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Prognostic factors of 30-day mortality in patients with COVID-19 pneumonia under standard remdesivir and dexamethasone treatment

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Abstract

Although some studies have reported prognostic factors for coronavirus disease 2019 (COVID-19), they were conducted before standard treatment with remdesivir and dexamethasone was implemented. This retrospective, observational study was conducted to evaluate various prognostic factors in patients with COVID-19 pneumonia receiving standard treatment with remdesivir and dexamethasone. Of 99 patients with COVID-19 pneumonia, 68 (68.7%) died within 30 days of hospitalization. The mean age was 71.3 years. Remdesivir and dexamethasone were administered to 80 (80.8%) and 84 (84.8%) patients, respectively. Early antibiotic treatment was administered to 70 patients (70.7%) within 5 days of hospitalization. Dexamethasone (79.4% vs 96.8%, $P = .033$) was more frequently administered in the survived group, whereas early antibiotics (60.3% vs 93.5%, $P = .001$) were less frequently administered. In the multivariate analysis, a high National Early Warning Score (NEWS; odds ratio [OR] 1.272), high Charlson Comorbidity Index (CCI; OR 1.441), and dyspnea (OR 4.033) were independent risk factors for 30-day mortality. There was no significant difference in age, sex, and vaccination doses between the survived and fatal groups. Lymphopenia, monocytopenia and high levels of C-reactive protein (CRP)/lactate dehydrogenase (LDH) reflected poor prognosis. NEWS, CCI, and dyspnea were predictors of 30-day mortality in patients with COVID-19 pneumonia. Early antibiotic use did not lower the 30-day mortality risk.

Abbreviations: CCI = Charlson Comorbidity Index, CI = confidence interval, COVID-19 = coronavirus disease 2019, CRP = C-reactive protein, LDH = lactate dehydrogenase, NEWS = National Early Warning Score, OR = odds ratio, pro-BNP = pro-B-type natriuretic peptide, RT-PCR = reverse transcription–polymerase chain reaction, SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2.

Keywords: COVID-19, mortality, pneumonia, prognosis, SARS-CoV-2

1. Introduction

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has spread rapidly worldwide since its emergence on January 7, 2020.[1] As of February 7, 2022, more than 350 million cases of coronavirus disease 2019 (COVID-19) occurred globally, resulting in 5,592,266 deaths.[2] Although most patients with COVID-19 present with a self-limiting mild respiratory disease, 30% to 40% of patients are affected by pneumonia, and in 5% of patients, the disease turns fatal.[2,3]

In the past 2 years, many studies have been conducted to identify the predictive factors of severe COVID-19, which showed that older age, high Sequential Organ Failure Assessment score, high procalcitonin levels, high lactate dehydrogenase (LDH) levels, and high D-dimer levels were associated with progression to severe disease and poor clinical outcomes.[4–6] Moreover, hypercalcemia in fragile elderly patients with COVID-19 is associated with shorter survival times,[7] and decreased vitamin K levels have also been reported as a poor prognostic factor in severe COVID-19.[8] During the COVID-19 pandemic, it is important to predict severe COVID-19 as it allows for efficient resource allocation.

However, most studies on the risk or prognostic factors for severe COVID-19 were conducted before standard treatment with remdesivir and dexamethasone. Current guidelines recommend remdesivir treatment for hospitalized patients requiring oxygen therapy and steroids for severe or critical patients.[9] Moreover, there is limited information because most studies have focused on host factors, such as age and underlying medical conditions. This study aimed to evaluate

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All data generated or analyzed during this study are included in this published article [and its supplementary information files]; the datasets generated during and/or analyzed during the current study are not publicly available, but are available from the corresponding author on reasonable request.

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the diverse prognostic factors in patients with COVID-19 pneumonia in terms of laboratory markers and treatment agents.

