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Clinical Characteristics and Predictors of Disease Progression in Severe Patients with COVID-19 Infection in Jiangsu Province, China: A Descriptive Study



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ABSTRACT

Background: We studied patients with coronavirus disease 2019 (COVID-19) infected by severe acute respiratory syndrome coronavirus 2, a virus that originated in Wuhan, China, and is spreading over the country including Jiangsu Province. We studied the clinical characteristics and therapies of severe cases in Jiangsu Province.

Methods: A multicenter retrospective cohort study was conducted to analyze clinical, laboratory data and treatment of 60 severe cases with COVID-19 infection in Jiangsu Province between January 24, 2020 and April 20, 2020. The improvement and deterioration subgroups were compared to identify predictors of disease progression.

Results: A total of 653 infected cases with COVID-19 were reported in Jiangsu Province, of which 60 severe cases were included in this study. Up until April 20, 2020, the mortality of severe patients was 0%. The median age was 57 years. The average body mass index of these patients was 25 kg/m². White blood cell counts decreased in 45.0% of patients, lymphopenia in 63.3%, thrombocytopenia in 13.3% and procalcitonin levels in 88.3% of the patients were less than 0.5 ng/mL. There were no statistically significant differences in immunoglobulin therapy and GCs therapy between the improvement and deterioration subgroups. Logistic regression analysis identified higher levels of troponin T (odds ratio [OR]: 1.04; 95% confidence interval [CI]: 1.00-1.08; $P=0.04$), antiviral therapy with aerosol inhalation of interferon (OR: 6.33; 95% CI: 1.18-33.98; $P=0.03$), and the application of non-invasive mechanical ventilation (OR: 1.99; 95%CI: 1.17-3.41; $P=0.01$) as predictors of disease progression, whereas higher lymphocyte count (OR: 0.11; 95% CI: 0.02-0.57; $P=0.01$) and early prone ventilation were associated with improvement (OR: 0.11; 95% CI: 0.01-0.98; $P=0.04$).

Conclusions: COVID-19 infection had a low mortality rate in Jiangsu Province, China. The higher levels of troponin T and lower lymphocyte count were predictors of disease progression. Early prone ventilation may be an effective treatment for severe cases.

Key Indexing Terms: COVID-19; Severe patients; Disease progression; Critical care. [[Am J Med Sci 2020;360\(2\):120-128.](#)]

INTRODUCTION

The coronavirus disease 2019 (COVID-19) is a novel highly contagious disease first reported from Wuhan, Hubei Province, China on Dec 8, 2019 and then rapidly spread globally by human-to-human transmission. Severe cases could cause difficulty breathing and acute respiratory distress syndrome.^{1,2} Increasing confirmed cases and deaths pose huge challenges to public health and governance.³ Cases have now spread to at least 6 continents.^{4,5} As of April 20, 2020, there were more than 84,237 cases with laboratory-confirmed COVID-19 infection, and over 4,642 deaths in China.⁶ In addition, more than 2,326,435 cases had been confirmed and 161,293 deaths in more than 100 countries, including America, Italy, Spanish, France, Germany, England and so on.⁷⁻¹¹

At present, several publications have described the epidemiological characteristics, clinical manifestations, clinical prognosis, genomic characteristics and antiviral treatment of cases with COVID-19 infection.^{9,12-16} The clinical spectrum of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pneumonia varies in different studies. In some patients, the disease changed rapidly and could quickly develop into progressive pneumonia, respiratory failure, and even death.^{17,18} However, the clinical characteristics and systematic review of treatment for COVID-19 infected patients in critical condition have rarely been reported. Up to April 20, 2020, a total of 653 cases were confirmed in Jiangsu Province, including 60 severe cases admitted to intensive care units (ICU). Although the epidemic occurred relatively late in Jiangsu, as an infectious disease, patients with COVID-19 had to come to the hospital as soon as possible and receive early diagnosis and treatment.

Our aim was to study the epidemiological, clinical, laboratory and radiological characteristics, treatment regimens and clinical outcomes of severe patients diagnosed with COVID-19 infection in Jiangsu Province, China. We hope that our findings can provide some reference experience and theoretical basis for the treatment of severe cases of COVID-19 infection in the global community.

