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ORIGINAL RESEARCH

Comparison of Platelet Indices, Lymphocyte, and Systemic Inflammation Indices on Days 1 and 8 in Surviving and Non-Surviving COVID-19 Patients at Hasan Sadikin General Hospital, Bandung, Indonesia

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Purpose: This study aimed to compare platelet count, platelet indices, lymphocyte, and systemic inflammation indices between surviving and non-surviving COVID-19 patients, measured at admission and on the eighth day of hospitalization.

Patients and Methods: A retrospective cohort study was conducted on COVID-19 patients hospitalized at Hasan Sadikin General Hospital, Bandung, from March to December 2020. Patient characteristics and laboratory data were sourced from medical records and the Clinical Pathology Laboratory. Bivariate analysis was performed to determine the comparison of platelet indexes between Surviving and Non-Surviving COVID-19 patients depending on data distribution. Significantly correlated variables in Bivariate analysis were included in the ROC analysis, with the AUC used to identify optimal threshold values for laboratory parameters.

Results: Data from 132 patients were analyzed, with 106 (80.3%) surviving and 32 (19.7%) not surviving. Non-surviving patients had lower platelet count, PLTCT, and lymphocyte levels but higher MPV and PDW compared to survivors. Receiver operating characteristic (ROC) analysis revealed that on day 1, lymphocytes had a higher area under the curve (AUC) than MPV. On day 8, lymphocytes had the highest AUC, followed by platelet count, MPV, PLTCT, and PDW.

Conclusion: Platelet indices, lymphocyte counts, and systemic inflammation index have the potential to distinguish the severity of COVID-19.

Keywords: mortality, platelet indices, thrombocytopenia, SII, NLR

Introduction

Coronavirus disease 2019 (COVID-19), caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), was first detected in Wuhan, China, in December 2019. In March 2020, the World Health Organization declared it a global pandemic. By March 2022, there were 474,805,725 confirmed cases and 6,123,387 deaths globally, with 154,000 deaths reported in Indonesia.[1,2] The mortality rate for COVID-19 reached 61.5% among confirmed cases.

The severity of COVID-19 symptoms varies from mild to moderate and severe.[3] A meta-analysis of over 50,000 cases showed that 18.1% of infections resulted in severe illness.[4] Clinical manifestations of COVID-19 are correlated with various laboratory parameters, emphasizing the importance of simple hematological analyses, such as complete blood count (CBC).[5] These analyses are widely utilized in both large and small laboratories, as well as in outpatient and

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inpatient settings.[6] The inexpensive and accessible laboratory tests can provide valuable insights into disease severity and guide treatment decisions.[6–9]

Monitoring hematological markers, such as platelet indices,[10–21] lymphocyte,[22–29] and neutrophil[25,26,30,31] levels, is crucial for assessing clinical progression and detecting potential deterioration in patient conditions.[5] The platelet index serves as a key marker of platelet activation and reflects platelet quality. It includes measurements of total platelet count, morphology, and proliferation.[12] The lifespan of platelets, typically 7–10 days, aligns with the estimated duration of COVID-19, which ranges from 7 to 14 days from the onset of symptoms to clinical manifestations.[8] During this period, infections can cause changes in platelets, which are detectable through the platelet index as a marker of activation.[14,32] Monitoring changes in platelet count from day 1 of disease onset and throughout treatment is crucial for assessing the disease's clinical progression.[13]

The relationship between lymphocytes and COVID-19 is being explored, with hypotheses suggesting that SARS-CoV -2 may directly infect T cells, leading to a reduction in CD4+ and CD8+ lymphocytes.[33] Numerous concurrent studies have also indicated that hematologic parameters, such as platelet indices[10–21] and lymphocyte[22–29] correlate with the severity and mortality of COVID-19 cases.

On the other hand, several parameters have been introduced to estimate the severity of COVID-19. The neutrophil-to-lymphocyte ratio (NLR)[25,26,30,31,34,35] and systemic inflammation index (SII)[34,36–39] is an inflammatory parameter that can estimate the severity of symptoms of COVID-19. The SII is obtained by calculating the number of lymphocytes, neutrophils, and platelets. A higher score of SII indicated a poor prognostic marker in several malignancies.[40] During the COVID-19 pandemic, SII has been used to predict the in-hospital mortality of the disease.[34] It is a marker to predict the need for invasive ventilators and poor patient outcomes.[41]

This study aimed to compare platelet indices, lymphocyte, and systemic inflammation index on admission and day 8 of hospitalization between surviving and non-surviving COVID-19 patients.

Materials and Methods

Study Design and Participants

This retrospective cohort study was conducted on COVID-19 patients hospitalized at Hasan Sadikin General Hospital, Bandung, from March to December 2020. We collected secondary data from day 1 (admission day) to day 8[12,42] of hospitalization, including patient characteristics and final outcomes from medical records. Laboratory data were obtained from the electronic records of the Clinical Pathology Laboratory at the hospital. Patients were categorized into two groups based on survival outcomes: survivors and non-survivors.

Inclusion criteria included confirmed COVID-19 patients over 18 years old with complete hematological and platelet index data in their medical records. Patients were excluded if they had autoimmune or hematologic disorders; were pregnant women; had malignant diseases, human immunodeficiency virus, or chronic liver; or were immunocompromised and receiving immunosuppressive therapy.

