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Clinical and laboratory characteristics of critically ill COVID-19 patients with chronic lung disease

Tunzala Yavuz[1], Omurhan Sarac[2], Ozcan Alpdogan[2], Hicret Yeniay[3], Didem Celik[1]

[1] *Izmir Tepecik Training and Research Hospital, Izmir, Turkey*
[2] *Izmir City Hospital, Izmir, Turkey*
[3] *Balikesir Ataturk City Hospital, Balikesir, Turkey*

Abstract

Introduction: Chronic lung diseases (CLD) are associated with increased susceptibility to respiratory infections and may influence COVID-19 outcomes. This research aims to assess the clinical, laboratory findings, and prognostic outcomes in critically ill COVID-19 patients with and without CLD, and to explore differences between various CLD types.

Methodology: A retrospective analysis was conducted on 406 critically ill COVID-19 patients, comparing those with CLD and those without. Clinical characteristics, laboratory markers, and mortality rates were assessed. Subgroup analyses evaluated differences between COPD, asthma, and other CLD types.

Results: Patients with CLD were older and had significantly lower lymphocyte and platelet levels than those without CLD (p values were 0.034, 0.021, and 0.013, respectively). The mean age, urea level, and platelet count in the COPD group showed significant differences compared to the other groups. Among critically ill COVID-19 patients, mortality rates were observed to be higher in the CLD group compared to those without CLD, and in the COPD group compared to other CLD types; however, these differences did not reach statistical significance.

Systemic steroid use was associated with reduced 3-month (OR: 0.403, 95% CI: 0.226-0.719, $p = 0.002$) and 1-year mortality (OR: 0.513, 95% CI: 0.288-0.914, $p = 0.023$). Inhaled corticosteroid use did not increase mortality and was predominantly utilized for symptom management. Laboratory markers such as lymphopenia and thrombocytopenia were significantly associated with worse outcomes.

Conclusions: CLD and its subtypes were not independently linked to mortality in critically ill COVID-19 patients; however, their association with older age and worse laboratory profiles highlights their clinical significance.

Key words: asthma; COPD; corticosteroids; COVID-19; lung diseases; mortality.

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Introduction

The COVID-19 pandemic, caused by the Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2), is associated with substantial rates of morbidity and mortality. The clinical presentation of COVID-19 varies from asymptomatic cases to severe outcomes, including acute respiratory distress syndrome (ARDS) and death. Certain risk factors, such as older age, male gender and cardiovascular diseases, obesity, and diabetes, have been linked to poorer outcomes in COVID-19 patients [1,2].

Chronic lung diseases (CLD) such as chronic obstructive pulmonary disease (COPD), asthma, and other lung diseases may increase the risk of serious infections, especially viral infections. Moreover, viral infections are among the primary triggers for exacerbations of chronic respiratory conditions, further complicating disease management and patient outcomes [1,3-5]. CLD, due to its distinct pathophysiological mechanisms, can significantly influence the clinical course of COVID-19 infection, the severity of the disease, and the response to treatment. In particular, viral infections affecting the respiratory system, such as COVID-19, can lead to marked differences in the prognosis of patients [6,7].

COPD is a progressive lung condition characterized by airflow restriction and persistent respiratory symptoms. COPD patients who have a COVID-19 infection may develop severe disease, in addition to a typical exacerbation. These patients are at a higher risk of poor outcomes and elevated mortality [1-5,7,8]. However, the literature provides inconsistent results regarding the effects of different chronic lung diseases on the course of COVID-19. While some studies have not found a meaningful association between COPD and increased mortality, some studies have provided information supporting this relationship [1,3-11].

Asthma, a chronic inflammatory disease of the airways, has generally not been associated with worse COVID-19 outcomes. However, patients with severe asthma, characterized by frequent exacerbations and persistent symptoms, may face an increased risk of

higher mortality rates when infected with COVID-19 [1,3-5].

Studies evaluating the impact of these conditions (asthma, COPD) on COVID-19 outcomes have yielded mixed results, with variations in severity and prognosis reported across different populations [1,3-5,7,8]. The use of inhaled corticosteroids may significantly influence the disease course in COVID-19 patients with asthma. In addition, laboratory markers such as lymphopenia and eosinopenia may indicate a severe course of the disease. The assessment of these biomarkers is critically important in the clinical management of COVID-19, not only for asthmatic patients but also for the broader patient population [1,3-5].