METHODS

Study Design and Patients

Since December 8, 2019, the COVID-19 originated in Wuhan, Hubei Province and had spread rapidly to almost all provinces and cities in China, including Jiangsu Province. For this multicenter retrospective cohort study, we recruited confirmed patients with COVID-19 infection between January 24 and April 20, 2020, from 12 hospitals in Jiangsu Province, China, and described in detail the 60 severe cases. The patients' medical records were sent to Nanjing, where data collection and analysis were

coordinated by the Health Department of Jiangsu Province.¹⁹ The research was approved by the institutional ethics board of the First Affiliated Hospital of Nanjing Medical University. Written informed consent was waived in view of the urgent need to collect clinical data.

Procedures

Information recorded included demographics (including age, sex, body mass index [BMI] and exposure history), symptoms, underlying diseases, complications, incubation period, APACHE II score²⁰ on admission, laboratory and chest radiographs findings prior to and during treatment. Treatment variables included antiviral therapy, antibiotic therapy, means of oxygen support, early prone position ventilation, the use of glucocorticoids (GCs), intravenous immunoglobulin therapy, and negative fluid balance. Clinical outcomes were followed up until April 20, 2020. If the records were missing or needed to be clarified, we obtained the data through direct communication with the attending physicians and other health care providers. The data was reviewed by a trained team of physicians.

The main end points were significant improvement or discharge, or deterioration by April 20, 2020. Since clinical observations are still ongoing and no patients have died, no fixed time horizon has been applied to these end points.

Throat-swabs or endotracheal specimens taken from suspected cases were sent to the Jiangsu Center for Disease Control and Prevention.¹⁹ After the initial detection of respiratory pathogens, samples were sent to the Chinese Center for Disease Prevention and Control (CDC). Laboratory confirmation of the 2019-nCoV was performed by the real-time reverse transcription polymerase chain reaction (RT-PCR) assays in accordance with the protocol established by the World Health Organization (WHO).^{15,21} RT-PCR detection reagents were provided by the following institutions: the Chinese Academy of Medical Science, the Chinese CDC, Academy of Military Medical Sciences, and Wuhan Institute of Virology.

Blood cultures were collected from patients with chills and shivering. Sputum or endotracheal aspirates were administered on admission to identify possible pathogenic bacteria, fungi or other viral infections [for instance, SARS coronavirus, influenza A virus (H1N1), influenza B virus, parainfluenza virus, Middle East respiratory syndrome (MERS) coronavirus, and so on]. In addition, all patients underwent chest computed tomography (CT) scans or chest x-rays.²²

DEFINITIONS

The following terms were defined prior to data analysis. The definitions of suspected and confirmed cases of COVID-19 infection were based on the *Diagnosis and Treatment of Pneumonia Caused by Novel Coronavirus (Pilot Version 5)*²³ issued by the National health and

fitness commission of China. Similarly, mild and severe patients were classified according to the above newly issued diagnostic criteria. Patients with mild symptoms were described as having no or only mild clinical and radiological manifestations. Severe patients were defined as obvious respiratory distress (respiratory rate greater than 30 breaths per minute), hypoxemia (oxygen saturation less than 93% or oxygenation index no more than 300 mmHg), and even respiratory failure being required to be admitted to ICU. In severe patients, oxygen support referred to high flow nasal cannula (HFNC), non-invasive mechanical ventilation, invasive mechanical ventilation or early prone position ventilation. The oxygenation index was calculated by dividing the partial pressure of arterial oxygen (PaO₂) by the inspiratory oxygen fraction (FiO₂), and the normal value was between 400 and 500 mmHg.²⁴ The definition of acute respiratory distress syndrome (ARDS) referred to the Berlin diagnostic criteria.²⁵ Clinical outcomes included discharge from hospital, improvement, and deterioration. Improvement was defined as PaO₂/FiO₂ ratio greater than 300 mmHg or transferred from ICU to a general ward after treatment.²³ Similarly, according to the fifth edition of the guidelines,²³ deterioration was defined as a significant decrease in a patient's PaO₂/FiO₂ ratio, and the need for invasive mechanical ventilation, or the onset of shock, or combined with other organs failure.

Statistical Analysis

Continuous variables were compared with Student t test (for normally distributed variables) or the Mann-Whitney U test (for non-normally distributed variables). Categorical variables were evaluated with the χ^2 or 2-tailed Fisher exact test. Results are expressed as mean \pm standard deviation (SD) or median (range; continuous variables) or as percentages of the group from which they were derived (categorical variables). Two-tailed tests were used to determine statistical significance; a value of *P* less than 0.05 was considered significant.²⁶ Univariate analysis and logistic regression were used to identify risk factors for disease deterioration. All statistical analyses were performed with the SPSS, version 20.0.

