, leukocytes, neutrophils, and lymphocytes, the neutrophil-to-lymphocyte ratio (NLR), and the platelet-to-lymphocyte ratio (PLR) between COVID-19 patients with and without PE. In contrast, no significant relationship was observed for platelet count or mean platelet volume (MPV) ($P > 0.05$) (23). Castillejo et al reported that only neutrophil and lymphocyte counts differed significantly between COVID-19 patients with and without PE, whereas no significant differences were observed for platelet count, ferritin, ESR, and CRP indices between the two groups (24).

Overall, the present findings suggest that laboratory indices, particularly hematological indices, may serve as useful biomarkers for monitoring COVID-19 patients with PE. These indices may contribute to the diagnostic and therapeutic strategies for patient management (25-27).

This study had several limitations. First, it had a retrospective design, which may have affected the quality of the data. Therefore, further prospective studies should be designed to enhance the reliability of the results. Second, this study was conducted in a single treatment center; thus, multicenter studies are needed to improve the generalizability of the results. It would also be valuable to

evaluate the effect of PE on patients' response to treatment. A total of 106 patients participated in this study, including 12 patients without PE and 94 patients with PE. The prevalence of PE in patients with COVID-19 is generally rare and depends on various factors. Furthermore, the single-center setting limited the number of patients. To address these limitations, future studies should employ larger patient populations.

Conclusion

Overall, the results indicated no statistically significant relationship between clinical or laboratory parameters and the incidence of PE in COVID-19 patients. However, further research is needed to explore these associations more thoroughly.

Authors' Contribution

Conceptualization: Somayeh Zamanifard

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Supervision: Somayeh Zamanifard

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Visualization: Somayeh Zamanifard

Writing–Original Draft: Zahra Habibi

Writing–Review & Editing: Somayeh Zamanifard

Competing Interests

The authors declare that they have no conflict of interests.

Consent for Publication

Not applicable.

Data Availability Statement

Data are available from the corresponding author upon reasonable request.

Ethical Approval

All procedures performed in this study involving human participants followed the ethical standards of the local ethics committee of Shahrekord University of Medical Sciences (IR. SKUMS.MED).

REC.1400.019), as well as the 1964 Helsinki Declaration.

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