This study aims to assess the clinical features and laboratory findings, and prognostic results in critically ill COVID-19 patients according to the presence and type of CLD. Additionally, the study aims to investigate the differences and similarities among the various types of CLD groups.

Methodology

Study design and Patients

This retrospective, single-center cohort study was conducted at a tertiary care hospital with approval from the local ethics committee (Approval No: 2023/02-28). The study included critically ill COVID-19 patients who were primarily hospitalized in the Intensive Care Unit (ICU) between April 1, 2020, and April 1, 2022. Data were retrospectively retrieved from medical records.

Data collection

Patient demographic and clinical information, including age, gender, and comorbid conditions, was obtained from patient medical records. Critically ill COVID-19 patients were categorized according to the presence of CLD, divided into subgroups of COPD, asthma, and other causes, and compared with a group of patients without CLD.

Clinical data included the reason for ICU admission, ICU length of stay, total hospitalization duration, development of organ failures during the ICU stay, respiratory support requirements (non-invasive and invasive), and the need for renal replacement therapy.

Laboratory parameters, including routine biochemistry and complete blood count results collected during ICU admission and follow-up, were analyzed retrospectively. Chest imaging findings, particularly chest computed tomography (CT) results, were reviewed and classified using the COVID-19 Reporting and Data System (CO-RADS) score, which stratifies involvement into five severity grades.

Mortality data were recorded and analyzed at 1 month, 3 months, and 1 year after admission.

Study Outcomes

Primary outcomes include mortality rates of COVID-19 patients with chronic lung diseases.

Secondary outcomes included independent predictors of mortality at 1, 3 months, and 1 year.

Inclusion criteria

Patients eligible for the study were those 18 years of age or older with a confirmed diagnosis of COVID-19, verified through reverse transcription-polymerase chain reaction (RT-PCR) testing.

Table 1. Clinical and demographic characteristics of patients.

Variable	n (%), median (min-max), median (IQR), (n: 406)
Age, years	67.00 (20.00)
Male	252 (62.1%)
ICU Length of stay, days	10.00 (11.00)
Hospital Length of stay days	16.00 (16.25)
Hypertension	196 (48.3%)
Diabetes mellitus	147 (36.2%)
Without CLD	332 (81.8%)
COPD	38 (9.4%)
Asthma	20 (4.9%)
Others, (PHT; malignancy)	16 (3.9%)
Coronary artery disease	97 (23.9%)
Heart failure	53 (13.1%)
Chronic kidney disease	46 (11.3%)
Hemodialysis at Admission	66 (16.3%)
Systemic steroids at admission	223 (54.9%)
Inhaled steroids at admission	50 (12.1%)
Systemic steroids during hospitalization	341 (84%)
Inhaled steroids during hospitalization	71 (17.1%)
Bronchodilator treatment	81 (20%)
Vasopressor treatment	70 (17.2%)
Tocilizumab treatment	7 (1.7%)
Mortality at 1 Month	245 (60.3%)
Mortality at 3 Months	272 (67%)
Mortality at 1 Year	282 (69.5%)
Albumin, g/dL	2.9 (1.5-4.9)
Urea, mg/dL	64 (8-321)
Creatinine, mg/dL	1.2 (0.3-14.4)
LDH, U/L	493 (139-7144)
CRP, mg/L	134.5 (1.5-686)
Ferritin, ng/mL	450 (23-9996)
INR	1.07 (0.8-16.2)
D-dimer, µg/L	1865 (220-27900)
Fibrinogen, mg/dL	545.4 (104-983)
WBC × 10^3/µL	10.6 (0.2-118)
Neutrophils × 10^3/µL	9.2 (0.1-83.9)
Lymphocytes × 10^3/µL	0.6 (0.1-13.0)
Eosinophils × 10^3/µL	0.1 (0.0-4.2)
Hemoglobin, g/dL	11.7 (4.7-17.6)
Platelets × 10^3/µL	241 (3-676)
Procalcitonin, ng/mL	0.34 (0.01-313.7)

ICU: Intensive Care Unit; CLD: chronic lung diseases; COPD: chronic obstructive pulmonary disease; PHT: pulmonary hypertension; LDH: lactate dehydrogenase; CRP: C-reactive protein; INR: international normalized ratio; WBC: white blood cell count.