RESULTS

Demographic, and Baseline Characteristics

By April 20, 2020, 84,237 symptomatic patients had been confirmed with the COVID-19 infection in China, of which 653 confirmed patients in Jiangsu Province, China. Further study and analysis were conducted on 60 severe cases of 653 confirmed patients from 12 hospitals in Jiangsu Province (Figure 1).

The demographic and clinical characteristics are shown in Table 1. The 60 confirmed severe cases were positive by real-time reverse transcription polymerase chain reaction (RT-PCR) test of secretions from throat

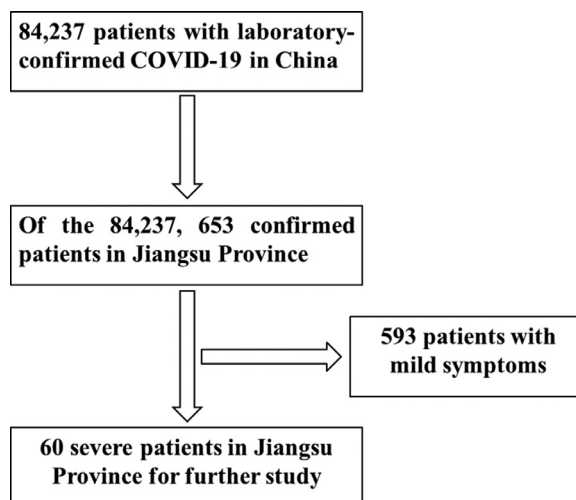


FIGURE 1. Patient recruitment flow chart in China. Shown are the official statistics of all documented laboratory-confirmed cases throughout China according to the National Health Commission (as of April 20, 2020).

swabs. 35 (58.3%) were male; the median age of the patients was 57 years (range, 26- 97 years); the proportion of patients over the age of 50 was 63.3%, higher than that of patients under the age of 50. The mean BMI of the severe patients was 25 ± 3.3 kg/m². A history of contact with people from Wuhan, contact with a confirmed patient, staying in the same train compartment with the patient, and dining together was documented in 41.7%, 16.7%, 5.0% and 3.3% of patients, respectively. 3.3% were healthcare workers. 30.0% were family cluster. The mean incubation period for these patients was 7.7 ± 3.9 days.

Fever (80.0%) and dry cough (51.7%) were the most common symptoms, whereas expectoration (5.0%), vomiting (3.3%) and chest pain (1.7%) were rare. Among the patients with fever, patients with a temperature above 38.5 accounted for 6.7%, significantly less than those with a temperature below 38.5. Thirty-one patients (51.7%) had at least 1 preexisting condition (i.e., hypertension, diabetes, autoimmune disease, stroke), including 1 pregnancy. Mean APACHE II score at admission were 14 ± 5 scores.

Radiologic and Laboratory Findings at Presentation

Table 2 showed the radiologic and laboratory findings of these 60 severe cases on admission. White blood cell counts were normal in 30 patients (50.0%) and decreased in 27 patients (45.0%); 38 patients (63.3%) had lymphopenia. Thrombocytopenia occurred in 8 patients (13.3%). The procalcitonin levels were less than 0.5 ng/mL in 53 (88.3%) of the patients. The average level of albumin for these patients was 34.7 ± 5.1 g/L. Lactate dehydrogenase was elevated in 48 patients (80%) patients; elevated levels of alanine aminotransferase (>50 U/L) and aspartate aminotransferase (>40 U/L) were present in 60% or more of patients. The increase of

TABLE 1. The demographic, epidemiologic, and clinical features of the 60 severe patients in Jiangsu, China.

Characteristics	Patients (n = 60)
Male sex	35 (58.3)
Age, yrs, median (range)	57 (26-97)
Age group	
<30 yrs	4 (6.7)
30-50 yrs	18 (30.0)
>50 yrs	38 (63.3)
BMI, kg/m ² , mean±SD	25 ± 3.3
Exposure to source of transmission	
Contact with people from Wuhan	25 (41.7)
Family cluster	18 (30.0)
Contact with a confirmed patient	10 (16.7)
Staying in the same train compartment with the patient	3 (5.0)
Dine together	2 (3.3)
Health care workers	2 (3.3)
Area of origin	
Nanjing	7 (11.7)
Non-Nanjing	53 (88.3)
Preexisting conditions	
At least 1 preexisting condition	31 (51.7)
Hypertension	14 (23.3)
Diabetes	10 (16.7)
Autoimmune disease	4 (6.7)
Stroke	4 (6.7)
Cardiovascular disease	3 (5.0)
Chronic obstructive pulmonary disease	2 (3.3)
Chronic kidney diseases	1 (1.7)
Pregnancy	1 (1.7)
Incubation period, days, mean±SD	7.7 ± 3.9
APACHE II score on admission to ICU, mean±SD	14 ± 5
Signs and symptoms	
Fever	48 (80.0)
<38.5°C	44 (73.3)
≥38.5°C	4 (6.7)
Dry cough	31 (51.7)
Muscle ache	15 (25.0)
Respiratory distress	7 (11.7)
Fatigue	4 (6.7)
Headache	4 (6.7)
Diarrhea	4 (6.7)
Expectoration	3 (5.0)
Nausea and vomiting	2 (3.3)
Chest pain	1 (1.7)

