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Medical

Mortality prognostic factors of COVID-19 in the emergency department during outbreak in Daegu, Korea: a multicenter retrospective study

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Objective: We aimed to investigate the characteristics and prognostic factors of coronavirus disease 2019 (COVID-19) patients in the emergency departments (EDs) in Daegu, Korea, the region with the second regional outbreak worldwide.
Methods: We conducted a retrospective observational multicenter study using a population-based COVID-19 registry of EDs. We included the demographic, clinical and laboratory data. Cox proportional hazard regression analysis was performed to identify the prognostic factors of mortality.
Results: A total of 241 patients were included in this study. In the Cox hazard regression model (hazard ratio [95% confidence interval]), age (65-79 years: 3.531 [1.529-8.156], ≥80 years: 5.335 [2.229-12.770]), respiratory rate (RR) (>20 breaths/min: 2.025 [1.205-3.403], ≤11 breaths/min: 111.292 [30.845-401.555]), lymphocyte counts <1.0×10^9/L (2.611 [1.494-4.739]), blood urea nitrogen (BUN) levels>23 mg/dL (2.047 [1.233-3.399]), aspartate aminotransferase (AST) levels>40 IU/L (1.785 [1.009-3.158]) and neutrophil counts>6.3×10^9/L (1.638 [1.014-2.644]) were associated with mortality.
Conclusion: Age, RR, lymphocyte counts, BUN levels, AST levels and neutrophil counts were prognostic factors in COVID-19 patients in the ED. These factors can help effectively treat and reduce mortality through optimized management of COVID-19 patients, in places with limited emergency medical resources such as massive regional outbreaks.

Keywords: Coronavirus; Disease outbreaks; Emergency treatment; Prognosis; Mortality

INTRODUCTION

Novel coronavirus disease 2019 (COVID-19) emerged in Wuhan, China, in December 2019, and the World Health Organization has declared it as a global pandemic.[1] In Korea, one of the countries closest to China geographically, confirmed cases were sporadically detected after the first patient was identified on January 20, 2020.[2] Daegu is the fourth largest city in Korea, with an area of 883.56 km^2 and a population of 2,487,829, located in the south-eastern part of the Korean peninsula.[3] On February 18, 2020, the second massive regional COVID-19 outbreak worldwide commenced in Daegu (Fig. 1). This resulted in repeated shutdowns of emergency departments (EDs), isolation of exposed hospital workers, and an overload on the emergency medical resources across the city.[4]

After the outbreak, city government and medical facilities in the Daegu prepared the screening and treatment of COVID-19 patients in Daegu area. Public health centers and major hospitals began operating screening centers for early diagnosis of COVID-19, and patients with mild symp-

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Capsule Summary

What is already known in the previous study

The World Health Organization has declared a global pandemic of novel coronavirus disease 2019 (COVID-19), and on February 18, 2020, the second massive regional outbreak worldwide commenced in Daegu, Korea. Patients with severe COVID-19 visited the major emergency departments (EDs) for critical care and screening.

What is new in the current study

Old age, abnormal respiratory rate, lymphocytopenia, neutrophilia, elevated blood urea nitrogen and elevated alanine aminotransferase were associated with higher mortality rates in COVID-19 patients assessed in the ED. These findings will help treat and reduce mortality rates of severe COVID-19 patients in places with limited emergency medical resources, such as massive regional outbreaks.

toms were admitted to the life treatment centers (LTCs) designated by the Korea Centers for Disease Control and Prevention.[5] Hospitals with six major EDs, which are research-participating EDs, have prepared isolation room and provided critical care for serious COVID-19 patients. However, people with severe symptoms directly visit the major EDs for critical care and screening. In addition, while these EDs constitute the front line of management for severe COVID-19 patients, they also have to handle the regular workload simultaneously. Therefore, it is almost impossible to predict the impact of a regional outbreak on the emergency medical preparedness for severe COVID-19 patients.[4,5] In this regard, the clinical features and prognostic factors of COVID-19 patients in the ED can be different from that encountered in the LTCs. As the pandemic is ongoing, there is a possibility of repeated regional outbreaks, and during these circumstances, a considerable chunk from the limited emergency medical resources will have to be diverted for COVID-19 management. Therefore, it is necessary to establish an optimal strategy and provide aggressive medical intervention efficiently by identifying the COVID-19 patients who may have a poor prognosis, in the ED.[5,6]

There have been several previous studies on COVID-19.[2,7,8] However, the characteristics of patients visiting EDs may differ from those of the regular patients in the community. In addition, to the best of our knowledge, most ED-based studies on COVID-19 have addressed the guidelines for medical staff protection or ED management, and there are no studies focusing on the clinical characteristics and outcomes based on the ED assessment, in a particular regional outbreak area.[4,5] Hence, we investigated the characteristics and prognostic factors of COVID-19 patients presenting to EDs in Daegu.

METHODS

1. Study design

This retrospective, observational, citywide, multicenter study was conducted on COVID-19 patients treated in the EDs of Daegu. Data collection was approved by the institutional review board of each study hospital. The need for informed consent was waived for this retrospective study.

2. Study participants and data collection

In Daegu, two regional and four local emergency medical centers provide majority of the emergency medical services. After the massive COVID-19 outbreak in Daegu, these six EDs collaborated and established a citywide clinical registry for COVID-19. In this registry, patients' data were collected from the electronic medical records of each study hospital. In addition, researchers in each study hospital followed up the patients' outcomes. These data were sent to data quality managers who provided feedback to all the researchers to increase the level of perfection. The study participants were those who had positive COVID-19 real-time reverse transcription-polymerase chain reaction (RT-PCR) results and were treated in one of the six major EDs from January 20, 2020 to April 30, 2020.