Statistical Analysis

Statistical analyses were performed using IBM SPSS Statistics version 27. The Kolmogorov-Smirnov and Shapiro-Wilk tests were utilized to evaluate the normality of data. Descriptive statistics were presented as mean ± standard deviation for variables with a normal distribution and as median (interquartile range) for those not normally distributed. For comparisons between groups, independent t-tests or one-way ANOVA were used for parametric data, and Mann-Whitney U or Kruskal-Wallis tests were applied for non-parametric data. Categorical data were analyzed using the chi-square test. Multivariate logistic regression analysis was used to identify independent predictors of the outcome variables. A *p*-value of less than 0.05 was considered to indicate statistical significance.

Results

This study involved 406 patients diagnosed with confirmed COVID-19 via RT-PCR, all of whom were hospitalized in the ICU between April 1, 2020, and April 1, 2022. The patients had a median age of 67 years (IQR 20), and 62.1% (n = 252) of them were male. The median ICU stay duration was 10 days (IQR:11) and the median hospital stay was 16 days (IQR: 16.25). Hypertension (48.3%) and diabetes mellitus (36.2%) were the most common comorbidities. Seventy-four (18.2%) patients had a previously diagnosed CLD, including COPD (9.4%, n = 38), asthma (4.9%, n = 20), and other lung diseases such as pulmonary hypertension or malignancy (3.9%, n = 16). Favipiravir therapy was part of the standard treatment protocol. Among corticosteroids, dexamethasone (6mg/day) was the most commonly used agent, administered to 300

Table 2. Comparison of clinical and biochemical parameters in patients with and without CLD.

	Without CLD n (%) median (IQR), mean ± SD, (n = 332, 81.8%)	With CLD n (%), median (IQR), mean ± SD (n= 74, 18.2%)	*p*
Clinical parameters			
Age, years	67 (20)	72 (19)	**0.034**
IMV at admission	55 (16.6%)	14 (18.9%)	0.335
Initiated MV	241 (72.6%)	54 (73%)	0.947
Initiated IMV	138 (41.6%)	39 (52.7%)	0.081
Length of stay in ICU, days	10 (10)	8.5 (11)	0.520
Length of stay in hospital, days	16 (17)	15 (15)	0.362
Hemodialysis at admission	55 (16.6%)	11 (14.9%)	0.720
Systemic steroid use at admission	180 (54.2%)	44 (58.1%)	0.543
Systemic steroid use during hospitalization	276 (83.1%)	65 (87.8%)	0.318
Dexamethasone treatment	244 (73.5%)	56 (75.7%)	0.533
Methylprednisolone treatment	32 (9.6%)	9 (12.2%)	
Inhaled steroid at admission	24 (7.2%)	26 (35.1%)	**< 0.001**
Inhaled steroid during hospitalization	38 (11.4%)	33 (44.6%)	**< 0.001**
Vasopressor use at admission	60 (18.1%)	12 (16.2%)	0.743
N-acetylcysteine treatment	**96 (28.9%)**	**38 (51.4%)**	**< 0.001**
Mortality at 1 month	196 (59%)	49 (66.2%)	0.254
Mortality at 3 months	217 (65.4%)	55 (74.3%)	0.138
Mortality at 1 Year	224 (67.5%)	58 (78.4%)	0.065
CORADS 1	14 (4.4%)	7 (9.6%)	NA
CORADS 2	34 (10.7%)	7 (9.6%)	NA
CORADS 3	36 (11.4%)	14 (19.2%)	0.133
CORADS 4	23 (7.3%)	4 (5.5)	0.140
CORADS 5	210 (66.2%)	41 (56.2%)	NA
Biochemical parameters			
Albumin, g/dL	2.9 (0.6)	2.9 (0.7)	0.392
Urea, mg/dL	63 (55)	76 (59)	0.232
Creatinine, mg/dL	1.2 (0.6)	1.2 (0.85)	0.386
LDH, U/L	502 (283)	494 (333)	0.155
CRP, mg/L	118 (139)	107 (109.7)	0.677
Ferritin, ng/mL	450 (297)	450 (297)	0.257
INR	1.06(0.16)	1.02 (0.2)	0.936
D-dimer, µg/L	1700 (2875)	1730 (4325)	0.237
Fibrinogen, mg/dL	496 (257)	510 (214)	0.683
WBC × 10^3/µL	110.816 ± 4.79	11.015 ± 4.8045	0.507
Neutrophils × 10^3/µL	8.8 (6.0)	8.4 (9.1)	0.884
Lymphocytes × 10^3/µL	0.6 (0.7)	0.5 (0.5)	**0.021**
Eosinophils × 10^3/µL	0.0 (0.1)	0.2 (0.2)	0.08
Hemoglobin, g/dL	11.426 ± 2.19	11.415 ± 2.57	0.543
Platelets × 10^3/µL	259.51 ± 119.37	223.69 ± 72.117	**0.013**
Procalcitonin, ng/mL	0.3 (0.65)	1.38 (2.94)	0.284