Data are expressed as number (%) unless otherwise specified. Abbreviations: APACHE, acute physiology and chronic health evaluation; BMI, body mass index; ICU, intensive care unit; SD, standard deviation.

creatinase kinase, creatine kinase isoenzyme and troponin T was documented in 30.0%, 26.7% and 31.7% of patients, respectively.

All patients had abnormal imaging presentations consistent with pneumonia. The most common pattern of chest CT was bilateral patchy shadows (85.0%). [Figure 2](#)

TABLE 2. The laboratory and radiographic findings of the 60 severe patients.

Characteristics	Patients (n = 60)
Laboratory index	
White blood cell count, *10 ⁹ /L, normal range 4-10	
<4	27 (45.0)
4-10	30 (50.0)
>10	3 (5.0)
Lymphocyte count, *10 ⁹ /L, normal range 1.0-3.2	
<1.0	38 (63.3)
≥1.0	22 (36.7)
Platelet count, *10 ⁹ /L, normal range 100-300	
<100	8 (13.3)
≥100	52 (86.7)
Procalcitonin, ng/mL, normal range 0-0.05	
<0.05	17 (28.3)
0.05-0.5	36 (60.0)
≥0.5	7 (11.7)
Albumin, g/L, normal range 40-55, mean±SD	34.7 ± 5.1
LDH, U/L, normal range 140-270	
≤270	12 (20.0)
>270	48 (80.0)
CK, U/L, normal range 18-198	
≤198	42 (70.0)
>198	18 (30.0)
CK-MB, U/L, normal range 0-24	
≤24	44 (73.3)
>24	16 (26.7)
cTnT, μg/L, normal range 0.02-0.13	
≤0.13	41 (68.3)
>0.13	19 (31.7)
ALT, U/L, normal range 9-50	
≤50	19 (31.7)
>50	41 (68.3)
AST U/L, normal range 15-40	
≤40	24 (40.0)
>40	36 (60.0)
Chest x-ray and CT findings	
Unilateral pneumonia	9 (15.0)
Bilateral pneumonia	51 (85.0)

Data are expressed as number (%) unless otherwise specified. Abbreviations: ALT, alanine aminotransferase; AST, aspartate aminotransferase; CK, creatine kinase; CK-MB, creatine kinase isoenzyme; CT, computerized tomography; cTnT, Troponin T; LDH, Lactate dehydrogenase; SD, standard deviation.

shows the representative radiologic findings of a severe patient at the early and deterioration stages of disease.

Treatment and Complications

A total of 9 patients (15.0%) developed ARDS after admission and 16 patients (26.7%) developed respiratory failure ([Table 3](#)). Secondary bacterial or fungal infections occurred in 4 patients (6.7%). Acute liver injury, defined by alanine aminotransferase greater than 50 U/L or aspartate aminotransferase greater than 40 U/L, was observed in 41 patients (68.3%).

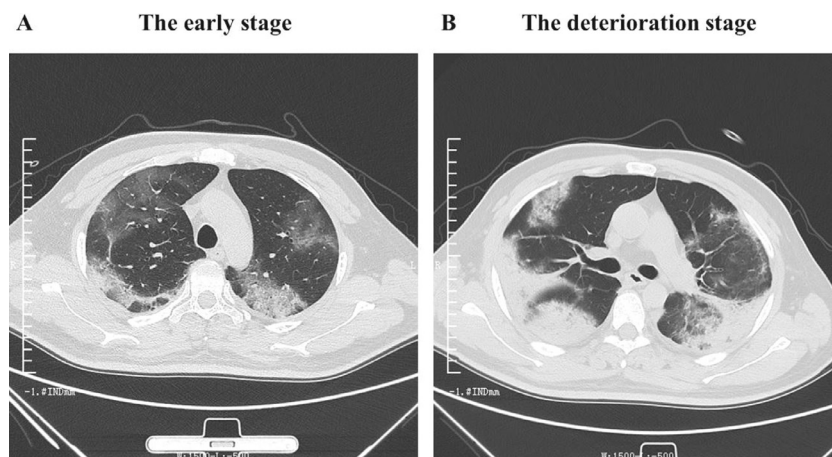


FIGURE 2. The representative radiologic findings of a severe COVID-19 patient. A: The early stage; B: The deterioration stage.