2. Methods

2.1. Study design and participants

We performed a single-center, retrospective, observational study of patients with COVID-19 admitted to the Korea University Guro Hospital from January 1, 2021 to February 16, 2022. To evaluate the prognostic factors of COVID-19 pneumonia, we defined the following inclusion criteria: diagnosis of COVID-19 by reverse transcription–polymerase chain reaction (RT-PCR) positivity, age >18 years, available laboratory data within 5 days after symptom onset, and pneumonia confirmed on chest X-ray.

Of 222 SARS-CoV-2 RT-PCR-positive patients with pneumonia, 123 were excluded; patients aged <18 years (9), hospitalized more than 5 days after symptom onset (82), missing information (10), and hospital-acquired infection (22). Finally, 99 patients who met the inclusion criteria were included in the analysis (Fig. 1).

2.2. Data sources

Demographic, clinical, and laboratory data were retrospectively collected from electronic medical records. The baseline data included age, sex, body mass index, comorbidities, symptoms, chest radiographic findings, and laboratory findings on the day of admission. The National Early Warning Score (NEWS) was calculated to assess COVID-19 severity, whereas the Charlson Comorbidity Index (CCI) was used to determine the underlying medical conditions, as previously described.[10,11] Data on treatment (remdesivir, regdanvimab, dexamethasone, and antibiotics) and clinical outcomes, including 30-day mortality, inotropic administration, mechanical ventilation, hemodialysis, and extracorporeal membrane oxygenation, were also collected.

Based on the epidemiologic data of circulating SARS-CoV-2, we divided the study periods into the period before delta dominance (from February 2020 to June 2021), delta-dominant period (from July 2021 to December 2021), and omicron-dominant period (from January 2022 to March 2022).[12] The vaccination history was based on the time before disease onset. Early antibiotic use was defined as treatment within 5 days after the diagnosis of pneumonia. The length of hospital stay was defined as the period from hospitalization to death or discharge.

2.3. Statistical analysis

We divided the participants into 2 groups: patients who survived (survived group) and those who died within 30 days of hospitalization (fatal group). Descriptive statistics were used for baseline characteristics. Categorical variables are presented as n (%) and continuous variables are presented as mean ± standard deviation. Independent Student *t* test was performed for statistical comparison between continuous variables, while the chi-square test (or Fisher exact test) was performed for categorical variables. Multivariate analysis was performed using a stepwise logistic regression model with the significant prognostic variables obtained from univariate analysis. All tests were 2 tailed, and significance was assessed at a P value <.05. All data were analyzed using the SPSS software (version 25.0; IBM Corp., New York, NY).

2.4. Ethics statement

The study was approved by the Institutional Review Board of the Korea University Guro Hospital (2020GR0123), and the requirement for informed consent was waived.

3. Results

Of 99 patients with COVID-19 pneumonia, 31 (31.3%) died within 30 days of hospitalization (Fig. 1). The mean age was 71.3 ± 12.5 years, and men accounted for 54.4% (54) of the cases. The mean interval from symptom onset to hospitalization was 2.5 ± 1.8 days. The most common symptom was dyspnea, which was noted in 55 patients (55.6%). Regdanvimab, remdesivir, and dexamethasone were administered to 16 (16.2%), 80 (80.8%), and 84 (84.8%) patients, respectively. Early antibiotic treatment was administered to 70 (70.7%) patients within 5 days of the diagnosis of pneumonia. Fifty-two (52.5%) patients were either unvaccinated or single-dose vaccinated, 34 (34.3%) patients received 2 doses of vaccine, and 13 (13.1%) patients received 3 doses. Most patients (63.6%) were hospitalized during the delta-dominant period.