CLD: chronic lung diseases; IMV: invasive mechanical ventilation; MV: mechanical ventilation; ICU: Intensive Care Unit; LDH: lactate dehydrogenase; CRP: C-reactive protein; INR: international normalized ratio; WBC: white blood cell count.

(73.9%) patients. Besides dexamethasone, methylprednisolone was used as an alternative corticosteroid in some patients. High-dose methylprednisolone was administered to 7 patients, while 34 patients received a dose of 1mg/kg/day. There was no statistically significant difference in mortality rates at 1-month, 3-month, and 1-year between patients treated with dexamethasone and those receiving methylprednisolone at a dose of 1 mg/kg/day. A total of 7 (1.7%) patients received tocilizumab treatment. N-acetylcysteine was added to the treatment of 134 (33%) patients, and vitamin C (1g) was given to 101 (24.9%) patients.

The mortality rate was 60.3% (n = 245) at 1 month, 67% (n = 272) at 3 months, and 69.5% (n = 282) at 1 year (Table 1). The majority of the patients (61.8%) were categorized as CORADS 5, indicating very high suspicion of COVID-19 pneumonia based on CT findings (Table 2).

ICU admission reasons and respiratory support

Out of the 406 patients, 368 (90,6%) were admitted to the ICU due to respiratory failure, 13 (3.2%) for neurological reasons, 9 (2.2%) for cardiac causes, and 16 (3.9%) for other reasons. Upon ICU admission, 257 (63.3%) patients were on oxygen therapy with a reservoir mask (RM), 10 (2.5%) were breathing room air, 34 (8.4%) were receiving oxygen via nasal cannula, 36 (8.9%) were on mask oxygen therapy, and 69 (17%) were on invasive mechanical ventilation (IMV) support. During their ICU stay, 44.6% of patients required non-invasive ventilation (NIMV), 11% required IMV, and 3.7% received high-flow nasal oxygen (HFNO).

Comparison of the patients with and without chronic lung disease

Among the 406 patients, 74 (18.2%) had CLD, while 332 (81.8%) did not have it. Patients with CLD were significantly older than those without (median age: 72 years vs. 67 years, $p = 0.034$). Patients with CLD had a slightly shorter median ICU stay, but not statistically significant ($p = 0.520$). The use of IMV was observed more frequently in the CLD group (52.7%) compared to the patients without CLD (41.6%), although this difference lacked statistical significance ($p = 0.081$).

Inhaled steroid use at ICU admission was significantly higher in patients with CLD compared to those without CLD (35.1% vs. 7.2%, $p < 0.001$). However, systemic steroid use at ICU admission was similar (58.1% vs. 54.2%, $p = 0.543$). Inhaled steroid use during ICU stay was significantly greater in patients with CLD (44.6% vs. 11.4%, $p < 0.001$); however, the

Table 3. Comparison of clinical parameters, mortality rates and biochemical parameters in patients with different types of CLD.