In the entire patients who visited the six major EDs during the study period, we excluded the patients who did not undergo testing or had negative RT-PCR results. Thereafter, we further excluded the patients who visited the ED only for COVID-19 screening. In addition, the patients who showed positive RT-PCR results 14 days after the ED visit were excluded since the purpose of their ED visit was not considered to be COVID-19 related, because the diagnosis were being made after the incubation period.[9]

We evaluated the demographic characteristics and clinical features including age, sex, major symptoms, comorbidities, visiting date, visiting methods, mode of arrival, symptom onset date, primary designated area, vital signs on arrival, radiological findings, ED disposition, date of ED discharge, hospital discharge date, and final outcome. Symptoms including fever, cough, sore throat, dyspnea, sputum, myalgia, and headache were considered as typical, and others were considered atypical.[7] In addition, we evaluated the initial laboratory results, including those of complete blood counts, blood biochemistry, and C-reactive protein (CRP) levels.

3. Statistical analysis

Demographic characteristics, clinical features, and hospital outcomes were evaluated. Continuous variables, expressed as medians and interquartile ranges (IQRs; 25-75th percentile), were evaluated using the Mann-Whitney U test, based on the positively skewed distribution noted in the Shapiro-Wilk test. In addition, the Pearson chi-square and Fisher's exact tests were used to compare categorical variables, which were presented as numbers and percentages.

We performed the Kaplan-Meier estimation and log rank tests to identify the factors associated with survival in COVID-19 patients. Univariable and multivariable Cox proportional hazard regression analyses with 95% confidence intervals (CIs) were performed to identify prognostic factors of mortality in COVID-19 patients. Sex, age, comorbidity, respiratory rate (RR), body temperature (BT), heart rate, systolic blood pressure (SBP), mental status, initial chest X-ray findings, lymphocyte, neutrophil, and platelet counts, alanine aminotransferase (ALT), aspartate aminotransferase (AST), blood urea nitrogen (BUN), serum creatinine, and CRP levels were considered as variables for multivariable analysis, based on the association in univariable model. Variance inflation factors were identified to confirm collinearity among the confounders.

All statistical analyses were performed using IBM SPSS ver. 21.0 (IBM Corp., Armonk, NY, USA), and results with P-values <0.05 were considered statistically significant.

4. Outcome measures

The main outcome was mortality, as of July 31, 2020 (the last date of follow-up). Patients who were discharged alive from the hospital and patients who were still hospitalized on the last date of follow-up were considered to have survived.

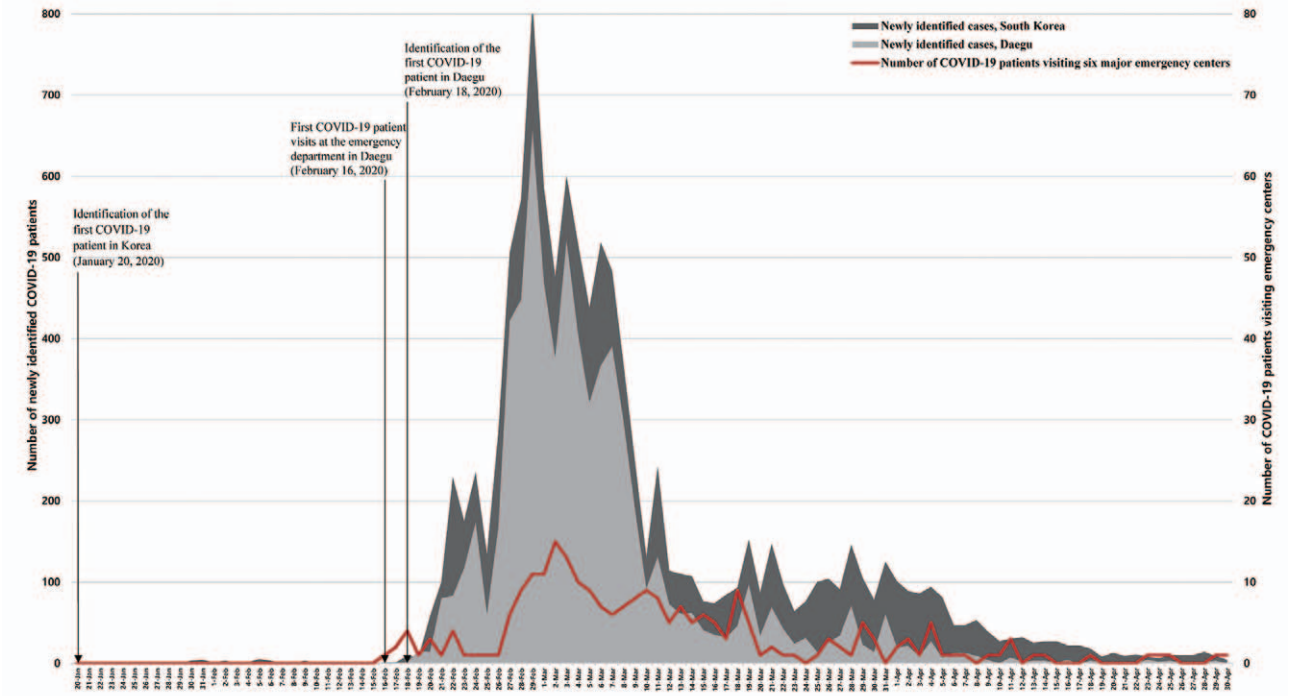

Fig. 1. Number of newly identified coronavirus disease 2019 (COVID-19) patients and the number of COVID-19 patients visiting six major emergency centers according to the date of visit, Daegu, South Korea.