Compared to the survived group, NEWS (7.4 ± 2.6 vs 4.4 ± 3.3, P < .001) and CCI (5.1 ± 2.7 vs 3.9 ± 2.3, P = .029) were

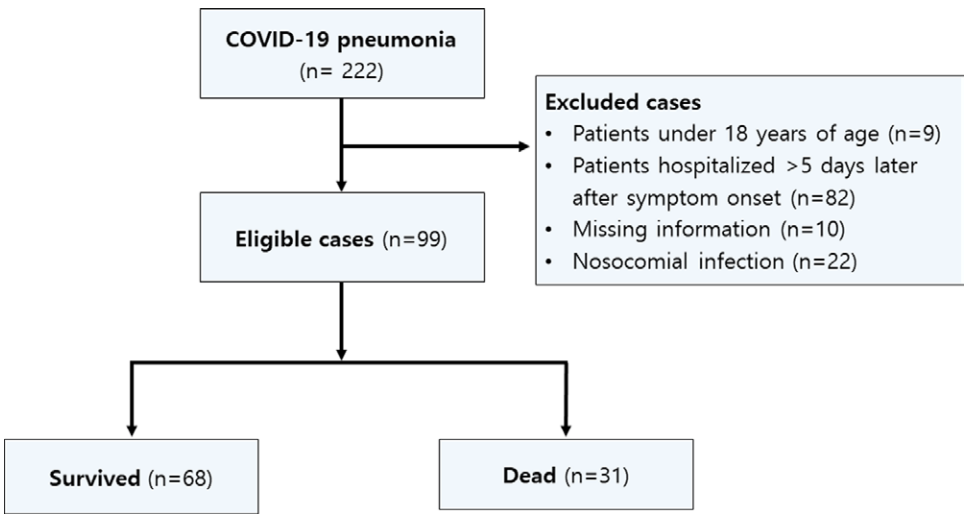

Figure 1. Study flowchart.

significantly higher in the fatal group. Moreover, the incidence of dyspnea on admission was significantly higher in the fatal group (80.6 vs 44.1, $P = .001$). Regdanvimab (23.5 vs 0, $P = .003$) and dexamethasone (79.4 vs 96.8, $P = .033$) were more frequently administered in the survived group, whereas early antibiotics (60.3 vs 93.5, $P = .001$) were less frequently administered. Patients in the fatal group were more likely to be treated with inotropic agents (90.3 vs 14.7, $P < .001$), mechanical ventilation (87.1 vs 25.0, $P < .001$), and hemodialysis (32.3 vs 2.9, $P < .001$) than those in the survived group. There were no significant differences in age, sex, number of vaccination doses, and periods (divided by SARS-CoV-2 strain dominance; wild type vs delta variant vs omicron variant) on the day of hospitalization between the 2 groups (Table 1).

There were several significant differences in the initial laboratory findings between the 2 groups (Table 2). As for the

Table 1

Demographic and clinical characteristics of COVID-19 pneumonia: comparison between survived and fatal cases.

