

# Early and critical care in severe patients with COVID-19 infection in Jiangsu Province, China: a descriptive study

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## Research

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# Abstract

**Background:** Patients with coronavirus disease 2019 (COVID-19) infected by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) which originated in Wuhan, China, and spreading over the country including Jiangsu Province. Our study aimed to study the epidemiological, clinical characteristics and therapies of these severe cases in Jiangsu Province.

**Methods:** A multicenter retrospective cohort study was conducted to extract and analyze epidemiological, clinical, laboratory data and treatment of 60 severe cases with COVID-19 infection from 12 large hospitals in Jiangsu Province between Jan 24 and Feb 23, 2020. Cases were identified by real-time reverse transcription polymerase chain reaction (RT-PCR). The improvement and deterioration subgroups were compared to identify predictors of disease progression. Clinical outcomes were followed up until Feb 23, 2020.

**Results:** A total of 631 infected cases with COVID-19 in Jiangsu Province, 60 of which were severe cases. Up until Feb 23, 2020, the mortality rate of these severe patients was 0%. The median age was 57 years (range, 26 to 97), and 58.3% were man. The body mass index (BMI) of these patients was higher, with an average of 25 kg/m<sup>2</sup>. More than 90 percent of the patients had a history of contact with an infected patient or dined together, and two patients were infected while staying in the same train compartment with a confirmed patient. 51.7% of severe cases had at least one underlying disease, and low fever (80.0%) and dry cough (51.7%) were the most common symptoms. Mean acute physiology and chronic health evaluation (APACHE) II score on admission was 14±5. Acute respiratory distress syndrome (ARDS) appeared in 15% of the patients. 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 glucocorticoids therapy between the improvement and deterioration subgroups (P>0.05). 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 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:** The 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. Antiviral therapy with interferon was not recommended. The early prone ventilation may be an effective treatment for severe cases.

## Background

The coronavirus disease 2019 (COVID-19) was 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, of which 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 four continents in global.[4, 5] As of Feb 23, 2020, there were more than 77,000 cases with laboratory-confirmed COVID-19 infection, and over 2,400 deaths in China.[6] In addition, more than 1,400 cases had been confirmed and 11 deaths in 28 countries, including Japan, Singapore, Thailand, South Korea, Australia, USA, Canada, India and so on[7–11].

At present, several publications have described the epidemiological characteristics, clinical manifestations, clinical prognosis, genomics characteristics and antiviral treatment of COVID-19 infection cases.[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 not been reported. Up to Feb 23, 2020, a total of 631 cases were confirmed in Jiangsu Province, among there were 60 severe cases admitted to intensive care unit (ICU).<sup>6</sup> 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 Dec 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 Jan 24 and Feb 23, 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, BMI and exposure history), symptoms, underlying diseases, complications, incubation period, APACHE II score[20] 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 Feb 23, 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 were reviewed by a trained team of physicians.

The main end points were significant improvement or discharge, or deterioration by Feb 23, 2020. Since clinical observations are still ongoing and no patients have died, no fixed time horizon has been applied to these endpoints.

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 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 defined 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 requiring 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 ( $P_{aO_2}$ ) by the inspiratory oxygen fraction ( $F_{iO_2}$ ), and the normal value was between 400 and 500 mmHg.[24] The definition of ARDS referred to the Berlin diagnostic criteria[25]. The clinical outcomes included discharge from hospital, improvement, and deterioration. Improvement was defined as  $P_{aO_2}/F_{iO_2}$  ratio greater than 300 mmHg or transferred from ICU to 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  $P_{aO_2}/F_{iO_2}$  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  $\chi^2$  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 was used to identify the risk factors for disease deterioration. All statistical analyses were performed with the SPSS, version 20.0.

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This research was not funded. Corresponding authors had access to all the data in the study and are ultimately responsible for the decision to submit for publication.

## Results

### Demographic, and Baseline Characteristics

By Feb 23, 2020, 77,048 symptomatic patients had been confirmed with the COVID-19 infection in China, of which 631 confirmed patients in Jiangsu Province, China. Further study and analysis were conducted on 60 severe cases of 631 confirmed patients from 12 hospitals in Jiangsu Province (Fig. 1).