RESULTS

1. Baseline characteristics

After February 18, when the day first COVID-19 patient was identified at the one of study EDs, number of COVID-19 infected patients was dramatically increased, and newly identified patients were peaked after two weeks. After the first case, the patient continued to develop for about two months, and finally entered a lull in the last week of April (Fig. 1). During this period, 44,322 patients were visited the study EDs, we excluded 44,056 patients who did not undergo testing or had negative RT-PCR results, 24 patients who visited the ED only for COVID-19 screening, and one patient who showed positive RT-PCR result 14 days after the ED visit. One patient who still hospitalized on the last accessed date was considered to have survived, and finally 241 patients were included in this study (Fig. 2).

Table 1 presents the baseline characteristics of the study participants. Of the 241 study participants, 75 (31.1%) were less than 64 years old, 102 (42.3%) were 65-79 years old, and 64 (26.6%) were over 80 years old; 115 (47.7%) were male. A total of 164 patients (68.0%) had more than one comorbidity, with hypertension being most common (n=114, 47.3%). Public emergency medical services were most commonly used to visit the ED (n=147, 61.0%), and primary visitation was the major mode of arrival (n=183, 75.9%). The median interval from symptom onset to ED visit was one day (IQR, 0.0-3.0 days). Most patients underwent inpatient management (193, 80.1%), 22 (9.1%) were transferred, 16 (6.6%) died in the ED, and 10 (4.1%) were discharged because they had mild disease. All deaths occurred in patients over 50 years of age (Fig. 3).

2. Clinical features

Table 2 presents the clinical features of the enrolled patients. Typical symptoms were not observed in 41 patients (17.0%). Upon arrival, 105 (43.6%) showed abnormal BT, 36 (14.9%) had an SBP less than 100 mmHg, 70 (29.0%) showed an abnormal heart rate, and 73 (30.3%) had either tachypnoea or bradypnea. Impaired mental function was observed in 26 patients (10.8%). In addition, 17 (7.1%) patients were included in the severe disease group based on their Modified Early Warning Scores (MEWS). On initial chest radiography, 55 (23.2%) did not show pneumonic infiltration. Primary isolation failure was seen in 49 patients (20.3%), which occurred mostly during the initial intensive outbreak period. The median length of ED stay was one day (IQR, 0.0-2.0 days), the median length of inpatient admission was 18.0 days (IQR, 9.5-34.5 days), and the median length of overall hospitalization was 16.0 days (IQR, 5.0-32.0 days).

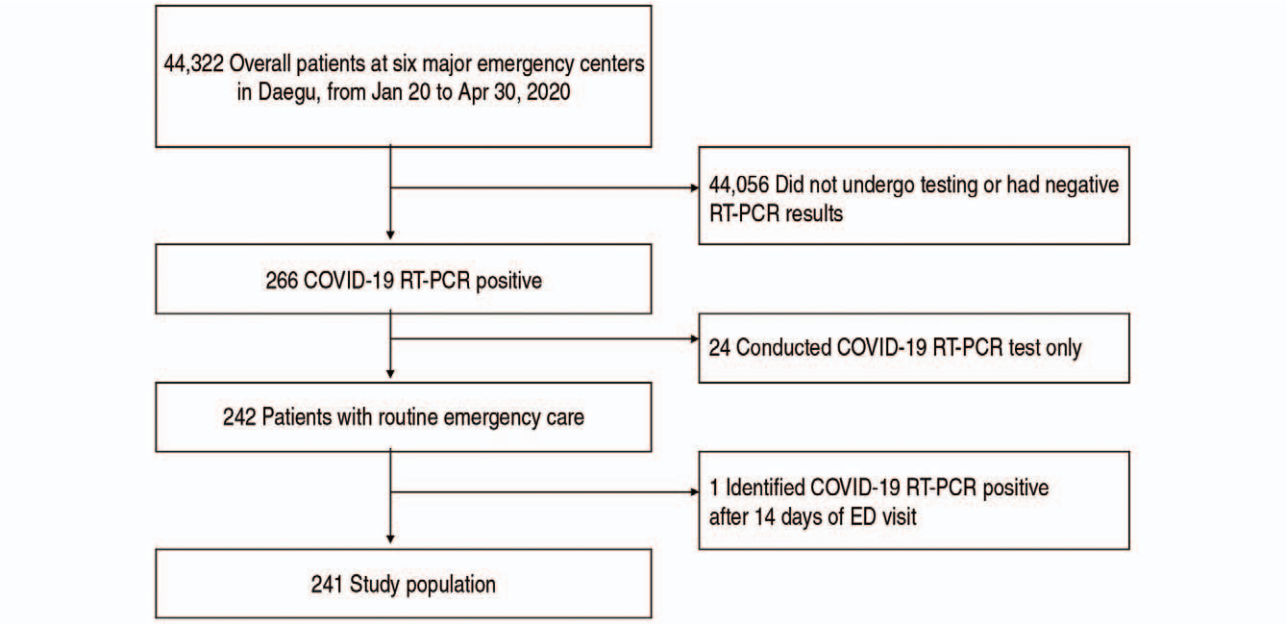

Fig. 2. Flow chart of inclusion of the study population. COVID-19, coronavirus disease 2019; RT-PCR, reverse transcription-polymerase chain reaction; ED, emergency department.