	Total (n = 99)	Survived group (n = 68)	Fatal group (n = 31)	*P* value
Demographics				
Men, no. (%)	54 (54.5)	30 (44.1)	15 (48.4)	.692
Age, yr (mean ± SD)	71.3 ± 12.5	69.8 ± 13.4	74.6 ± 9.7	.077
<50	9 (9.1)	8 (11.8)	1 (3.2)	.254
50–65	11 (11.1)	9 (13.2)	2 (6.5)	
>65	79 (79.8)	51 (75.0)	28 (90.3)	
BMI (mean ± SD)	23.6 ± 4.5	23.3 ± 4.8	24.5 ± 3.9	.226
Days of symptom onset to hospitalization	2.9 ± 1.8	2.6 ± 1.7	2.3 ± 1.9	.429
National Early Warning Score (mean ± SD)	5.3 ± 3.4	4.4 ± 3.3	7.4 ± 2.6	<.001
Comorbidities, no. (%)				
Chronic heart diseases	8 (8.1)	4 (5.9)	4 (12.9)	.253
Neurovascular diseases	12 (12.1)	6 (8.8)	6 (19.4)	.184
Chronic renal diseases	3 (3.0)	1 (1.5)	2 (6.5)	.230
Diabetes	38 (38.4)	23 (33.8)	15 (48.4)	.167
COPD	3 (3.0)	2 (2.9)	1 (3.2)	1.000
Asthma	3 (3.0)	2 (2.9)	1 (3.2)	1.000
Hematologic malignancy	2 (2.0)	2 (2.9)	0 (0)	1.000
Solid cancer	17 (17.2)	11 (16.2)	6 (19.4)	.697
Charlson comorbidity index (mean ± SD)	4.3 ± 2.5	3.9 ± 2.3	5.1 ± 2.7	.029
Symptoms, no. (%)				
Fever	34 (34.3)	23 (33.8)	11 (35.5)	1.000
Cough	32 (32.3)	23 (33.8)	9 (29.0)	.636
Sputum production	26 (26.3)	14 (20.6)	12 (38.7)	.057
Dyspnea	55 (55.6)	30 (44.1)	25 (80.6)	.001
Mental status change	14 (14.1)	8 (11.8)	6 (19.4)	.358
Therapeutic agents, no. (%)				
Regdanvimab	16 (16.2)	16 (23.5)	0 (0)	.003
Remdesivir	80 (80.8)	52 (76.5)	28 (90.3)	.105
Dexamethasone	84 (84.8)	54 (79.4)	30 (96.8)	.033
Early antibiotic use within 5 days	70 (70.7)	41 (60.3)	29 (93.5)	.001
Factors related to severity				
Inotropics, no. (%)	38 (38.4)	10 (14.7)	28 (90.3)	<.001
MV, no. (%)	55 (55.6)	17 (25.0)	27 (87.1)	<.001
Hemodialysis, no. (%)	12 (12.1)	2 (2.9)	10 (32.3)	<.001
ECMO, no. (%)	5 (5.1)	3 (4.4)	2 (6.5)	.647
Length of hospital stay, day (mean ± SD)	19.7 ± 12.0	20.7 ± 13.2	17.5 ± 8.9	.231
Vaccination				.716
0–1 dose	52 (52.5)	36 (52.9)	16 (51.6)	
2 doses	34 (34.3)	22 (32.4)	12 (38.7)	
3 doses	13 (13.1)	10 (14.7)	3 (9.7)	
Period by the predominant viral strain, no. (%)				.310
Wild type	16 (16.2)	13 (19.1)	3 (9.7)	
Delta variant	63 (63.6)	40 (58.8)	23 (74.2)	
Omicron variant	20 (20.2)	15 (22.1)	5 (16.1)	

BMI = body mass index, COPD = chronic obstructive pulmonary disease, COVID-19 = coronavirus disease 2019, ECMO = extracorporeal membrane oxygenation, MV = mechanical ventilation, SD = standard deviation.

Table 2

Initial laboratory and radiologic findings of COVID-19 pneumonia: comparison between survived and fatal cases.