Clinical parameters	Without CLD, median (IQR) (n = 332)	COPD, median (IQR) (n = 38)	Asthma, median (IQR) (n = 20)	Other, median (IQR) (n = 16)	*p*
Age, years	67 (20)	75.5 (14)	60 (22)	71 (20)	0.002
Length of stay in ICU, days	10 (10)	10 (12)	10.5 (16)	5 (10)	0.118
Length of stay in hospital, days	16 (17)	16 (19)	17 (17)	13 (9)	0.213
Mortality at 1 month	196 (59%)	28 (73.7%)	10 (50%)	11 (68.8%)	0.219
Mortality at 3 months	217 (65.4%)	32 (84.2%)	11 (55%)	12 (75%)	0.064
Mortality at 1 year	224 (67.5%)	33 (86.8%)	13 (65%)	12 (75%)	0.092
CORADS 1	14 (4.4%)	3 (7.9%)	1 (5.0%)	3 (20%)	
CORADS 2	34 (10.7%)	4 (10.5%)	2 (10.0%)	1 (6.7%)	
CORADS 3	36 (11.4%)	10 (26.3%)	1 (5.0%)	3 20.0%)	0.055
CORADS 4	23 (7.3%)	2 (5.3%)	0 (0%)	2 (13.3%)	
CORADS 5	210 (66.2%)	19 (50%)	16 (80%)	6 (40%)	
Biochemical parameters					
Albumin, g/dL	2.9 (3)	2.9 (0.7)	3.05 (0.4)	2.8 (1.0)	0.316
Urea, mg/dL	62 (59)	86 (51)	53.5 (51)	62 (51)	0.049
Creatinine, mg/dL	1.2 (0.8)	1.4 (1)	1 (0.48)	1.1 (0.7)	0.181
LDH, U/L	492 (358)	494 (358)	512 (265)	342 (561)	0.532
CRP, mg/L	134.5 (143.1)	125 (139.5)	117.5 (113)	156.7 (211)	0.658
Ferritin, ng/mL	450 (343)	450 (309)	450 (227)	450 (1080)	0.162
INR	1.07(0.19)	1.06 (0.23)	1.02 (0.28)	1.15 (0.7)	0.509
D-dimer, µg/L	1900 (3935)	1830 (2860)	1080 (1928)	5000 (8390)	0.107
Fibrinogen, mg/dL	580 (284)	545 (326)	520 (225)	496.5 (345)	0.838
WBC × 10^3/µL	10.4 (7)	12.2 (5.8)	9.4 (7.8)	10.3 (11.6)	0.740
Neutrophils × 10^3/µL	9.2 (6.1)	10.1 (5.4)	8.25 (6.0)	8.0 (10.1)	0.645
Lymphocytes × 10^3/µL	0.6 (0.7)	0.4 (0.4)	0.55 (0.6)	0.3 (1.1)	0.061
Eosinophils × 10^3/µL	0.1 (0.1)	0.1 (0.2)	0.05 (0.2)	0.1 (0.2)	0.724
Hemoglobin, g/dL	11.7 (3.1)	11.6 (4.2)	12.2 (2.5)	10.3 (2.4)	0.136
Platelets × 10^3/µL	244.5 (153)	176 (150)	250.5 (170)	224 (101)	0.043
Procalcitonin, ng/mL	0.3 (0.92)	0.86 (4.66)	0.28 (0.72)	0.48 (6.6)	0.239

CLD: chronic lung diseases; COPD: chronic obstructive pulmonary disease; ICU: Intensive Care Unit; LDH: lactate dehydrogenase; CRP: C-reactive protein; INR: international normalized ratio; WBC: white blood cell count.

use of systemic steroids did not differ (87.8% vs. 83.1%, $p = 0.318$). Furthermore, N-acetylcysteine therapy was administered more frequently in patients with CLD than those without CLD (51.4% vs. 28.9%, $p < 0.001$).

Mortality rates at 1 month, 3 months, and 1 year were consistently higher among patients with CLD; however, these differences were not statistically significant ($p > 0.05$).

Among the radiological findings, reticular patterns (12.5% vs. 5.8%, $p = 0.048$), emphysema (25% vs. 12.6%, $p = 0.008$), and atelectasis (34.7% vs. 17.5%, $p = 0.001$) were notably more frequent in patients with CLD compared to those without. Other findings, such as ground-glass opacities, consolidations, fibrosis, and pleural effusion, did not show significant differences between the groups. No statistically significant differences were identified between the two groups based on CORADS scoring.