Data Collection

Data from days 1 and 8 of hospitalization for COVID-19 patients were gathered from the hospital's information system. Patient characteristics such as age, gender, comorbidities, treatment, COVID-19 outcomes, severity levels, and laboratory results were collected. Laboratory data included hemoglobin, hematocrit, leukocyte count, segmented neutrophils, total neutrophils, total platelets, absolute lymphocytes, and platelet indices. MPV reflects the average platelet size, PDW indicates variability in platelet size and anisocytosis, and PLTCT represents total platelet mass, calculated using the following formula: platelet count × MPV / 10,000. Systemic inflammatory index (SII) was calculated as platelet count × neutrophil count/lymphocyte count. COVID-19 diagnosis was confirmed through reverse transcription-polymerase chain reaction (RT-PCR) using nasal swabs. COVID-19 severity was classified as mild, moderate, or severe. Severe cases included patients with oxygen saturation below 94% without oxygen supplementation, PaO2/FiO2 ratio under 300 mmHg, rapid breathing (over 30 breaths per minute), more than 50% lung infiltration, acute respiratory distress syndrome, septic shock, or those requiring invasive ventilation or vasopressor therapy. Moderate patients were classified

as patients with clinical signs of pneumonia, including fever, cough, dyspnea, and rapid breathing, without evidence of severe pneumonia. These patients generally do not exhibit signs of respiratory failure or significant hypoxia, while mild cases were classified as patients with non-specific clinical signs such as fever, cough, sore throat, nasal congestion, malaise, headache, and muscle aches.[43]

Statistical Analysis

Demographic and clinical data were presented as the median and interquartile range (IQR) for continuous variables and as frequencies and proportions for categorical variables. The normality of data distribution was assessed using the Kolmogorov–Smirnov test. Statistical comparisons between the survived and non-survived groups were made using the Chi-square test, Fisher's exact test, unpaired *t*-test for normal distributed data, and Mann–Whitney test for skewed data, with a *p*-value of <0.05 considered statistically significant.

Significantly correlated variables in bivariate analysis were included in the ROC analysis, with the AUC used to identify optimal threshold values for laboratory parameters. Cut-off points, sensitivity, and specificity were determined using ROC analysis and were presented as descriptive statistics. All statistical analyses were conducted using IBM SPSS version 27, GraphPad PRISM version 9, and MedCalc version 20.011.

Ethical Consideration

The study was conducted in accordance with the Declaration of Helsinki and approved by the Health Research Ethics Committee of Dr. Hasan Sadikin General Hospital, Bandung, with ethics number LB.02.01/X.6.5/451/2022 with the approval date of 13 December 2022, and performed with a waiver of informed consents, as it utilized anonymized secondary data and had no additional examination directly contact to the patients.

Results

We screened data from 691 confirmed COVID-19 patients admitted from March to December 2020. Most patients (559) had incomplete records of hematological and platelet indices, leaving 132 patients who met the inclusion criterion for the study (Figure 1). This group consisted of 106 (80.3%) survivors and 26 (19.7%) non-survivors. The characteristics of the group are detailed in Table 1. The non-survivors had a significantly older median age compared to the survivors. Males predominated in both groups, comprising 59.4% of the survivors and 88.4% of the non-survivors. Hypertension was the most prevalent risk factor in both groups. The non-survivors also had a higher proportion of severe cases compared to the survivors, with rates of 65.4% and 28.3%, respectively, which was statistically significant.

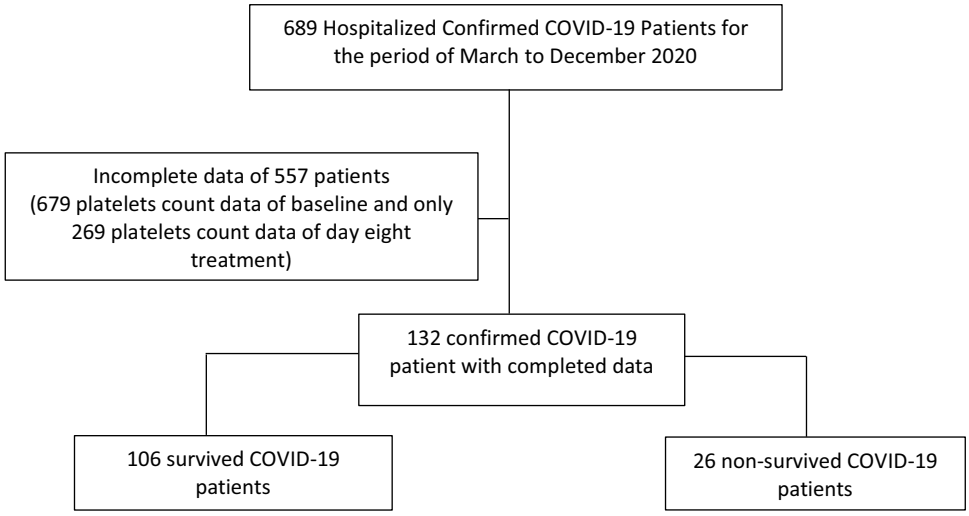

Figure 1 Subject selection process.
Abbreviations: COVID-19, coronavirus disease 2019; IQR, Interquartile range.