3. Laboratory results

The initial laboratory results are presented in Table 3. Leukopenia (white blood cell count<4.0×10^9/L) was present in 31 patients (13.0%), and leukocytosis was present in 30 patients (12.6%). Neutrophilia was present in 82 patients (34.5%), and lymphocytopenia (lymphocyte count <1.0×10^9/L) was present in 133 patients (55.9%). Thrombocytopenia (platelet count<150×10^9/L) was present in 54 patients (22.7%). AST levels were elevated in 114 (47.9%), ALT levels were elevated in 63 (26.5%), and hyperbilirubinemia was present in 33 (13.9%). BUN levels were elevated in 71 patients (30.0%), and serum creatinine levels were elevated in 108 patients (45.6%). CRP levels were elevated in 186 patients (78.5%).

Table 1. Baseline characteristics of COVID-19 patients in the emergency departments in Daegu

Variable	Total (n=241)	Final outcomes		P-value
		Survive (n=159)	Death (n=82)	
Age (yr)	73.0 (61.0-80.0)	68.0 (58.0-78.0)	78.0 (71.0-81.0)	<0.001
≤64	75 (31.1)	66 (41.5)	9 (11.0)	<0.001[a]
65-79	102 (42.3)	62 (39.0)	40 (48.8)	
≥80	64 (26.6)	31 (19.5)	33 (40.2)	
Sex				0.003[a]
Male	115 (47.7)	65 (40.9)	50 (61.0)	
Female	126 (52.3)	94 (59.1)	32 (39.0)	
Comorbidities[b]				
Existence of comorbidities				0.002[a]
No	76 (31.6)	61 (38.4)	15 (18.5)	
Yes	164 (68.3)	98 (61.6)	66 (81.5)	
Detailed comorbidities				
Hypertension	114 (47.5)	71 (44.7)	43 (53.1)	0.216[a]
Diabetics mellitus	64 (26.7)	34 (21.4)	30 (37.0)	0.010[a]
Malignancy	24 (10.0)	13 (8.2)	11 (13.6)	0.187[a]
Cardiovascular disease	23 (9.6)	12 (5.0)	11 (4.6)	0.133[a]
Dementia	22 (9.2)	10 (6.3)	12 (14.8)	0.030[a]
Cerebrovascular disease	20 (8.3)	9 (5.7)	11 (13.6)	0.036[a]
Chronic liver disease	4 (1.7)	3 (1.9)	1 (1.2)	>0.99[c]
Old pulmonary tuberculosis	3 (1.3)	2 (1.3)	1 (1.2)	>0.99[c]
Visiting methods				0.001[a]
Public EMS	147 (61.0)	84 (52.8)	63 (76.8)	
Other ambulance	16 (6.6)	11 (6.9)	5 (6.1)	
Other vehicles/walking	78 (32.4)	64 (40.3)	14 (17.1)	
Mode of arrival				0.608[a]
Primary visitation	183 (75.9)	118 (74.2)	65 (79.3)	
Transfer from the other hospitals	49 (20.3)	34 (21.4)	15 (18.3)	
Refer from the outpatient department	9 (3.7)	7 (4.4)	2 (2.4)	
Interval from symptom to visit (day)[d]				0.746[a]
0-6	197 (84.2)	126 (82.9)	71 (86.6)	
7-13	26 (11.1)	18 (11.8)	8 (9.8)	
≥14	11 (4.7)	8 (5.3)	3 (3.7)	
ED disposition				<0.001[a]
Admission	193 (80.1)	131 (82.4)	62 (75.6)	
Transfer	22 (9.1)	18 (11.3)	4 (4.9)	
Death	16 (6.6)	0	16 (19.5)	
Discharge	10 (4.1)	10 (6.3)	0	

Values are presented as median (interquartile range, 25-75th percentile) or number (%).
COVID-19, coronavirus disease 2019; EMS, emergency medical services; ED, emergency department.
[a] Pearson chi-square test. [b] One missing datapoint. [c] Fisher's exact test. [d] Seven missing datapoints.

4. Prognostic factors in COVID-19 patients

The survival curves and prognostic factors for mortality in COVID-19 patients in the ED are presented in Fig. 4 and Table 4. According to the multivariable Cox proportional hazards regression analysis performed after Kaplan-Meier estimation and log rank tests (hazard ratio [95% CI]), age (65-79 years: 3.53 [1.53-8.16]; ≥80 years: 5.34 [2.23-12.77]), RR (>20 breaths/min: 2.03 [1.21-3.40]; ≤11 breaths/min: 11.29 [30.85-401.56]), lymphocyte counts $<1.0\times10^9$/L (2.61 [1.49-4.74]), BUN levels >23 mg/dL (2.05 [1.23-3.40]), AST levels >40 IU/L (1.79 [1.01-3.16]), and neutrophil counts>6.3×10^9/L (1.64 [1.01-2.64]) were associated with mortality. In addition, the same variables were found to be significant except for RR and BUN levels in in COVID-19 patients with MEWS 0 to 4.

DISCUSSION

To the best of our knowledge, this study is the first to identify the prognostic factors of mortality in COVID-19 patients based on the ED during a massive regional outbreak in Korea. In this study, old age, abnormal RR, lymphocytopenia, increased BUN levels, AST elevation, and neutrophilia were associated with poor prognosis in COVID-19 patients.