All patients received antiviral therapy. Abidor was given to 50 patients (83.3%), lopinavir and ritonavir to 41 (68.3%), aerosol inhalation of interferon to 12 (20.0%), ribavirin to 7 (11.7%) and oseltamivir to 2 (3.3%). The mean course of antiviral was 10.9 ± 4.2 days.

In addition, 56 patients (93.3%) were treated with antibiotics, of which fluoroquinolones (61.7%) was the most commonly used antibiotics. Thirty-four patients (56.7%), which had higher serum levels of interleukin-1 and interleukin-6, received intravenous glucocorticoid administration at doses ranging from 40-80mg/d. Twenty-eight patients (46.7%) received immunoglobulin (IgG enriched) injections for a period of 5-9 days immunoregulation. In addition, 20 patients (33.3%) were treated with negative fluid balance therapy.

For respiratory support, 14 patients (23.3%) received the noninvasive mechanical ventilation, 15 (25.0%) received high-flow nasal cannula (HFNC) therapy, and 6 (10.0%) received a combination of the above. Three patients (5.0%) were treated with invasive mechanical ventilation with tidal volumes of 4-7 mL/kg predicted body weight in accordance with lung protective ventilation strategy.²⁷ In the invasive or noninvasive respiratory support, 29 patients (48.3%) were given early prone ventilation. The average time from admission to noninvasive mechanical ventilation was 3.5 ± 3.8 days. In addition, 2 patients received continuous renal replacement therapy (CRRT) and 1 received extracorporeal membrane oxygenation (ECMO).

Clinical Outcomes

As of Apr 20, 2020, no patients had died, 50 patients had significantly improved, 2 patients had been discharged and 8 patients were still in serious conditions. The clinical outcomes are shown in the last section of Table 3. Based on the clinical outcome, patients were assigned to an improvement group and deterioration group for further analysis.

Univariate analysis revealed significant differences between the patients who had improved and patients with aggravated conditions subgroups. Patients in the latter group were more likely to have lower lymphocyte count, higher levels of troponin T, and antiviral therapy with aerosol inhalation of interferon. Also, this group had lower rates of application of early prone ventilation and higher rates of non-invasive mechanical ventilation. There were no statistically significant differences between the 2 groups in BMI, preexisting conditions, APACHE II score, white blood cell count, platelet count, administration of glucocorticoid, immunoglobulin therapy, negative fluid balance, or HFNC (All $P > 0.05$).

Logistic regression analysis showed higher levels of troponin T (OR: 1.04; 95% CI: 1.00-1.08; $P = 0.04$), antiviral therapy with aerosol inhalation of interferon (OR: 6.33; 95% CI: 1.18-33.98; $P = 0.03$), and the application of non-invasive mechanical ventilation (OR: 1.99; 95% CI: 1.17-3.41; $P = 0.01$) as predictors of disease progression, whereas higher lymphocyte count (OR: 0.11; 95% CI: 0.02-0.57; $P = 0.01$) and early prone ventilation were associated with improvement (OR: 0.11; 95% CI: 0.01-0.98; $P = 0.04$; Table 4).

After the application of early prone position ventilation, the change trend of patients' oxygenation index ($\text{PaO}_2/\text{FiO}_2$ ratio) on the first, third, fifth and seventh days were shown in Figure 3. It was found that the oxygenation index of severe patients improved after the application of early prone position ventilation.

DISCUSSION

The study presented a cohort of 60 severe patients of COVID-19 in Jiangsu Province, China. The overall mortality rate in Jiangsu Province was 0% by Apr 20, 2020. There were 86.7% of severe patients improved or were discharged from hospital, suggesting that the COVID-19 had been effectively controlled and treated in Jiangsu Province.

TABLE 3. The complications, treatments and clinical outcomes of the 60 patients.