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Table 1 Comparison of Background Characteristics of Subjects

Characteristics	Total (n = 132)	Classification		*p*-value
		Survived COVID-19 Patients (n = 106)	Non-Survived COVID-19 Patients (n = 26)	
Age (years), median (IQR)[a]	56 (43–65)	54 (43–64)	60 (52–74)	0.020*
Gender, n (%)[b]				
Female	46 (34,8)	43 (93,5)	3 (6,5)	
Male	86 (65,2)	63 (73,3)	23 (26,7)	0.005*
Comorbidity, n (%)[b]				
Hypertension	48 (36.4)	36 (34.0)	12 (46.2)	0.492
Diabetes	21 (15.9)	17 (16.0)	4 (15.4)	0.599
Chronic heart failure	15 (11.4)	11 (10.4)	4 (15.4)	0.584
Chronic kidney disease	10 (7.6)	9 (8.5)	1 (3.8)	0.382
No comorbidity	51 (38.6)	43 (40.6)	8 (30.8)	0.358
Severe level, n (%)[b]				
Mild–moderate	85 (64.4)	76 (71.7)	9 (34.6)	<0.001*
Severe	47 (35.6)	30 (28.3)	17 (65.4)	
Hematology parameters, median (IQR)[a]				
Hemoglobin (g/dL)	13.8 (12.4–15.1)	13.7 (12.3–15.0)	14.0 (13.0–15.6)	0.405
Hematocrit	40.0 (36.7–43.63)	40.0 (36.6–15.1)	39.1 (36.7–44.1)	0.429
Leukocytes (10^3/µL)	7.9 (5.8–11.2)	7.9 (5.8–10.6)	8.3 (6.4–14.7)	0.170
Segmented neutrophils	77.0 (67.0–84.7)	75.5 (65.6–84.0)	84.5 (73.8–89.3)	0.002*
Neutrophils (%)	78.0 (67.0–85.0)	76.5 (66.0–84.0)	84.5 (74.0–90.0)	0.003*
Absolute neutrophils (10^3/µL)	5950 (4338–9115)	5885 (3725–8380)	7160 (5445–12,763)	0.037*
Lymphocytes (%)	15.0 (8.0–23.0)	16.0 (10.0–24.0)	6.0 (7.0–7.0)	0.004*
Absolute lymphocytes (10^3/µL)	1127 (816–1511)	11 88 (847–1638)	513 (872–1142)	0.003*
Platelets (10^3/µL), (n = 131)	255 (189–325)	258 (193–336)	240 (175–309)	0.354
Plateletcrit (%)	0.25 (0.20–0.31)	0.25 (0.20–0.32)	0.23 (1.88–0.29)	0.375
PDW	10.8 (9.7–12.6)	10.7 (9.7–12.2)	11.3 (9.8–13.0)	0.058
MPV	10.0 (9.4–10.8)	10.7 (9.7–12.2)	10.6 (9.6–11.2)	0.011*
NLR	5.1 (3.1–10.6)	4.7 (2.8–8.6)	12.6 (5.2–15.0)	<0.001*
SII	1498.7 (656–2548)	1149.8 (563–2422)	2129.3 (1128.9–3918.1)	<0.001*
Treatment, n (%)[b]	n = 96	n = 82	n = 14	
Favipiravir	55 (57.3)	50 (61.0)	5 (35.7)	0.077
Remdesivir	51 (53.1)	38 (46.3)	13 (92.9)	0.001*
Steroid	72 (75.0)	59 (72.0)	13 (50.0)	0.095

(*Continued*)

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Table 1 (Continued).

Characteristics	Total (n = 132)	Classification		*p*-value
		Survived COVID-19 Patients (n = 106)	Non-Survived COVID-19 Patients (n = 26)	
Convalescent plasma	8 (8.3)	8 (9.8)	0 (0.0)	0.222
Antiviral treatment	87 (90.6)	73 (89.0)	0 (0.0)	0.193
Oseltamivir	1 (1.0)	0 (0.0)	1 (7.1)	NA
Antibiotics	77 (80.2)	64 (78.0)	13 (92.9)	0.199

Notes: [a]Analyzed using independent *t*-test; [b]Analyzed using Chi-square test; *$p < 0.05$: statistically significant.
Abbreviations: COVID-19, coronavirus disease 2019; IQR, Interquartile range; NLR, neutrophil-lymphocyte ratio; SII, systemic inflammatory index.

From the hematological parameters, the levels of segmented neutrophils, total neutrophils, and absolute neutrophils were higher in the non-survivor group, with values of 75.5 (IQR, 65.6–84.0), 76.5 (IQR, 66.0–84.0), and 5.885 (IQR, 3725–8380), respectively, compared to the survivor group, which had values of 84.5 (IQR, 73.8–89.3), 84.5 (IQR, 74.0–90.0), and 7.160 (IQR, 5.445–12.763). These differences were statistically significant. In contrast, the total lymphocyte count and absolute lymphocytes were lower in the non-survivor group, with values of 2.0 (IQR, 6.0–17.3) and 872 (IQR, 513–1.142), respectively, compared to the survivor group, which had values of 16.0 (IQR, 10.0–24.0) and 1.188 (IQR, 847–1.638), respectively, and these differences were also statistically significant. The non-survivor also shows a statistically higher NLR and SII, with a value of 12.6 (IQR, 5.2–15.0) and 2129.3 (IQR, 1128.9–3918.1), respectively, compared to the survivors with a value of 4.7 (IQR, 2.8–8.6) and 1149.8 (IQR, 563–2422), respectively.