Previous studies have reported that older people show severe COVID-19 outcomes.[6,10,11] Similarly, ageing was associated with a higher mortality rate in this study; in particular, all the deceased patients were over 50 years old (Fig. 3). However, there was a difference in mortality rates compared to those in previous reports. Verity et al.[12] reported a mortality rate of 6.4% in patients aged 60 or older in Hubei, China. Richardson et al.[13] reported a 26.6% mortality rate in patients over 65 years who did not receive ventilator support in New York City. The Korean Office for Government Policy Coordination reported that 452 of 7,765 (5.8%) aged 60 or more COVID-19 patients were deceased, with mortality rates of 1.2% for patients in their sixties, 7.1% for patients in their seventies, and 20.3% for those aged 80 and above.[14] In our study, the mortality rate for COVID-19 patients aged 60 and above in the ED was 41.1%, and was 51.6% in those older than 80 (Fig. 3). In

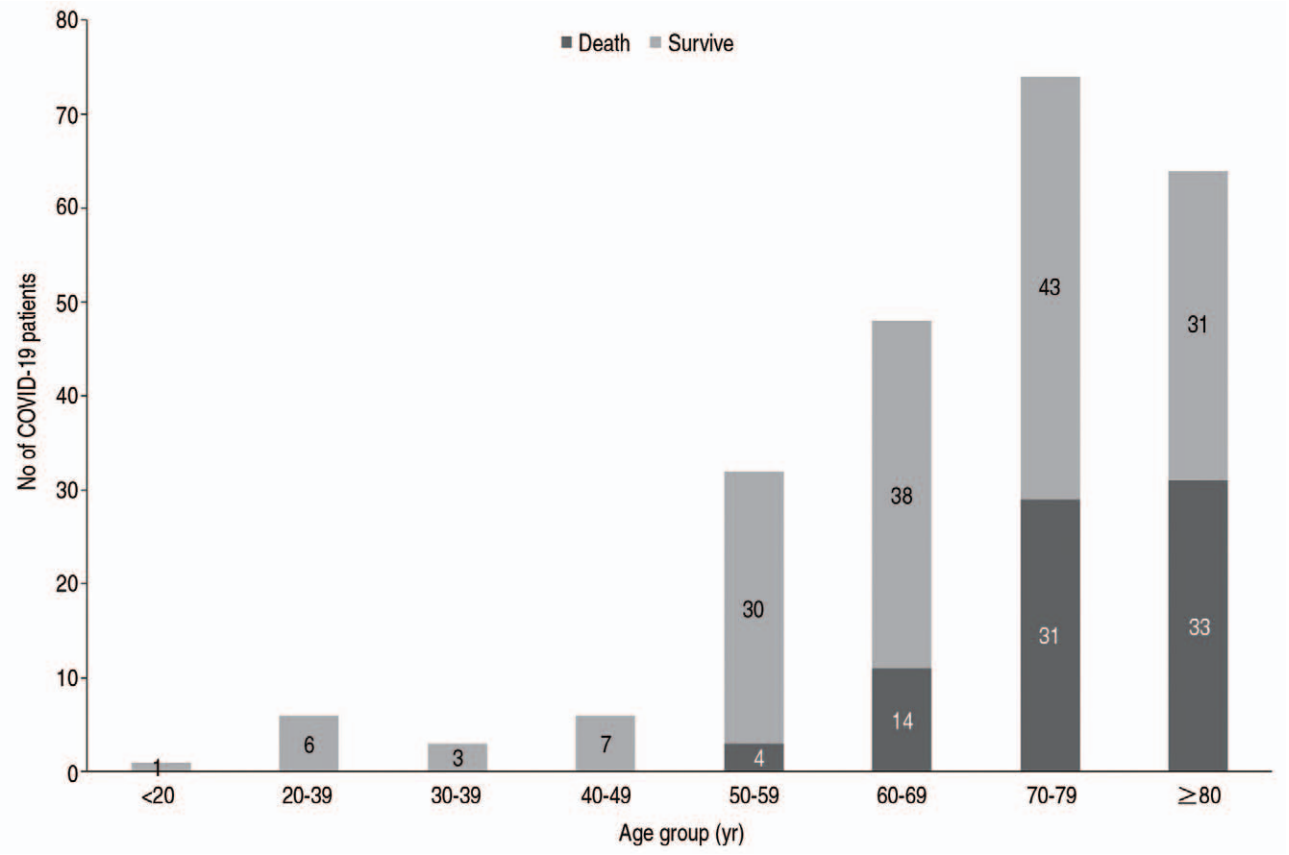

Fig. 3. Outcomes of coronavirus disease 2019 (COVID-19) patients at six major emergency centers in Daegu according to age groups.

a study of Sung et al.[2] based on the COVID-19 patients in South Korea, 4.0% SBP ≤100 mmHg, 6.5% RR ≥22, and 0.2% altered mentality were reported, but in this study, 14.9% and 26.1% and 10.8%, respectively. In addition, in a study of Jang et al.[15] based on the COVID-19 patients via ED and outpatient department in Daegu, 21.8% lymphocytopenia, 11.8% increased BUN levels, 26.4% AST elevation, and 21.8% neutrophilia were reported, but in this study, 55.9% and 30.0%, 47.9%, and 34.5%, respectively. The higher mortality observed in this study may have been due to the higher severity of illness of the study participants compared with that in the previous studies, since the char-

Table 2. Clinical features of COVID-19 patients in the emergency departments in Daegu