In terms of laboratory findings, lymphocyte counts were significantly lower in patients with CLD (median 0.5 vs. 0.6, $p = 0.021$), and platelet counts were also significantly lower in the CLD group (median 235 vs. 347, $p = 0.013$). Other parameters showed no statistically significant differences between the two groups (Table 2).

Subgroup analysis: COPD, asthma, and other lung diseases

The analysis of demographic and clinical features among patients without CLD (n = 332), COPD (n = 38), asthma (n = 20), and other lung diseases (n = 16) revealed the following results: The median age differed significantly among the groups ($p = 0.002$). COPD patients had the highest median age (75.7 years, IQR 14), while patients with asthma had the lowest (60 years, IQR 22). No significant differences were found among the groups in ICU length of stay ($p = 0.118$) or total hospital stay ($p = 0.213$).

Mortality rates were higher in the COPD group across all time points, but these differences were not statistically significant ($p > 0.05$). Additionally, no significant differences between the groups according to CORADS categories (Table 3).

Statistical analysis revealed significant variations in urea levels among the groups ($p = 0.014$).

According to the post-hoc analysis results, patients in the COPD group had significantly higher mean age, urea levels, and platelet counts compared to those without CLD, asthma, and other groups ($p < 0.05$). In

Table 4. Predictive factors for 1-month, 3-month and 1-year mortality identified by logistic regression analysis.

	B	SE	Odds ratio (OR)	Confidence interval (CI) (95%)	*p*
Predictive factors for 1-Month mortality identified by logistic regression analysis					
Age	0.040	0.009	1.041	1.023-1.060	< 0.001
Use of NIMV	-0.630	0.251	0.532	0.326-0.870	0.012
Creatinine	0.321	0.096	1.379	1.142-1.665	< 0.001
LDH	0.002	0.000	1.002	1.001-1.003	< 0.001
CRP	0.003	0.001	1.003	1.000-1.005	0.021
WBC	0.105	0.026	1.111	1.056-1.168	< 0.001
Lymphocyte	-0.299	0.110	0.741	0.598-0.920	0.006
Eosinophil	-1.436	0.730	0.238	0.057-0.994	0.049
Predictive factors for 3-Month mortality identified by logistic regression analysis					
Age	0.031	0.010	1.031	1.011-1.052	0.003
Female	-0.645	0.304	0.525	0.289-0.952	0.034
Use of NIMV	-1.166	0.429	0.312	0.134-0.722	0.007
Application of IMV	-1.060	0.452	0.346	0.143-0.841	0.019
Systemic steroid during hospitalization	-0.910	0.296	0.403	0.226-0.719	0.002
Urea	0.009	0.004	1.009	1.001-1.017	0.03
LDH	0.003	0.001	1.003	1.002-1.004	< 0.001
CRP	0.003	0.001	1.003	1.000-1.006	0.016
WBC	0.112	0.032	1.119	1.051-1.191	< 0.001
Lymphocyte	-0.373	0.114	0.689	0.551-0.861	0.001
Platelets	-0.004	0.001	0.996	0.993-0.999	0.010
Predictive factors for 1-Year mortality identified by logistic regression analysis					
Age	0.034	0.010	1.035	1.014-1.056	< 0.001
Use of NIMV	-1.285	0.427	0.277	0.120-0.638	0.003
Application of IMV	-1.176	0.450	0.309	0.128-0.745	0.009
Systemic steroid during hospitalization	-0.667	0.294	0.513	0.288-0.914	0.023
Urea	0.010	0.004	1.010	1.002-1.019	0.014
LDH	0.002	0.001	1.002	1.001-1.004	< 0.001
WBC	0.111	0.032	1.117	1.049-1.190	< 0.001
Lymphocyte	-0.250	0.103	0.779	0.636-0.953	0.015
Hemoglobin	-0.147	0.068	0.863	0.755-0.987	0.031
Platelets	-0.004	0.001	0.996	0.993-0.998	0.001

MV: mechanical ventilation; IMV: invasive mechanical ventilation; LDH: lactate dehydrogenase; CRP: C-reactive protein; WBC: white blood cell count.

the COPD group, both age and urea levels were observed to be significantly higher, while platelet levels were comparatively lower. However, no significant differences were detected between the asthma and other CLD groups ($p > 0.05$).