The differences in platelet indices between the survived and non-survived groups on day 1 and day 8 of treatment are shown in Table 2. Our study indicated that platelet levels were lower in the non-survivor group than in the survivor group on both day 1 and day 8 of admission (Table 2). However, only the platelets measured on day 8 showed statistical significance ($p = <0.001$) (Figure 2A). PLTCT counts were lower in the non-survivor group compared to the survivor group on day 1 and day 8 as well, with only the day 8 results being statistically significant ($p = 0.002$) (Figure 2B).

Compared to the survivor group, the MPV levels were higher in the non-survivor group on both day 1 and day 8 of treatment, with *p*-values of 0.039 and 0.001, respectively (Figure 2C). The PDW levels were also higher in the non-

Table 2 Comparison of Hematology Parameters, NLR, and Systemic Inflammation Indices in Survived and Non-Survived COVID-19 Patients

Characteristics	Survived COVID-19 Patients (n = 106) Median (IQR)	Non-Survived COVID-19 Patients (n = 26) Median (IQR)	p-value[a]
Hematology parameters			
Platelets (10^3/μL)			
Day 1	258 (193–336)	241 (176–309)	0.354
Day 8	376 (272–460)	262 (202–321)	<0.001*
Delta	106 (37–204)	52 (−87–106)	0.001*
Delta %	41.8 (11.5–95.6)	24.5 (−28.5–51.7)	0.014*
p-value[b] (within)	<0.001*	0.461	

(*Continued*)

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Table 2 (Continued).

Characteristics	Survived COVID-19 Patients (n = 106) Median (IQR)	Non-Survived COVID-19 Patients (n = 26) Median (IQR)	p-value[a]
Plateletcrit (%)			
Day 1	0.25 (0.20–0.32)	0.23 (0.19–0.29)	0.375
Day 8	0.36 (0.29–0.46)	0.30 (0.22–0.34)	0.002*
Delta	0.11 (0.03–0.19)	0.07 (−0.07–0.12)	0.030*
Delta %	39.1 (11.4–87.9)	34.4 (−27.6–58.3)	0.106
p-value[b] (within)	<0.001*	0.134	
Mean platelet volume (fL)			
Day 1	9.9 (9.4–10.7)	10.6 (9.8–11.2)	0.039*
Day 8	9.9 (9.3–10.7)	10.8 (9.9–11.3)	0.001*
Delta	−0.1 (−0.5–0.3)	0.4 (−0.5–0.7)	0.67
Delta %	−1.0 (−4.1–3.2)	3.6 (−4.5–7.1)	0.70
p-value[b] (within)	0.329	0.140	
Platelet distribution width (fL)			
Day 1	10.7 (9.7–12.2)	11.3 (9.8–12.9)	0.234
Day 8	10.5 (9.7–12.4)	12.1 (10.7–13.6)	0.009*
Delta	−0.2 (−0.9–0.7)	0.6 (−0.9–2.0)	0.108
Delta %	−0.1 (−7.9–7.3)	6.0 (−8.1–18.5)	0.083
p-value[b] (within)	0.989	0.121	
Lymphocyte (%)			
Day 1	16.0 (10.0–24.0)	7.0 (6.0–15.3)	<0.001*
Day 8	14.0 (7.0–25.0)	4.6 (3.0–8.0)	<0.001*
Delta	−2.0 (−8.3–5.0)	−4.0 (−9.0–−1.8)	0.58
Delta %	−11.4 (−50.0–32.9)	−57.1 (−70.1–14.0)	<0.001*
p-value[b] (within)	0.225	<0.001*	
Absolute lymphocyte (/μL)			
Day 1	1188 (847–1638)	872 (513–1142)	0.003*
Day 8	1173 (737–1623)	554 (364–1029)	<0.001*
Delta	−19 (−391–386)	−194 (−508–92)	0.124
Delta %	−2.1 (−26.9–36.7)	−21.1 (−52.7–23.1)	0.045*
p-value[b] (within)	0.907	0.066	

(*Continued*)

Table 2 (Continued).

Characteristics	Survived COVID-19 Patients (n = 106) Median (IQR)	Non-Survived COVID-19 Patients (n = 26) Median (IQR)	p-value[a]
NLR (Neutrophil-lymphocyte ratio)			
Day 1	4.66 (2.78–8.62)	12.57 (5.21–14.93)	<0.001*
Day 8	5.50 (2.56–12.51)	20.38 (10.80–31.47)	<0.001*
Delta	0.63 (−1.78–7.58)	10.57 (2.23–24.57)	<0.001*
Delta %	16.5 (−36.5–148.3)	143.8 (20.6–294.3)	0.002*
p-value[b] (within)	0.012*	<0.001*	
SII (Systemic inflammatory index)			
Day 1	1149 (563–2422)	2129 (1128–3918)	<0.006*
Day 8	1991 (821–1991)	5860 (3090–7867)	<0.001*
Delta	378.0 (−107.2–2795)	3195 (−114.3–5447)	0.06
Delta %	53.49 (−12.13–222.5)	141.0 (−3.507–552.0)	0.12
p-value[b] (within)	<0.001*	<0.001*	

Notes: Analyzed using [a]mann–Whitney *U*-test, [b]Wilcoxon test *p < 0.05: statistically significant.
Abbreviations: COVID-19, coronavirus disease 2019; IQR, Interquartile range.

survivor group compared to the survivor group, but statistical significance was only observed on day 8 with a *p*-value of 0.009 (Figure 2D).