Variable	Total (n=241)	Final outcomes		P-value
		Survive (n=159)	Death (n=82)	
Symptoms				0.073[a]
Typical	200 (83.0)	127 (79.9)	73 (89.0)	
Atypical	41 (17.0)	32 (20.1)	9 (11.0)	
Vital signs				
Body temperature (°C)[b]				0.003[a]
36.1-37.4	134 (56.1)	98 (61.6)	36 (45.0)	
≥37.5	87 (36.4)	55 (34.6)	32 (40.0)	
≤36.0	18 (7.5)	6 (3.8)	12 (15.0)	
SBP (mmHg)				<0.001[a]
>100	205 (85.1)	145 (91.2)	60 (73.2)	
≤100	36 (14.9)	14 (8.8)	22 (26.8)	
Heart rate (bpm)				<0.001[a]
60-100	171 (71.0)	124 (78.0)	47 (57.3)	
>100	56 (23.2)	32 (20.1)	24 (29.3)	
<60	14 (5.8)	3 (1.9)	11 (13.4)	
Respiratory rate (breaths/min)				<0.001[a]
12-20	168 (69.7)	127 (79.9)	41 (50.0)	
>20	63 (26.1)	32 (20.1)	31 (37.8)	
≤11	10 (4.1)	0	10 (12.2)	
Impaired mentality				<0.001[a]
No	215 (89.2)	153 (96.2)	62 (75.6)	
Yes	26 (10.8)	6 (3.8)	20 (24.4)	
MEWS				<0.001[a]
Minor (0-4)	212 (88.0)	152 (95.6)	60 (73.2)	
Moderate (5-6)	12 (5.0)	6 (3.8)	6 (7.3)	
Severe (≥7)	17 (7.1)	1 (0.6)	16 (19.5)	
Chest X-ray finding[c]				<0.001[a]
No infiltration	55 (23.2)	47 (29.7)	8 (10.1)	
Unilateral infiltration	28 (11.8)	24 (15.2)	4 (5.1)	
Bilateral infiltration	154 (65.0)	87 (55.1)	67 (84.8)	
Initial designated area				0.912[a]
Isolation zone	192 (79.7)	127 (79.9)	65 (79.3)	
Ordinary treatment area	49 (20.3)	32 (20.1)	17 (20.7)	
Length Hospitalization (day)				
ED stay	1.0 (0.0-2.0)	1.0 (0.0-1.0)	1.0 (0.0-2.0)	0.217
Inpatient admission[d]	18.0 (9.5-34.5)	25.0 (14.0-39.0)	9.0 (4.8-21.3)	<0.001
Overall hospitalization	16.0 (5.0-32.0)	20.0 (9.0-36.0)	8.0 (2.0-17.0)	<0.001

Values are presented as number (%) or median (interquartile range, 25th-75th percentile).
COVID-19, coronavirus disease; SBP, systolic blood pressure; MEWS, Modified Early Warning Score; ED, emergency department.
[a] Pearson chi-square test. [b] Two missing datapoints. [c] Four missing datapoints. [d] Forty-eight cases of non-admission were excluded.

acteristics that all these patients visited hospitals for emergency care. In addition, deaths in the ED in severe patients that were not identified in other hospitalization-based studies and limitations of emergency medical resources during massive outbreaks may also have contributed to the high mortality in this study.[16]

Among the initial vital signs, only RR was associated with mortality in this study. There are many previous reports suggesting the association between respiratory difficulty and COVID-19 severity. Dyspnea is likely related to severe COVID-19 infection and poor outcomes.[6,8,17] Hypoxia can be caused due to various reasons in COVID-19 infections, and is related to poor outcomes.[18,19] Tachypnoea could reflect dyspnea or hypoxia; thus, the results of this study could have reflected this association. In addition, bradypnea was strongly associated with death in this study. This result may be related to very serious cases such as cardiac arrest or impending cardiac arrest associated with COVID-19 infection. In fact, 10 patients who showed bradypnea in this study had a cardiac arrest or impending cardiac arrest, all

Table 3. Initial laboratory findings of COVID-19 patients in the emergency departments in Daegu

Variable	Total[a] (n=238)	Final outcome		P-value[b]
		Survive (n=159)	Death (n=79)	
White blood cell count ($\times 10^9$/L)				0.001
4.0-12.0	177 (74.4)	125 (78.6)	52 (65.8)	
<4.0	31 (13.0)	23 (14.5)	8 (10.1)	
>12.0	30 (12.6)	11 (6.9)	19 (24.1)	
Neutrophil count ($\times 10^9$/L)				0.011
≤6.3	156 (65.5)	113 (71.1)	43 (54.4)	
>6.3	82 (34.5)	46 (28.9)	36 (45.6)	
Lymphocyte count ($\times 10^9$/L)				0.001
≥1.0	105 (44.1)	82 (51.6)	23 (29.1)	
<1.0	133 (55.9)	77 (48.4)	56 (70.9)	
Hemoglobin (g/dL)				0.366
≥12.0	157 (66.0)	108 (67.9)	49 (62.0)	
<12.0	81 (34.0)	51 (32.1)	30 (38.0)	
Platelet count ($\times 10^9$/L)				0.001
≥150	184 (77.3)	133 (83.6)	51 (64.6)	
<150	54 (22.7)	26 (16.4)	28 (35.4)	
Aspartate aminotransferase (IU/L)				<0.001
≤40	124 (52.1)	101 (63.5)	23 (29.1)	
>40	114 (47.9)	58 (36.5)	56 (70.9)	
Alanine aminotransferase (IU/L)				0.057
≤35	175 (73.5)	123 (77.4)	52 (65.8)	
>35	63 (26.5)	36 (22.6)	27 (34.2)	
Total bilirubin (mg/dL)[c]				0.111
≤1.2	204 (86.1)	140 (88.6)	64 (81.0)	
>1.2	33 (13.9)	18 (11.4)	15 (19.0)	
Blood urea nitrogen (mg/dL)[c]				<0.001
≤23.0	166 (70.0)	130 (82.3)	36 (45.6)	
>23.0	71 (30.0)	28 (17.7)	43 (54.4)	
Serum creatinine (mg/dL)[c]				<0.001
≤0.9	129 (54.4)	105 (66.5)	24 (30.4)	
>0.9	108 (45.6)	53 (33.5)	55 (69.6)	
C-reactive protein (mg/dL)[c]				0.019
≤1.0	51 (21.5)	41 (25.9)	10 (12.7)	
>1.0	186 (78.5)	117 (74.1)	69 (87.3)	

Values are presented as number (%).
COVID-19, coronavirus disease 2019.
[a] Three missing datapoints in the overall study population. [b] Pearson chi-square test. [c] One additional missing datapoint.

of which died. Given these results, we believe that abnormal RRs may be associated with death and physicians should be careful about this.