The demographic and clinical characteristics are shown in Table 1. The 60 confirmed severe cases were positive by real-time RT-PCR test of secretions from throat swabs. 35 (58.3%) were man; the median age of the patients was 57 years (range, 26 to 97); 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  $25 \pm 3.3$  kg/m<sup>2</sup>. 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  $7.7 \pm 3.9$  days.

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 <sup>2</sup> , 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 one 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)
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.	

Characteristics	Patients (n = 60)
Chronic obstructive pulmonary disease	2 (3.3)
Chronic kidney diseases	1 (1.7)
Pregnancy	1 (1.7)
Incubation period, days, mean $\pm$ SD	7.7 $\pm$ 3.9
APACHE II score on admission to ICU, mean $\pm$ SD	14 $\pm$ 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.	

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 temperature above 38.5 accounted for 6.7%, significantly less than those with temperature below 38.5. Thirty-one patients (51.7%) had at least one preexisting condition (i.e., hypertension, diabetes, autoimmune disease, stroke), including one pregnancy. Mean APACHE II score at admission was 14  $\pm$  5.

## 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 (50.0%) patients and decreased in 27 patients (45.0%); 38 (63.3%)

patients had lymphopenia. Only 8 (13.3%) patients occurred thrombocytopenia. 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  $34.7 \pm 5.1$  g/L. Lactate dehydrogenase was elevated in 48 (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 creatine kinas, creatine kinase isoenzyme and troponin T was documented in 30.0%, 26.7% and 31.7% of patients, respectively.

Table 2  
The Laboratory and Radiographic Findings of the 60 Severe Patients

Characteristics	Patients (n = 60)
Laboratory index	
White blood cell count, *10 <sup>9</sup> /L, normal range 4–10	
< 4	27 (45.0)
4–10	30 (50.0)
> 10	3 (5.0)
Lymphocyte count, *10 <sup>9</sup> /L, normal range 1.0-3.2	
< 1.0	38 (63.3)
≥ 1.0	22 (36.7)
Platelet count, *10 <sup>9</sup> /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	

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.

Characteristics	Patients (n = 60)
≤ 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.	

All patients had abnormal imaging presentations consistent with pneumonia. The most common pattern of chest CT was bilateral patchy shadows (85.0%). Figure 2 showed 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). Hospital-acquired infection 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 observed in 41 patients (68.3%).

Table 3  
The Complications, Treatments and Clinical Outcomes of the 60 Patients

	<b>Patients (n = 60)</b>
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 $\pm$ SD	10.9 $\pm$ 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)

Data are expressed as number (%) unless otherwise specified.

Abbreviations: SD, standard deviation.

	<b>Patients (n = 60)</b>
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 $\pm$ SD	3.5 $\pm$ 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.	

All patients received antiviral therapy. Abidor was given to 50 patients (83.3%), lopinavir and ritonavir to 41 (68.3%), interferon to 12 (20.0%), ribavirin to 7 (11.7%), and oseltamivir to 2 (3.3%). The mean course of antiviral was 10.9  $\pm$  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%) received intravenous glucocorticoid administration at doses ranging from 40 to 80 mg/d. Twenty-eight patients (46.7%) received immunoglobulin (IgG enriched) injections for a period of five to nine days immunoregulation. In addition, 20 patients (33.3%) were treated with negative fluid balance therapy.

For respiratory support, 14 patients (23.3%) received the non-invasive 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 (48.3%) patients were given early prone ventilation. The average time from admission to noninvasive mechanical ventilation was  $3.5 \pm 3.8$  days. In addition, two patients received continuous renal replacement therapy (CRRT) and one received extracorporeal membrane oxygenation (ECMO).

## Clinical Outcomes

As of Feb 23, 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 were shown in the last section of Table 3. Based on the clinical outcome, patients were assigned to 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 interferon. Also, this group had lower rates of the application of early prone ventilation and higher rates of non-invasive mechanical ventilation. There were no statistically significant differences between the two 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 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, wherea 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).

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 <sup>2</sup> , 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 <sup>3</sup> /L	4.7 ± 2.4	4.9 ± 2.5	0.66	1.08 (0.77–1.51)
Lymphocyte count, *10 <sup>3</sup> /L	0.9 ± 0.6	0.4 ± 0.2	0.01	0.11 (0.02–0.57)
Platelet count, *10 <sup>3</sup> /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)

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.