	Total (n = 99)	Survived group (n = 68)	Fatal group (n = 31)	*P* value
Laboratory findings, mean ± SD				
Ct value	20.9 ± 5.6	21.0 ± 5.8	20.8 ± 5.2	.876
Hb	12.5 ± 2.2	12.8 ± 2.2	11.8 ± 2.1	.039
MCV	91.8 ± 8.3	91.3 ± 9.2	93.1 ± 5.9	.328
WBC	8474.8 ± 6500.9	8355.9 ± 7478.1	8735.5 ± 3614.0	.789
Monocyte	6.5 ± 3.8	7.2 ± 4.0	4.9 ± 2.7	.006
Lymphocyte	12.5 ± 9.5	14.1 ± 10.6	9.1 ± 4.9	.002
Platelet (k)	186.9 ± 73.3	181.9 ± 74.9	197.7 ± 69.6	.327
BUN	24.5 ± 15.4	21.8 ± 13.6	30.5 ± 17.6	.021
Creatinine	1.1 ± 1.1	0.9 ± 0.6	1.5 ± 1.7	.085
Albumin	3.4 ± 0.5	3.5 ± 0.5	3.2 ± 0.5	.014
Total cholesterol	139.5 ± 49.0	144.1 ± 51.1	129.4 ± 43.3	.169
ESR	53.7 ± 27.3	48.7 ± 24.9	71.6 ± 29.1	.013
CRP	102.7 ± 91.6	82.8 ± 89.1	146.2 ± 82.5	.001
Procalcitonin	1.5 ± 4.9	1.0 ± 3.0	2.7 ± 7.9	.183
Pro-BNP	1661.6 ± 3693.7	806.6 ± 1748.1	3927.6 ± 5991.0	.033
D-dimer	1.9 ± 3.1	1.6 ± 2.5	2.7 ± 4.1	.139
LDH	840.3 ± 503.6	723.5 ± 357.9	1190.8 ± 698.4	.001
Ferritin	732.7 ± 929.9	545.9 ± 1397.0	1397.0 ± 1422.3	.115
HCO_3	24.3 ± 5.0	25.3 ± 4.1	22.7 ± 6.0	.030
PH	7.5 ± 0.1	7.5 ± 0.1	7.4 ± 0.1	.101
Lactic acid	1.9 ± 1.8	1.6 ± 0.9	2.65 ± 2.6	.040
Radiological findings, no. (%)				
Bilateral	77 (77.8)	49 (72.1)	28 (90.3)	.079
Shape				.002
GGO only	31 (31.3)	27 (39.7)	4 (12.9)	
Consolidation only	30 (30.3)	23 (33.8)	7 (22.6)	
Mixed type	37 (37.4)	17 (25.0)	20 (64.5)	
Density				.024
Patchy	61 (61.6)	46 (67.6)	15 (48.4)	
Confluent	14 (14.1)	11 (16.2)	3 (9.7)	
Mixed type	23 (23.2)	10 (14.7)	13 (41.9)	

BUN = blood urea nitrogen, COVID-19 = coronavirus disease 2019, CRP = C-reactive protein, Ct = cyclic threshold, ESR = erythrocyte sedimentation rate, GGO = ground glass opacity, Hb = hemoglobin, HCO_3 = bicarbonate, LDH = lactate dehydrogenase, MCV = mean corpuscular volume, PH = hydrogen ion, pro-BNP = pro-B-type natriuretic peptide, SD = standard deviation, WBC = white blood cell.

complete blood counts, the hemoglobin (11.8 ± 2.1 vs 12.8 ± 2.2, $P = .039$), monocyte (4.9 ± 2.7 vs 7.2 ± 4.0, $P = .006$), and lymphocyte (9.1 ± 4.9 vs 14.1 ± 10.6, $P = .002$) levels were significantly lower in fatal group. The fatal group showed lower albumin levels (3.2 ± 0.5 vs 3.5 ± 0.5, $P = .014$) but higher blood urea nitrogen level (30.5 ± 17.6 vs 21.8 ± 13.6, $P = .021$), erythrocyte sedimentation rate (71.6 ± 29.1 vs 48.7 ± 24.9, $P = .013$), C-reactive protein (CRP) level (146.2 ± 82.5 vs 82.8 ± 89.1, $P = .001$), pro-B-type natriuretic peptide (pro-BNP) level (3927.6 ± 5991.0 vs 806.6 ± 1748.1, $P = .033$), LDH levels (1190.8 ± 698.4 vs 723.5 ± 357.9, $P = .001$), and lactic acid levels (2.7 ± 2.6 vs 1.6 ± 0.9, $P = .040$) compared to the survived group. The baseline cycle threshold value of RT-PCR was indistinguishable between the survived and fatal groups. With regard to radiological findings, mixed patterns of shape (ground glass opacity and consolidation, $P = .002$) and density (patchy and confluent, $P = .024$) were associated with higher fatality rates.

In the multivariate analysis, high NEWS (odds ratio [OR], 1.27; 95% confidence interval [CI], 1.01–1.60), high CCI (OR, 1.44; 95% CI, 1.02–2.04), and dyspnea (OR, 4.03; 95% CI, 1.17–13.89) were independent risk factors for 30-day mortality (Table 3). Early antibiotic use did not lower the 30-day mortality risk.