Lymphocytopenia and neutrophilia were associated with high mortality in this study. Previous studies have reported that lymphocytopenia and neutrophilia are important indicators of COVID-19 severity.[17,20] Lymphocytopenia may be related to the cytokine storm, an uncontrolled systemic hyperinflammatory syndrome that causes destruction of the immune system, respiratory distress syndrome, and systemic organ failure.[21] Neutrophilia is associated with pulmonary pathologies and is linked to severity.[22] In addition, a high neutrophil-lymphocyte ratio could predict poor prognosis.[23] Lymphocyte and neutrophil counts can be easily and quickly identified in the ED. Therefore, we believe that lymphocytopenia and neutrophilia might be useful in monitoring COVID-19 patients in the ED.

Increased BUN levels were associated with higher mortality in COVID-19 patients in this study. There have been previous studies about the relationship between COVID-19 outcomes and renal injury. Ok et al.[24] reported that the BUN/creatinine ratio could predict the outcomes of COVID-19 patients. Na et al.[3] reported that acute kidney injury (AKI) was frequent in severe COVID-19 patients. AKI is a phenomenon characterized by the acute loss of renal function, and BUN is one of the major indicators of renal function.[25,26] Therefore, the initial increase in BUN levels may be related to impending AKI in COVID-19 patients in the ED. In addition, since presently, no definite treatment exists for AKI caused by COVID-19 infection, aggressive prevention will be important in reducing the mortality rate of COVID-19 patients.[25] Considering this, we believe that BUN levels could help provide better management in COVID-19 patients in the ED.

In this study, AST elevation was associated with poor outcomes. COVID-19 patients could show varying degrees of hepatic dysfunction, and some biomarkers could represent disease severity.[27] Huang et al.[28] reported that the AST level was an independent risk factor for poor COVID-19 outcome. Lei et al.[29] reported that COVID-19 infection was related to liver injury and increased levels of hepatic indicators, especially AST. It was also associated