	Patients (n = 60)
Complications	
Acute respiratory distress syndrome	9 (15.0)
Respiratory failure	16 (26.7)
Secondary bacterial or fungal infections	4 (6.7)
Acute liver injury	41 (68.3)
Treatments	
Antiviral therapy	60 (100.0)
Abidor	50 (83.3)
Lopinavir and Ritonavir Tablets	41 (68.3)
Interferon	12 (20.0)
Ribavirin	7 (11.7)
Oseltamivir	2 (3.3)
Duration of antiviral therapy, days, mean±SD	10.9 ± 4.2
Antibiotic therapy	56 (93.3)
Fluoroquinolones	37 (61.7)
Cephalosporins	9 (15.0)
Imipenem or meropenem	5 (8.3)
Linezolid	4 (6.7)
Penicillins	4 (6.7)
Azithromycin	1 (1.7)
Antifungal therapy	2 (3.3)
Glucocorticoid therapy	34 (56.7)
Immunoglobulin therapy	28 (46.7)
Negative fluid balance	20 (33.3)
Oxygen support	4 (6.7)
Non-invasive mechanical ventilation	14 (23.3)
High-flow nasal cannula	15 (25.0)
High-flow nasal cannula combined with Non-invasive mechanical ventilation	6 (10.0)
Invasive mechanical ventilation	3 (5.0)
Interval from hospital admission to noninvasive mechanical ventilation, days, mean±SD	3.5 ± 3.8
Early prone ventilation	29 (48.3)
Continuous renal replacement therapy	2 (3.3)
Extracorporeal membrane oxygenation	1 (1.7)
Clinical outcomes	
Discharge	2 (3.3)
Improvement	50 (83.3)
Deterioration	8 (13.3)
Death	0 (0.0)

Data are expressed as number (%) unless otherwise specified.
Abbreviations: SD, standard deviation.

There was no significant difference between males and females in these severe cases. The median age of the patients was 57 years, and the proportion of patients over the age of 50 was 63.3%. The age distribution was similar to seasonal influenza.²⁸ The mean BMI of the severe patients was $25 \pm 3.3 \text{ kg/m}^2$, which was overweight. More than 90 percent of the patients had a history of contact with an infected patient or dined together, and 2 patients were infected while staying in the same train compartment with a confirmed patient. Our study provided further evidence for human-to-human

transmission and airborne transmission within a certain area. Recently, several studies²⁹ have confirmed that SARS-CoV-2 could also be detected in the gastrointestinal tract, saliva or urine, and proposed transmission by way of the digestive tract. The findings could provide useful evidence for curbing the rapid spread of the disease around the world.

The severe patients with COVID-19 infection usually presented with low fever (temperature $<38.5^\circ\text{C}$), dry cough and muscle soreness whereas gastrointestinal symptoms were rare, and 51.7% of the patients had at least 1 underlying disease, suggesting that the tropism of the virus was different from that of SARS-CoV, MERS-CoV and influenza.³⁰⁻³² For example, the symptoms of diarrhea occurred in only 6.7% of patients with COVID-19 infection, significantly less than that in SARS-CoV (38.4%)³² and MERS-CoV (26%)³⁰ infection. In addition, Yang Y et al¹⁹ demonstrated in their study that high fever (temperature $\geq 39^\circ\text{C}$), cough and sputum production at onset were the most common symptoms among patients with influenza A virus infection. The APACHE II score on admission were not high, and the illness progressed slowly, and ARDS appeared in 15% of the patients and secondary bacterial or fungal infections occurred in 6.7% of the patients, indicating a low fatality rate of the disease. Based on some published studies with a large sample and national official statistics, the cumulative mortality rate was 5.51% in China out of 84,237 confirmed cases as of April 20, 2020, lower than that of SARS-CoV, MERS-CoV and influenza.^{6,11,29}

Most patients had normal or low white blood cell count, low lymphocyte count, and less than 0.5 ng/mL of procalcitonin level. It also caused elevated levels of liver enzymes and troponin T. Lung imaging in most patients showed bilateral ground-glass lesions. These laboratory and radiological characteristics were similar to those of some recently published studies.^{14,29}

Patients with COVID-19 infection should also be followed up, in accordance with WHO guidelines for the early initiation of antiviral therapy for patients with influenza.³³ Due to the long incubation period of the disease, pneumonia patients with suspected COVID-19 infection could be given empirical antiviral treatment until COVID-19 infection was ruled out.¹⁹ All patients in this study were treated with antiviral drugs, including abidor, lopinavir and ritonavir, aerosol inhalation of interferon, ribavirin and oseltamivir. The mean course of antiviral was 10.9 ± 4.2 days. The protocol on antiviral drugs was based on the recommendation of the *Diagnosis and Treatment of Pneumonia Caused by Novel Coronavirus (Pilot Version 5)*²³ issued by the National health and fitness commission of China. We selected appropriate antiviral drugs according to the liver and kidney function of the patients. For example, the use of lopinavir and ritonavir should be avoided if the patient had a previous liver disease or abnormal liver function. Similarly, patients with renal dysfunction should avoid using the ribavirin. In terms of antibiotics, the above guidelines²³

TABLE 4. Univariate analysis of factors associated with prognosis among patients with COVID-19 infection.