Figure 2E illustrates that total lymphocyte levels were lower in the non-survivor group than in the survivor group on both day 1 and day 8 of treatment, with statistically significant *p*-values of <0.001 for both days. The absolute lymphocyte levels were similarly lower in the non-survivor group compared to the survivor group on day 1 and day 8 (Figure 2F), with significant differences on both days, yielding *p*-values of 0.003 and <0.001, respectively.

Additionally, NLR and SII also exhibited a statistically higher value in the non-survivor group compared to the survivor group on both day 1 and day 8 of treatment with the p-values of <0.001 from both days for NLR (Figure 2G), and <0.006* and <0.001, respectively for SII (Figure 2H).

The ROC analysis was conducted on total lymphocytes, absolute lymphocytes, MPV, NLR, and SII, for the non-survivor group on day 1 of treatment and on total lymphocytes, absolute lymphocytes, platelet count, MPV, PLTCT, PDW, NLR, and SII for the non-survivor group on day 8. This analysis aimed to identify the most reliable hematologic indicator for predicting mortality in COVID-19 patients. The NLR value exhibited the highest AUC of 0.740 as a mortality predictor on day 1 of treatment, with a cutoff of >12.4, a sensitivity of 53.8%, and a specificity of 90.6% (Figure 3A). This was followed by total lymphocyte, absolute lymphocytes, SII and MPV, which had AUCs of 0.729, 0.691, 0.674, and 0.631, respectively (Figure 3B–E). On day 8, the total lymphocyte value showed the highest AUC of 0.814 as a mortality predictor, with a cutoff value of $\leq 910^3/\mu L$, sensitivity of 88.5%, and specificity of 64.2% (Figure 4A) followed by NLR, absolute lymphocyte, platelet count, SII, MPV, PLTCT, and PDW with AUCs of 0.813, 0.750, 0.747, 0.726, 0.701, 0.691, and 0.665 respectively (Figure 4).

Discussion

In this study, we noted variations in platelet indices, lymphocytes, NLR, and SII between COVID-19 patients who survived and those who did not. The non-survivor group exhibited lower levels of platelet count, PLTCT, and lymphocytes, along with higher levels of MPV, PDW, NLR, and SII compared to the survivor group.