4. Discussion

In this study, we evaluated various prognostic factors of COVID-19 pneumonia in patients receiving standard treatment with remdesivir and dexamethasone. Underlying medical condition (CCI) and disease severity (NEWS) on admission were independent prognostic factors with statistical significance. The majority of hospitalized COVID-19 pneumonia cases occurred in older adults aged ≥65 years (79%); therefore, there was no significant difference in prognosis according to age. Early antibiotic treatment had no beneficial effect on 30-day mortality rate.

Previous studies have shown that COVID-19 pneumonia is more common and represents a more serious disease in the elderly population.[13] Although there was no significant age-dependent difference in the 30-day mortality, there was a significant correlation between old age and chronic disease ($R = 0.574$, $P < .001$; Figure S1, Supplemental Digital Content 1, http://links.lww.com/MD/H223) in this study. The CCI score increased the risk of death by 1.48-fold in the regression analysis. As for the clinical manifestations, the

Table 3

Prognostic factors related to 30-day mortality in patients with COVID-19 pneumonia.

Variables	OR	95% CI	*P* value
Age	1.01	0.9–1.07	.831
National Early Warning Score	1.27	1.01–1.60	.039
Dyspnea	4.03	1.17–13.89	.027
Charlson comorbidity index	1.44	1.02–2.04	.039
Dexamethasone use	0.97	0.05–17.99	.984
Early antibiotic use	5.34	0.80–35.63	.084
Vaccination			.795
0–1 dose	Reference	Reference	
2 doses	0.67	0.21–2.75	.671
3 doses	0.53	0.07–3.82	.527
Period by the predominant viral strain			.617
Wild type	Reference	Reference	
Delta variant	2.15	0.40–11.73	.375
Omicron variant	2.72	0.31–23.98	.367

CI = confidence interval, COVID-19 = coronavirus disease 2019, OR = odds ratio.

most common initial symptom was dyspnea (55.6%), followed by fever, cough, and sputum production. Most patients complained of dry cough, and sputum was noted in only 26% of patients. As expected, dyspnea and mechanical ventilation were associated with poor prognosis, reflecting disease severity.

In clinical practice, it is common to administer antibiotics to hospitalized patients with COVID-19 pneumonia because the accompanying bacterial pneumonia cannot be excluded. According to a large meta-analysis, only 3.5% of patients with COVID-19 pneumonia were reported to have bacterial co-infection, but antibiotics were administered in more than 70% of cases (Rawson et al, 2020). Similarly, early antibiotics were administered to 70.7% of patients in this study. It was difficult for clinicians to avoid empirical antibiotic use in severe cases; 60% of the survived group received antibiotics, while 93.5% of the fatal group received antibiotics in this study (Table S1, Supplemental Digital Content 2, http://links.lww.com/MD/H224). However, contrary to expectations, early antibiotic treatment had no beneficial effect on the 30-day mortality rate. Unlike other viral pneumonias, bacterial co-infection is rare in patients with COVID-19.[14] Therefore, it is necessary to avoid abuse of antibiotics when managing COVID-19 pneumonia.