Prognostic Factors	Patients (n = 60)		P value	OR (95% CI)
	Improvement (n = 52)	Deterioration (n = 8)		
BMI, kg/m ² , mean±SD	25.2 ± 3.4	23.7 ± 2.5	0.29	0.87 (0.68-1.12)
Preexisting conditions			0.40	1.94 (0.42-9.00)
Yes	24 (46.2)	5 (62.5)		
No	28 (53.8)	3 (37.5)		
APACHE II score on admission, mean±SD	13 ± 6	15 ± 6	0.85	1.02 (0.85-1.22)
White blood cell count, *10 ⁹ /L	4.7 ± 2.4	4.9 ± 2.5	0.66	1.08 (0.77-1.51)
Lymphocyte count, *10 ⁹ /L	0.9 ± 0.6	0.4 ± 0.2	0.01	0.11 (0.02-0.57)
Platelet count, *10 ⁹ /L	160 ± 55	133 ± 51	0.20	1.00 (0.98-1.01)
Troponin T, µg/L	7.6 ± 26.0	70.0 ± 12.7	0.04	1.04 (1.00-1.08)
Antiviral therapy with interferon	8 (15.4)	4 (50.0)	0.03	6.33 (1.18-33.98)
Glucocorticoid	27 (51.9)	7 (87.5)	0.09	6.48 (0.74-56.47)
Immunoglobulin therapy	22 (42.3)	6 (75.0)	0.10	4.09 (0.75-22.22)
Negative fluid balance	15 (28.8)	5 (62.5)	0.07	4.11 (0.87-19.41)
High-flow nasal cannula	14 (26.9)	1 (12.5)	0.40	0.39 (0.04-3.44)
Non-invasive mechanical ventilation	9 (17.3)	5 (62.5)	0.01	1.99 (1.17-3.41)
Interval from hospital admission to noninvasive mechanical ventilation, days, mean±SD	3.5 ± 4.2	3.4 ± 2.7	0.99	1.00 (0.78-1.29)
Early prone ventilation	28 (53.8)	1 (12.5)	0.04	0.11 (0.01-0.98)

Data are expressed as number (%) unless otherwise specified.
 Abbreviations: APACHE, acute physiology and chronic health evaluation; BMI, body mass index; CI, confidence interval; COVID-19, 2019 coronavirus disease; ICU, intensive care unit; OR, odds ratio; SD, standard deviation.

recommended avoiding blind or inappropriate use of antibiotics, especially in combination with broad-spectrum antibiotics. In our cohort, we mainly used a single fluoroquinolone to prevent secondary bacterial infections in severe patients. No significant adverse reactions were observed during antiviral and antibiotic therapy. Referring to the latest seventh edition of the *Diagnosis and Treatment of Pneumonia Caused by Novel Coronavirus*,³⁴ above antiviral drugs were still recommended,

while antiviral therapy of chloroquine phosphate was also recommended in the latest guidelines. However, the clinical efficacy of these antiviral and antibiotic treatments in patients is needed to be further studied in the future.

Early studies have shown that increased serum levels of pro-inflammatory cytokines (e.g., interleukin-1 beta, interferon γ, monocyte chemotactic protein 1 and inducible protein 10) in patients with COVID-19 infection were associated with pulmonary inflammatory responses and extensive lung injury.¹⁵ In consideration of the high amount of cytokines and inflammatory storm induced by COVID-19, GCs were frequently used to reduce inflammatory lung injury in patients with severe illness. The guidelines^{23,34} also recommended intravenous glucocorticoid therapy in the short term (3-5 days) for patients with an overactive inflammatory response to the body. In our study, 34 patients with COVID-19 infection, which had higher serum levels of interleukin-1 and interleukin-6, were treated with GCs. Four of 34 patients developed secondary infections, but there were no statistically significant differences between the improvement and deterioration subgroups. In our study, the effect of GCs was not significant. Furthermore, low lymphocyte count was found in most patients, nearly half of whom received intravenous immunoglobulin therapy in accordance with the advice of critical care specialists and guidelines, but the incidence of secondary infections was not significantly different between the 2 groups. Further larger sample size studies results are pending to provide more efficient evidence.