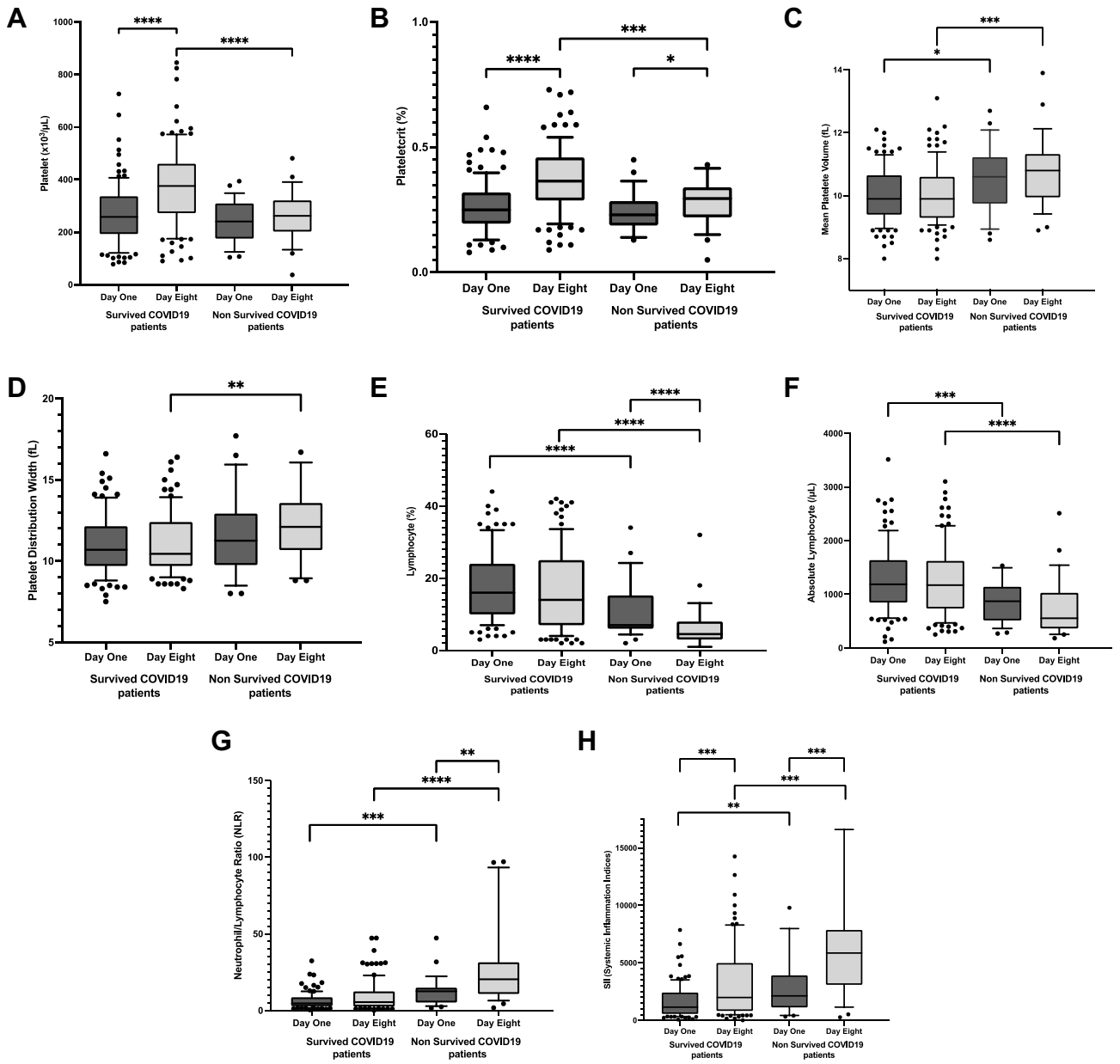

Figure 2 Boxplot distribution on day 1 and day 8 for survived and non-survived COVID-19 patients. (**A**) platelet count, (**B**) PLTCT, (**C**) MPV, (**D**) PDW, (**E**) total lymphocyte, (**F**) absolute lymphocyte, (**G**) NLR, and (**H**) SII.
Notes: *$p < 0.05$, ** $p < 0.01$, ***$p < 0.005$, ****$p < 0.001$.

The platelet count and PLTCT in the non-survivor group were significantly lower than in the survivor group on day 8 of treatment. A meta-analysis indicated that thrombocytopenia was associated with a threefold increased risk of severe COVID-19, with lower platelet counts associated with higher mortality.[44] Wang et al identified a correlation between thrombocytopenia and mortality. In contrast, Guclu et al reported that thrombocytopenia was more common in non-survivors than in survivors but found no correlation between platelet levels and mortality.[17] Additionally, Huang et al observed no significant difference in platelet counts between COVID-19 patients in ICU and non-ICU settings, which may be attributed to the limited sample size in their study.[4]

It has been reported that mortality increases as platelet count decreases.[11] Immunopathological damage to lung tissues has led to histological examination of platelet activation and aggregation in the lungs.[45,46] Studies from post-mortem examinations of COVID-19 patients revealed elevated platelet–fibrin thrombin in the small arteries and capillaries of the