Logistic regression analysis of mortality risk factors

First-month mortality: Increased age, elevated creatinine, lactate dehydrogenase (LDH), C-reactive protein (CRP), and white blood cell count (WBC) levels were identified as significant risk factors for 1-month mortality. In contrast, the use of NIMV, as well as higher lymphocyte and eosinophil counts, was associated with lower mortality risk.

Third-month mortality: Increased age, elevated urea, LDH, CRP, and WBC levels, lymphopenia, and thrombocytopenia were associated with higher 3-month mortality. Systemic steroid use was linked to a protective effect. In addition, the application of NIMV and IMV further contributed to a reduction in mortality risk.

At 1 year, increased age, elevated urea, LDH, and WBC levels, low hemoglobin levels, lymphopenia, and thrombocytopenia were significant risk factors for mortality. Consistent with 3-month findings, systemic steroid use and the application of NIMV and IMV were associated with reduced mortality risk (Table 4).

Discussion

In this study, we evaluated the impact of CLD on the clinical course and outcomes of critically ill COVID-19 patients admitted to the ICU. Our findings demonstrate that CLD wasn't significantly associated with increased mortality. However, patients with CLD were older, had lower lymphocyte and platelet levels. Additionally, systemic steroid use was associated with reduced mortality, particularly among patients with CLD.

CLD and clinical outcomes

The possibility of severe COVID-19 infection in CLD patients has been discussed in many studies [5,12,13]. Some studies have suggested that CLD is an important risk factor for severe COVID-19 disease [5,13]. However, Riou *et al.* reported that CLD did not significantly influence mortality rates [11]. These varying results emphasize the necessity for additional investigation to clarify the role of CLD in COVID-19 outcomes. In our study of critically ill COVID-19 patients, the mortality rates of CLD patients were found to be higher than those of the group without CLD, but this difference was not statistically significant, which is consistent with the result being similar to some studies [10,11].

In our study, patients with CLD were found to be older and had lower lymphocyte and platelet levels compared to those without CLD. This data is consistent with other studies in the literature. Additionally, numerous studies have reported that older age is a significant risk factor for more severe COVID-19 infections, worse clinical outcomes, and increased mortality [1,2]. These findings indicate that age and the status of the immune system may affect the course of COVID-19 infection. Due to the effect of the aging process on tissue repair and remodeling, COVID-19 infection may be adversely affected and lead to worse clinical outcomes, especially in older individuals with CLD [14].

Radiological findings revealed that reticular patterns, emphysema, and atelectasis were more common in the CLD group, consistent with expectations based on preexisting lung damage. However, according to CORADS scoring, there were no statistically significant differences observed between the two groups regarding lung involvement. A similar level of lung involvement in critically ill COVID-19 patients may explain the lack of difference in mechanical ventilation requirement between the groups [1].

Asthma and COPD in COVID-19

Studies on the prognosis and mortality rates of patients with CLD diseases during the COVID-19 pandemic provide important information on how these patient groups are affected by the course of infection. In the early phases of the pandemic, it was suggested that asthma could increase the severity of COVID-19 disease and mortality, but later studies did not support this. Studies have shown that there were no significant differences in ICU admission rates, mechanical ventilation needs, or mortality among asthmatic patients with COVID-19 [15-17].

Patients with COPD are vulnerable to COVID-19 due to their advanced age and chronic deterioration in lung function. However, studies on the relationship between COVID-19 infection and mortality show conflicting results. While some studies have indicated that COPD exacerbates the severity of COVID-19 and increases mortality, other studies have shown that this relationship is not statistically significant [1,2,5-10,18]. For instance, Finnerty *et al.* emphasize that asthma does not correlate with a higher risk of mortality, whereas COPD is identified as a predictor of mortality among hospitalized COVID-19 patients [1]. The study by Liu

et al. suggests that asthma and eosinophilia may offer protection against severe COVID-19 and mortality, whereas COPD is strongly linked to increased mortality [2]. In contrast, Toppen *et al.* revealed that COPD did not significantly increase mortality in COVID-19 patients [10].