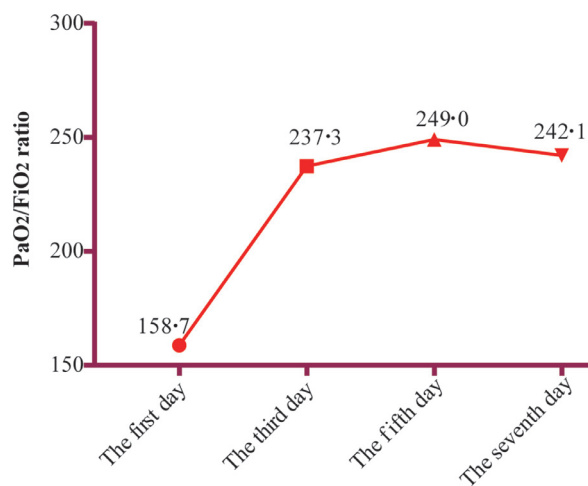


FIGURE 3. The tendency chart of patients' oxygenation index on the 1st, 3rd, 5th and 7th days after the prone ventilation.

Abbreviations: PaO₂, partial pressure of arterial oxygen; FiO₂, fraction of inspiration O₂.

The lung was an important target organ for COVID-19 viral infection, and severe infection could lead to hypoxemia and respiratory failure, even multiple organ dysfunction syndrome (MODS). The severity of hypoxemia assessed by the PaO₂/FiO₂ ratio was associated with mortality. Oxygen therapy was an important treatment measure to correct hypoxemia and avoid hypoxemia damage of vital organs. Having a full rest in the early stage may decrease oxygen consumption. In this group of cases, early and active oxygen therapy, including non-invasive mechanical ventilation, high-flow nasal cannula, and prone ventilation, maintaining PaO₂ above 60mmHg, and protecting important organs from hypoxemia were the key to effective treatment.

Our univariate analysis and logistic regression analysis demonstrated that early prone ventilation was significantly linked to an improvement of the disease. The mechanism of the improvement while ventilation under prone position reduces might due to the reduction/homogenization of lung stress/strain. However, higher levels of troponin T, lower lymphocyte count and antiviral therapy with aerosol inhalation of interferon were predictors of disease progression. Therefore, treatment of COVID-19 infection with aerosol inhalation of interferon was not recommended in this study. There were also significantly statistical differences in the application of noninvasive mechanical ventilation between the improvement and deterioration subgroups. It could be explained by the fact that most patients with disease progression received the therapy of noninvasive mechanical ventilation, but noninvasive mechanical ventilation did not improve the prognosis of severe patients. We hope that our findings can provide some reference experience and theoretical basis for the treatment of severe cases of COVID-19 in the global community.

Our study has some limitations. First, as an early report on a novel human infectious disease, this study only collected data of severe patients from 12 hospitals in Jiangsu Province, China, and the sample size was limited. Second, most of the patients still under hospitalization, the comparison between different prognostic subgroups might be biased. Moreover, it was likely that some patients did not receive confirmed diagnosis and/or systemic treatment leading to missing data. Finally, this is a retrospective study. We referred to internal and existing international guidelines for the diagnosis and treatment of COVID-19 infections.^{23,35} The data in this study permit a preliminary guidance of optimal management for critical patients with SARS-CoV-2 infection. Further studies are still needed.

CONCLUSIONS

The mortality rate for patients with severe COVID-19 infection in Jiangsu Province was 0%. The BMI of these patients was higher, with an average of 25 kg/m². It could spread rapidly by human-to-human transmission and airborne transmission within a certain

area, with a mean incubation period of 7.7 days. More than half of severe cases had at least one underlying disease, and low fever and dry cough were the most common symptoms. ARDS appeared in 15% patients. Antiviral therapy with aerosol inhalation of interferon was not recommended. The higher levels of troponin T and lower lymphocyte count were predictors of disease progression. While noninvasive mechanical ventilation did not improve the prognosis of patients, further analysis showed early prone ventilation appeared to be the effective approach to the treatment of COVID-19 pneumonia.

AUTHOR CONTRIBUTIONS

WW and CQ came up with the idea and design of the study, had full access to all data in the study and were responsible for the integrity and accuracy of the data. LL, HX, LA, ZH, GQ, SY, LJ, XX, LK and DY collected the epidemiological and clinical data. ZW contributed to the statistical analysis of the data. ZY and SF contributed to finish the first draft of the article. HM and YY contributed to further polish and revise the manuscript. All authors participated in the analysis or interpretation of the data, and reviewed and approved the final version.

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