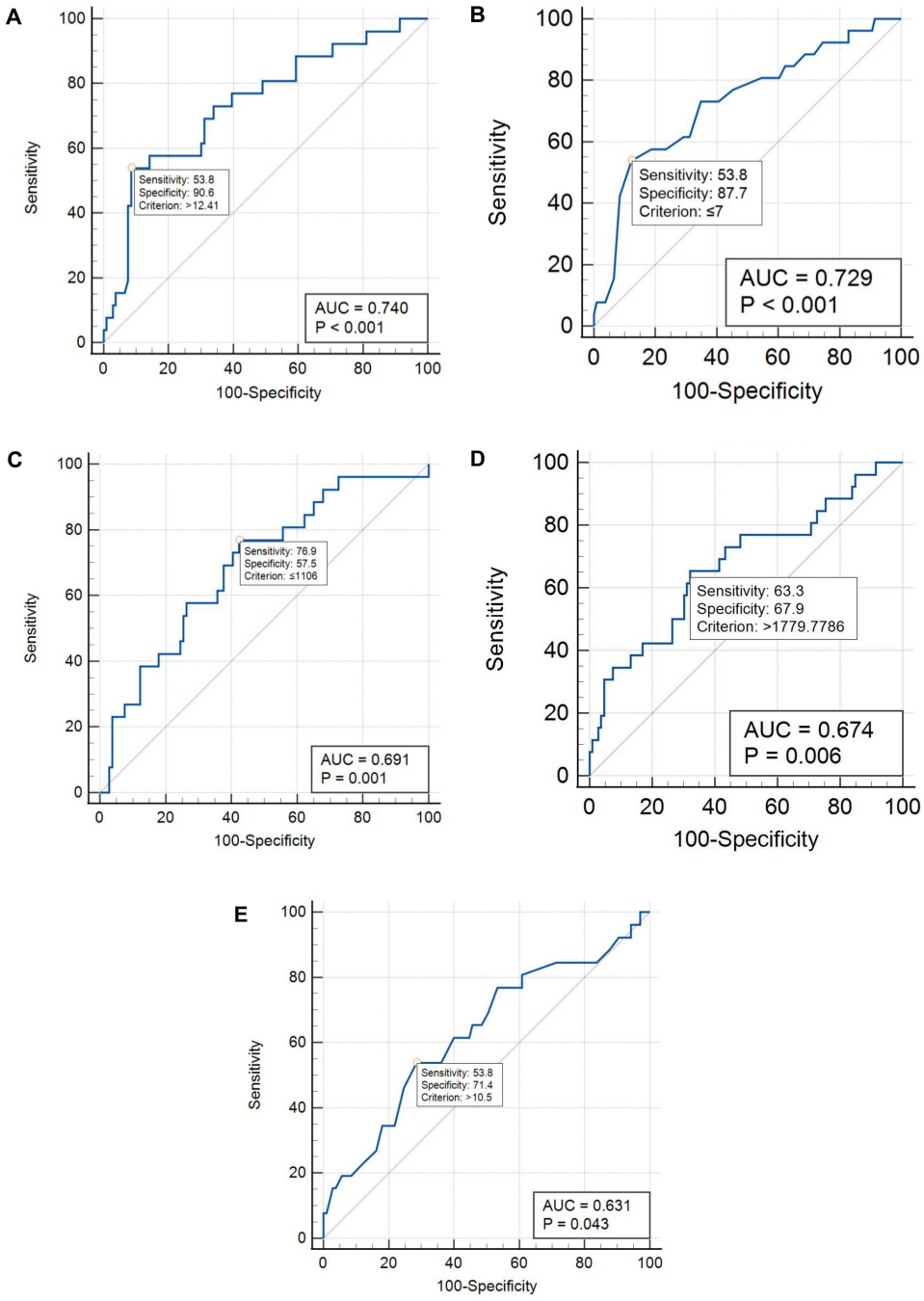

Figure 3 ROC curves of day 1 treatment of non-survived COVID-19 patients. (**A**) NLR, (**B**) total lymphocyte, (**C**) absolute lymphocyte, (**D**) SII, and (**E**) MPV. The blue line represents the ROC curve based on sensitivity and specificity calculations at various cutoff levels.

pulmonary vasculature, indicating a hypercoagulable state that can increase the risk of both venous and arterial thrombosis in critically ill COVID-19 patients, resulting in reduced platelet count and PLTCT.[47–50]

We found that the non-survivor group had a lower lymphocyte count than the survivor group on days 1 and 8 of treatment, with a statistically significant difference. A study indicated that lymphocyte levels were notable lower in severe cases and in patients requiring ICU care, serving as a prognostic marker for COVID-19 patients.[29,31,51] The meta-analysis showed that patients with severe COVID-19 experienced a decrease in lymphocytes. Additionally, other studies found that lymphopenia is associated with a threefold increased risk of severe COVID-19 infection.[24] However, another

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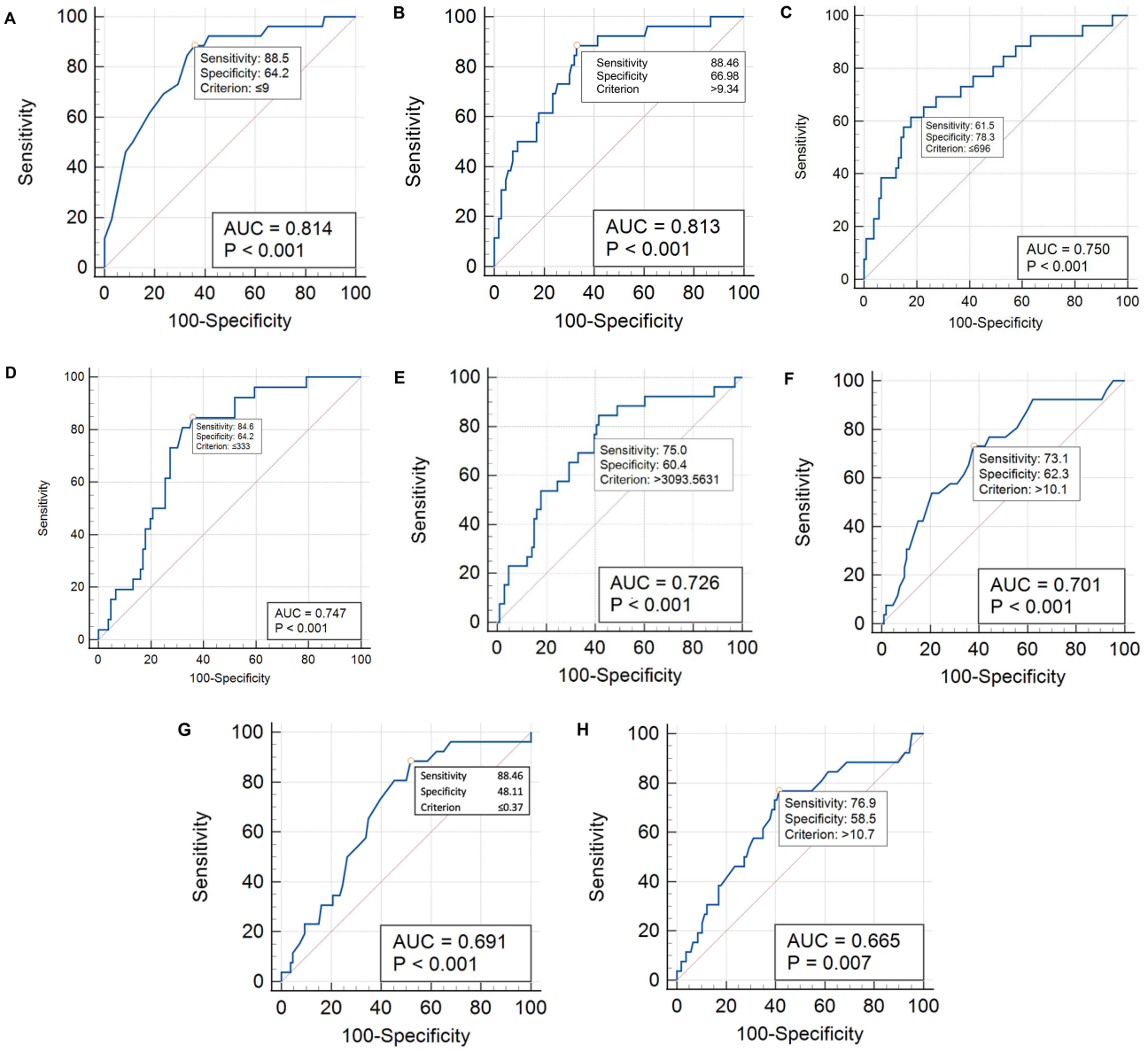