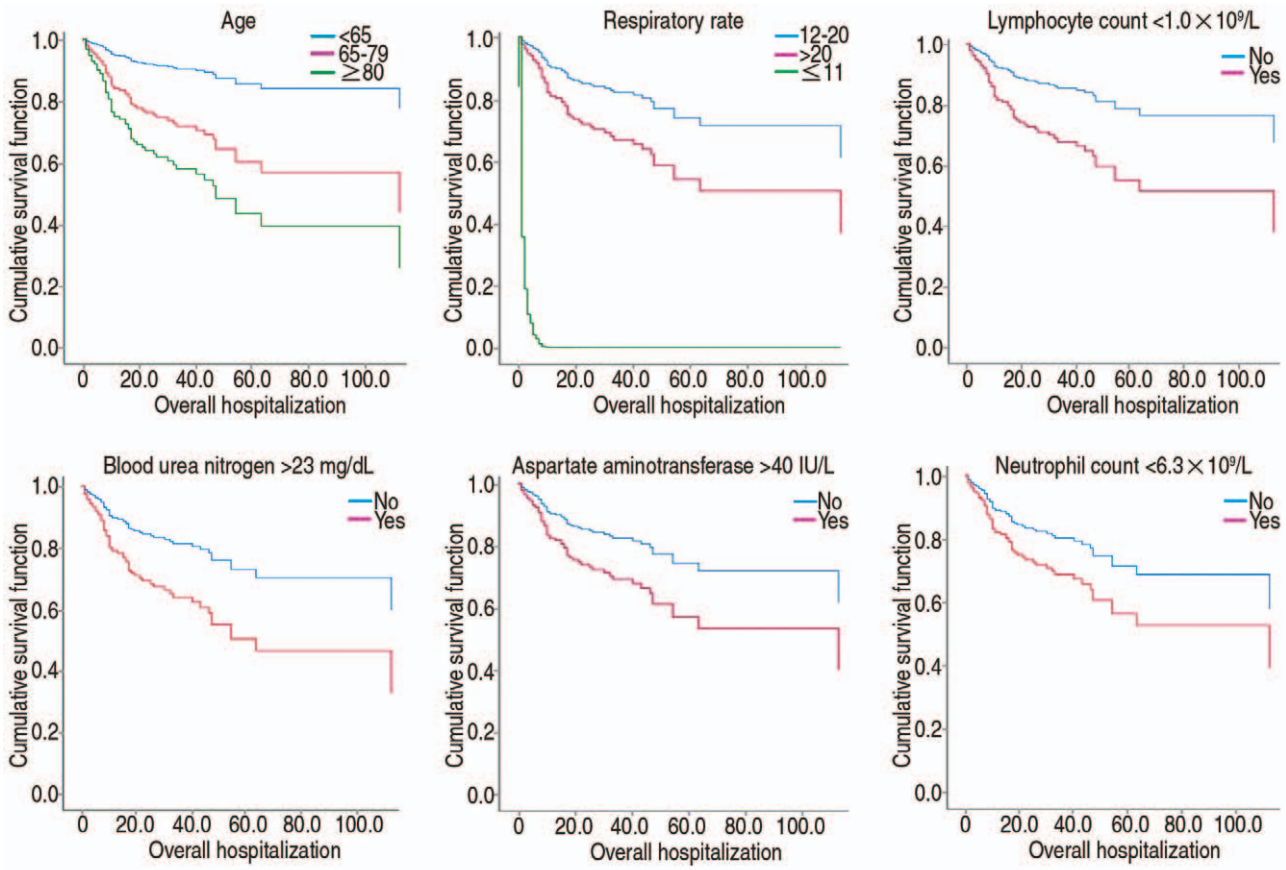

Fig. 4. Survival curves of coronavirus disease 2019 patients visiting six major emergency centers, Daegu, South Korea. Data were analyzed using a Cox proportional hazards model.

with mortality in COVID-19 patients.[29] It is still uncertain whether COVID-19 infection directly causes liver injury.[30] However, we believe that emergency physicians should evaluate hepatic biomarkers, especially AST levels, to monitor patient severity, based on the results of the current clinical studies.

This study has several limitations. First, this study was conducted in a specific city in Korea. As this is an unprecedented pandemic period, the impact of COVID-19 may vary from country to country due to differences in the available medical resources and emergency medical preparedness. Therefore, the results of this study must be generalized carefully. Second, it is possible that there were unidentified severe COVID-19 patients, such as those with out-of-hospital cardiac arrests related to COVID-19 infection, who would likely be missed from our study. However, this aspect could not be controlled. Third, we used data from a population-based registry; therefore, factors related to specific clinical management, such as the use of antiviral agents, mechanical ventilation support, or extracorporeal

Table 4. Cox proportional hazards regression analysis for the mortality of COVID-19 patients in the emergency departments in Daegu

Variable	HR (95% CI)	
	Univariable	Multivariable
Baseline characteristics		
Male sex	1.68 (1.08-2.63)	1.65 (0.97-2.79)
Age (yr)		
<65	Reference	Reference
65-79	3.31 (1.60-6.84)	3.53 (1.53-8.16)
≥80	4.37 (2.08-9.19)	5.34 (2.23-12.77)
Existence of comorbidity	1.89 (1.08-3.31)	1.24 (0.68-2.27)
Clinical features on arrival		
Respiratory rate (breaths/min)		
12-20	Reference	Reference
>20	1.94 (1.21-3.10)	2.03 (1.21-3.40)
≤11	52.06 (22.22-121.99)	111.29 (30.85-401.56)
Body temperature (°C)		
36.1-37.4	Reference	Reference
≥37.5	1.31 (0.82-2.12)	1.07 (0.63-1.81)
≤36.0	2.74 (1.43-5.28)	0.63 (0.25-1.56)
Heart rate (bpm)		
60-100	Reference	Reference
<60	8.28 (4.22-16.22)	1.62 (0.20-13.08)
>100	1.63 (1.00-2.68)	1.21 (0.69-2.11)
SBP≤100 mmHg	2.92 (1.79-4.77)	1.50 (0.77-2.93)
Impaired mentality	4.09 (2.46-6.80)	0.95 (0.43-2.12)
Initial chest X-ray finding		
No infiltration	Reference	Reference
Unilateral infiltration	0.89 (0.27-2.97)	0.57 (0.17-1.96)
Bilateral infiltration	2.77 (1.33-5.77)	1.30 (0.58-2.88)
Initial laboratory findings on the ED		
Lymphocyte count<1.0×10^9/L	2.02 (1.24-3.29)	2.61 (1.49-4.74)
Blood urea nitrogen>23 mg/dL	3.00 (1.92-4.70)	2.05 (1.23-3.40)
Aspartate aminotransferase>40 IU/L	2.95 (1.82-4.80)	1.79 (1.01-3.16)
Neutrophil count>6.3×10^9/L	1.52 (0.98-2.37)	1.64 (1.01-2.64)
C-reactive protein>1.0 mg/dL	1.81 (0.93-3.51)	1.58 (0.76-3.29)
Serum creatinine>0.9 mg/dL	2.89 (1.79-4.68)	1.07 (0.51-2.22)
Platelet count<150×10^9/L	1.86 (1.17-2.96)	0.99 (0.51-1.93)
Alanine aminotransferase>35 IU/L	1.67 (1.05-2.66)	0.83 (0.45-1.53)

COVID-19, coronavirus disease 2019; HR, hazard ratio; CI, confidence interval; SBP, systolic blood pressure; ED, emergency department.

membrane oxygenation, could not be considered. The aim of our study was to identify the prognostic factors associated with mortality in COVID-19 patients, upon arrival at the ED. There is a possibility that a specific treatment influenced the patient outcome, but still no definite investigations about these managements for COVID-19 patients via the ED. Finally, certain laboratory parameters with possible correlations to COVID-19 outcomes, such as arterial blood gas analysis, could not be considered in this study because these parameters were not assessed in all the patients during primary evaluation in the ED.

In conclusion, older age, abnormal RR, lymphocyte counts<1.0×10^9/L, AST levels>40 IU/L, BUN levels>23 mg/dL, and neutrophil counts>6.3×10^9/L were associated with higher mortality rates in COVID-19 patients assessed in the ED. In this unpredictable era of the COVID-19 pandemic, physicians must strive for efficient treatment of specific patients because of limited medical resources, especially in regions with massive outbreaks. The mortality of COVID-19 patients could be reduced by optimizing early management tailored to the severity of each patient, and we believe that the findings of our study could be significant in this regard.

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CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

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