As for the laboratory findings, complete blood count (CBC) is the most convenient test and is correlated with the severity of many other infectious diseases. In patients with COVID-19, a lower neutrophil-to-lymphocyte ratio and lymphopenia may be associated with poor prognosis.[15,16] This study supports that lower monocyte and lymphocyte levels are prognostic factors for COVID-19 pneumonia. Recent studies have revealed that white and red blood cells have the potential to predict mortality in non-infectious cardiovascular diseases.[17] Moreover, in cases of infectious diseases, red cell distribution width is known to be an independent prognostic factor for early mortality and poor outcomes.[18,19] Anemia was significantly associated with a higher risk of COVID-19 mortality in one meta-analysis but not in another meta-analysis.[20] The CBC parameters may require further investigation with respect to the prognosis of COVID-19. Second, factors previously known to be related to the prognosis of sepsis, such as erythrocyte sedimentation rate, CRP, pro-BNP, LDH, and lactic acid, were also found to be related to the prognosis of COVID-19 pneumonia.[21] Both LDH and CRP have been suggested to be associated with respiratory failure in patients with COVID-19 pneumonia, and serum CRP levels >40 mg/dL have been suggested as indicators of high disease severity and high mortality.[22–24] In addition, malnutrition affects the prognosis of patients with COVID-19.[25] In this study, 59.6% of patients with COVID-19 pneumonia had hypoalbuminemia (<3.5 g/dL), and mortality was higher in patients with low albumin levels. Finally, recent studies have revealed an association between cardiac dysfunction and 30-day all-cause mortality.[26] Similarly, high pro-BNP levels were associated with 30-day mortality in the present study. If patients with COVID-19 pneumonia have these factors at the time of admission, clinicians should carefully consider poor prognosis.

Contrary to expectation, we could not find significant vaccine effectiveness in lowering the disease severity and mortality among patients with COVID-19 pneumonia. Previous studies reported that vaccination significantly reduced COVID-19-related hospitalization and mortality rates.[27,28] Unlike previous studies, this study was limited to patients with pneumonia. In addition, because of the retrospective observational study design, both primary series completion rate (2-doses) and booster vaccination rate (3-doses) were significantly higher in older adults and chronically ill patients with higher CCI, which might have offset the vaccine effectiveness (Table S2, Supplemental Digital Content 3, http://links.lww.com/MD/H225).

This study had several limitations. First, sputum culture was not possible due to the institutional infection control strategy; therefore, it was difficult to confirm or exclude bacterial pneumonia. Second, this is a single-center retrospective study. Although the sample size is small, we identified several significant factors associated with mortality in this study. Further studies are warranted to verify causal relation of these factors.

In conclusion, high NEWS, high CCI, and dyspnea were predictors of 30-day mortality in patients with COVID-19 pneumonia. Diverse laboratory markers (lymphopenia, monocytopenia, hypoalbuminemia, and increased CRP, LDH, and pro-BNP levels) are useful indicators of poor prognosis. Early antibiotic use did not lower the case fatality rate in patients with COVID-19 pneumonia.