Figure 4 ROC curves of day 8 treatment of non-survived COVID-19 patients. (**A**) total lymphocyte, (**B**) NLR, (**C**) absolute lymphocyte, (**D**) platelet count, (**E**) SII, (**F**) MPV, (**G**) PLTCT, and (**H**) PDW. The blue line represents the ROC curve based on sensitivity and specificity calculations at various cutoff levels.

study noted an increase in lymphocyte count from day 1 to day 7 in non-survivor COVID-19 patients, although this increase was not statistically significant.[22]

Lymphocytes are crucial for regulating immune responses during inflammation. Changes in lymphocyte counts during COVID-19 may result from an inflammatory cytokine storm and T-cell interference.[28] Tan et al proposed several potential mechanisms for the changes in lymphocytes during COVID-19 infection: the virus targets the ACE2 receptor on lymphocytes, causing their death, and it may also directly damage lymphatic organs.[23,52–54] Another study indicated that the virus can suppress bone marrow function or trigger immune-mediated destruction of lymphocytes.[27,55–59] These mechanisms may collectively contribute to lymphopenia. Based on these findings, lymphocyte count could be an effective tool for quickly assessing the prognosis of COVID-19 patients.

In this study, the non-survivor group exhibited higher levels of MPV and PDW, with MPV being significant on both days 1 and 8 of treatment, while PDW was only significant on day 8. Similar findings were reported by Guclu et al and Sertbas et al, indicating a relationship between MPV, PDW, and mortality.[13] Their research showed that a one-unit

increase in MPV was linked to a 1.76 times higher risk of mortality.[17] However, other studies found no significant differences in MPV values among COVID-19 patients in the ICU, despite observing an increase in MPV that was not statistically significant.[9,60]

A study found that inflammatory cytokines might promote thrombopoiesis through various mechanisms, leading to the release of large and active platelets that could cause thromboembolism.[13] Three hypotheses regarding platelet count and structure are proposed: First, thrombocytopenia may result from the infection of the bone marrow, similar to other coronaviruses. Second, platelet destruction may occur due to the immune system. Third, platelet consumption may arise from aggregation in the lungs. Generally, as platelet count decreases, platelet production increases, which may account for the increase in MPV and PDW.[17] In addition to its inflammatory effects, COVID-19 has been shown to influence the hematopoietic system and hemostasis.[61] The study suggests that findings related to platelet count, PLTCT, MPV, and PDW may serve as prognostic indicators for predicting mortality in COVID-19 patients.

Based on the multicellular involvement in the pathophysiology of COVID-19, it was no surprise that more indicators were developed, such as the systematic immunoinflammatory index (SII).[34,62] This indicator is calculated based on the NLR and platelet count and is used to predict COVID-19 severity and mortality.[63,64] Our study found that both NLR and SII were significantly higher in the non-survived group compared to the survived group. These findings align with those of previous studies, which reported significantly higher SII values in non-survived patients compared to those who recovered.[65] Xue et al also showed that severe symptoms patients had an elevated SII compared to mild to moderate patients with SII.[66] Furthermore, a study also found that SII was an independent prognostic marker for hospitalized COVID-19 patients in the intensive care unit.[38] Recently, it has also been reported that the SII was significantly altered in COVID-19 patients when compared to healthy controls, suggesting a diagnostic role in SARS-CoV2-infected patients.[67]

Additionally, T lymphocytes CD4+ and CD8+ decrease is associated with disease severity, leading to increased NLR values, which have been reported to be a more sensitive biomarker of inflammation than the individual levels of neutrophils and lymphocytes.[68] In COVID-19 infection, neutrophil activation stimulates the formation of neutrophil extracellular trap (NET), platelet aggregation, and cell damage.[69] In addition, lymphopenia is a major immunological disorder in most severe COVID-19 patients and is significantly associated with mortality. Lymphopenia can cause immunosuppression and trigger a cytokine storm, which plays an important role in viral persistence, replication, multiorgan failure, and eventually death.[70] Platelets are also crucial in the severity of the development of COVID-19 and responsible for hemostasis and thrombus formation that can induced by the proinflammatory microenvironment, contributing to the existence of cytokine storm that characterizes the aggressive course of COVID-19.[71] In this context, NLR and SII value may serve as reliable predictors of severity in hospitalized COVID-19 patients.

The ROC analysis revealed that NLR showed the highest AUC, followed by lymphocytes, SII, and MPV on the first day of hospitalization. On the eighth day of follow-up, lymphocytes showed the highest AUC, followed by NLR, platelet count, SII, MPV, PLTCT, and PDW, indicating that NLR was more effective in predicting mortality in COVID-19 patients on eight days of hospitalization.

This study has some limitations. It is a retrospective cohort study based on existing data with a relatively small sample size. Additionally, less than half of the registered COVID-19 patients were included, and the sample primarily consists of hospitalized male patients under 60 years old with mild to moderate symptoms.

Conclusion

Platelet indices, lymphocyte counts, NLR, and systemic inflammation index have the potential to distinguish the severity of COVID-19.

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Disclosure

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