In our study, although there was an increase in all mortality rates in the COPD group, it was not statistically significant. We think that these varying results stem from the differing degrees of lung damage in critically ill COVID-19 patients.

Relationship between steroid therapy and mortality

Systemic steroids: There are many studies in the literature on steroid treatment in patients diagnosed with COVID-19. The RECOVERY study is one of the largest studies demonstrating the importance of steroid treatment in COVID-19 management. Steroids are suggested to inhibit viral replication and cytokine release, potentially preventing lung damage and the progression to severe conditions like ARDS in CLD patients [3,12]. Systemic steroid therapy has been demonstrated to lower 28-day mortality in COVID-19 patients and is recommended for treating severe cases requiring oxygen or mechanical ventilation [3,19]. Similarly, our study demonstrated that systemic steroid use reduced 3-month and 1-year mortality, suggesting that steroid therapy may have favorable effects on both short-term and long-term clinical outcomes.

Inhaled Corticosteroids (ICS): Two meta-analyses suggested that ICS might increase the risk of viral infections; however, further studies are necessary to establish and confirm this relationship [20,21]. In a systematic review by Halpin *et al.,* ICS use was evaluated for its effects on COVID-19, and no significant impact on mortality was found [22]. Similarly, Schultze *et al.* reported no meaningful correlation between ICS use and the risk of COVID-19-related mortality [23]. ICS is commonly used alone or in combination with bronchodilators for asthma management. Studies recommend that stable asthma patients continue their ICS treatment to prevent exacerbations [16,24]. For COPD, ICS is also used with bronchodilators as part of standard therapy [24]. Labor *et al.* highlighted that ICS might reduce the risk of severe COVID-19 in patients with COPD [25]. Similarly, Kiliç *et al.* recommended that ICS therapy should not be discontinued in asthma and COPD patients with COVID-19 [24].

In our study, ICS use was not linked to higher mortality in patients with CLD. This finding aligns with the current literature, suggesting that ICS can be safely used in the management of COVID-19 patients with CLD.

We also observed that ICS use was more prevalent during ICU admission and hospitalization among CLD patients, likely for respiratory symptom management, whereas systemic steroid use was comparable in both groups, reflecting its role in COVID-19 treatment protocols. This distinction highlights the different therapeutic purposes of ICS and systemic steroids.

In our study, adjunctive therapies such as bronchodilators, N-acetylcysteine, and vitamin C were used as supportive treatment options, especially in patients with CLD.

Certain laboratory biomarkers hold prognostic significance in critically ill COVID-19 patients. Studies have shown that elevated serum LDH levels, along with lymphopenia and thrombocytopenia, are associated with poor outcomes in severe COVID-19 cases [3,6,26].

Consistent with prior studies, our findings demonstrate that high-level serum LDH levels, lymphopenia, and thrombocytopenia are associated with increased mortality. The statistically significant lower levels of lymphocytes and platelets in our CLD patients compared to patients without CLD further emphasize the prognostic importance of such laboratory markers in this population.

Although high urea levels were identified as a predictor of 3-month and 1-year mortality in our study, it should be kept in mind that urea is a nonspecific marker affected by various factors such as the patient's hydration status, presence of infection, nutritional status, and renal perfusion. Therefore, its prognostic value should be interpreted with caution, especially in critically ill patients.

Limitations of this study

The retrospective, single-center design of this study limits the ability to determine causal relationships between CLD, steroid use, and mortality outcomes and may reduce the generalizability of the findings. The study did not evaluate the specific doses or durations of systemic or ICS therapies, limiting detailed insights into their impact on outcomes.

Conclusions

In conclusion, our study demonstrated that while CLD does not independently increase mortality in critically ill COVID-19 patients, these individuals are typically older, emphasizing the significant role of age in disease outcomes. Additionally, the observed mortality-reducing effect of systemic steroids,

particularly in patients with CLD, especially COPD, highlights the need for personalized therapeutic approaches in this high-risk population.

Corresponding author
Tunzala Yavuz, MD
Critical care specialist
Izmir Tepecik Training and Research Hospital, Turkey
Tel: +905308759242
Email: tunzala.yavuz@hotmail.com

Conflict of interest
No conflict of interest is declared.

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