Author contributions

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References

[1] World Health Organization. Novel Coronavirus (2019-nCoV). Situation report – 22, Data as reported by 11 February 2020. 2020. Available at: https://covid19-evidence.paho.org/handle/20.500.12663/837 [access date February 25, 2022].
[2] Guan WJ, Ni ZY, Hu Y, et al. Clinical characteristics of Coronavirus disease 2019 in China. N Engl J Med. 2020;382:1708–20.
[3] Chen N, Zhou M, Dong X, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. Lancet. 2020;395:507–13.
[4] Liu W, Yang C, Liao YG, et al. Risk factors for COVID-19 progression and mortality in hospitalized patients without pre-existing comorbidities. J Infect Public Health. 2022;15:13–20.
[5] Poudel A, Poudel Y, Adhikari A, et al. D-dimer as a biomarker for assessment of COVID-19 prognosis: D-dimer levels on admission and its role in predicting disease outcome in hospitalized patients with COVID-19. PLoS One. 2021;16:e0256744.
[6] Zhou F, Yu T, Du R, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. Lancet. 2020;395:1054–62.
[7] Pamart D, Otekpo M, Asfar M, et al. Hypercalcemia as a biomarker of poor prognosis in frail elderly patients with COVID-19. J Nutr Health Aging. 2021;25:1140–4.
[8] Dofferhoff ASM, Piscaer I, Schurgers LJ, et al. Reduced vitamin K status as a potentially modifiable risk factor of severe Coronavirus disease 2019. Clin Infect Dis. 2021;73:e4039–46.
[9] Zuin M, Rigatelli G, Quadretti L, et al. Prognostic role of anemia in COVID-19 patients: a meta-analysis. Infect Dis Rep. 2021;13:930–7.
[10] Tuty Kuswardhani RA, Henrina J, Pranata R, et al. Charlson comorbidity index and a composite of poor outcomes in COVID-19 patients: a systematic review and meta-analysis. Diabetes Metab Syndr. 2020;14:2103–9.
[11] Prytherch DR, Smith GB, Schmidt PE, et al. ViEWS--towards a National Early Warning Score for detecting adult inpatient deterioration. Resuscitation. 2010;81:932–7.
[12] Kim I, Park AK, Lee H, et al. Status and characteristics of the SARSCoV-2 variant outbreak in the Republic of Korea in January 2021.Pub Health Week Rep. 2022;15:505–10.
[13] CDC COVID-19 Response Team. Severe outcomes among patients with Coronavirus Disease 2019 (COVID-19) - United States, February 12-March 16, 2020. MMWR Morb Mortal Wkly Rep. 2020;69:343–6.
[14] Sieswerda E, de Boer MGJ, Bonten MMJ, et al. Recommendations for antibacterial therapy in adults with COVID-19—an evidence based guideline. Clin Microbiol Infect. 2021;27:61–6.
[15] Lee J, Park SS, Kim TY, et al. Lymphopenia as a biological predictor of outcomes in COVID-19 patients: a nationwide cohort study. Cancers (Basel). 2021;13:471.
[16] Yan X, Li F, Wang X, et al. Neutrophil to lymphocyte ratio as prognostic and predictive factor in patients with coronavirus disease 2019: a retrospective cross-sectional study. J Med Virol. 2020;92:2573–81.
[17] Perlstein TS, Weuve J, Pfeffer MA, et al. Red blood cell distribution width and mortality risk in a community-based prospective cohort. Arch Intern Med. 2009;169:588–94.
[18] Bazick HS, Chang D, Mahadevappa K, et al. Red cell distribution width and all-cause mortality in critically ill patients. Crit Care Med. 2011;39:1913–21.
[19] Jo YH, Kim K, Lee JH, et al. Red cell distribution width is a prognostic factor in severe sepsis and septic shock. Am J Emerg Med. 2013;31:545–8.
[20] Taneri PE, Gómez-Ochoa SA, Llanaj E, et al. Anemia and iron metabolism in COVID-19: a systematic review and meta-analysis. Eur J Epidemiol. 2020;35:763–73.
[21] Gallo Marin B, Aghagoli G, Lavine K, et al. Predictors of COVID-19 severity: a literature review. Rev Med Virol. 2021;31:1–10.
[22] Liu Y, Yang Y, Zhang C, et al. Clinical and biochemical indexes from 2019-nCoV infected patients linked to viral loads and lung injury. Sci China Life Sci. 2020;63:364–74.
[23] Poggiali E, Zaino D, Immovilli P, et al. Lactate dehydrogenase and C-reactive protein as predictors of respiratory failure in CoVID-19 patients. Clin Chim Acta. 2020;509:135–8.
[24] Stringer D, Braude P, Myint PK, et al. The role of C-reactive protein as a prognostic marker in COVID-19. Int J Epidemiol. 2021;50:420–9.
[25] Bedock D, Bel Lassen P, Mathian A, et al. Prevalence and severity of malnutrition in hospitalized COVID-19 patients. Clin Nutr ESPEN. 2020;40:214–9.
[26] Rath D, Petersen-Uribe A, Avdiu A, et al. Impaired cardiac function is associated with mortality in patients with acute COVID-19 infection. Clin Res Cardiol. 2020;109:1491–9.
[27] Lopez Bernal J, Andrews N, Gower C, et al. Effectiveness of the Pfizer-BioNTech and Oxford-AstraZeneca vaccines on covid-19 related symptoms, hospital admissions, and mortality in older adults in England: test negative case-control study. BMJ. 2021;373:n1088.
[28] Tenforde MW, Self WH, Adams K, et al. Association between mRNA vaccination and COVID-19 hospitalization and disease severity. JAMA. 2021;326:2042–54.