Prognostic Factors	Patients (n = 60)		P value	OR (95% CI)
	Improvement (n = 52)	Deterioration (n = 8)		
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.				

After the application of early prone position ventilation, the change trend of patients' oxygenation index (PaO<sub>2</sub>/FiO<sub>2</sub> ratio) on the first, third, fifth, and seventh days were shown in Fig. 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 Feb 23, 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.

There was no significant difference between male and female 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 ± 3.3 kg/m<sup>2</sup>, which was overweight. More than 90 percent of the patients had a history of contact with an

infected patient or dined together, and two 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 studies[29] have confirmed that SARS-CoV-2 could also be detected in gastrointestinal tract, saliva or urine, and proposed the transmission way of 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, dry cough and muscle soreness whereas gastrointestinal symptoms were rare, and more than 50% of the patients had at least one underlying disease, suggesting that the tropism of the virus was different from that of SARS-CoV, MERS-CoV and influenza[30–32]. The APACHE II score on admission was 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 3.17% in China out of 77,048 confirmed cases as of Feb 23, 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 radiologic characteristics were similar to those of some recently published studies.[14, 29]

At present, the commonly used antiviral drugs are abidor, lopinavir and ritonavir tablets, interferon and so on, among which the most commonly used is abidor in Jiangsu Province, China. Patients with COVID-19 infection should also be followed up, in accordance with WHO guidelines about 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] In our study, all severe patients were treated with antiviral therapy. In terms of antibiotics, blind or inappropriate use of antibiotics should be avoided, especially in combination with broad-spectrum antibiotics. In our cohort, we mainly used a single fluoroquinolone to prevent secondary bacterial infections in severe patients.

Early studies have shown that increased serum levels of pro-inflammatory cytokines (e.g., interleukin-1 beta, interferon  $\gamma$ , 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, glucocorticoids were frequently used to reduce inflammatory lung injury in patients with severe illness. In our study, 34 patients with COVID-19 infection were treated with glucocorticoids. All 4 patients who developed secondary infections were received glucocorticoids, although there were no statistically significant differences between the improvement and deterioration subgroups. In our study, the effect of glucocorticoids was not significant. Furthermore, low lymphocyte count were found in most patients and

nearly half of them were treated with intravenous immunoglobulin, but the incidence of secondary infections did not show significance between the two groups as well. Further larger sample size studies results are pending to provide more efficient evidence.

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  $\text{PaO}_2/\text{FiO}_2$  ratio was associated with mortality. Oxygen therapy to correct hypoxemia and avoid hypoxemia damage of vital organs was an important treatment measure. Having a full rest in early stage may decrease oxygen consumption. In this group of cases, through early and active oxygen therapy, including non-invasive mechanical ventilation, high-flow nasal cannula, and prone ventilation were performed early, keeping  $\text{PaO}_2$  above 60 mmHg, protecting important organs from hypoxemia are 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 interferon were predictors of disease progression. Therefore, the treatment of COVID-19 infection with interferon was not recommended in this study. There were also significant statistical differences in the application of non-invasive 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 non-invasive mechanical ventilation, but non-invasive 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, 34]. 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 severe patients with COVID-19 infection in Jiangsu Province was 0%. The BMI of these patients was higher, with an average of 25 kg/m<sup>2</sup>. More than half of severe cases had at least one underlying disease. ARDS appeared in 15% patients. Antiviral therapy with interferon was not recommended. The higher levels of troponin T and lower lymphocyte count were predictors of disease progression. While non-invasive mechanical ventilation did not improve the prognosis of patients, further

analysis showed with early prone ventilation method appeared to be the effective approach to the treatment of COVID-19 pneumonia. Further research will be needed to verify the significance of these results in clinical practice.

## **Declarations**

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### **Promotion**

None

### **Authors' contributions**

WW and CQ came up with the idea and design of the study, which 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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None

### **Availability of data and materials**

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

### **Ethics approval and consent to participate**

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.

### **Declaration of interests**

The authors declare no financial conflicts of interest.

### **Consent for publication**

Each patient gave written informed consent for their data to be used for research and publication.

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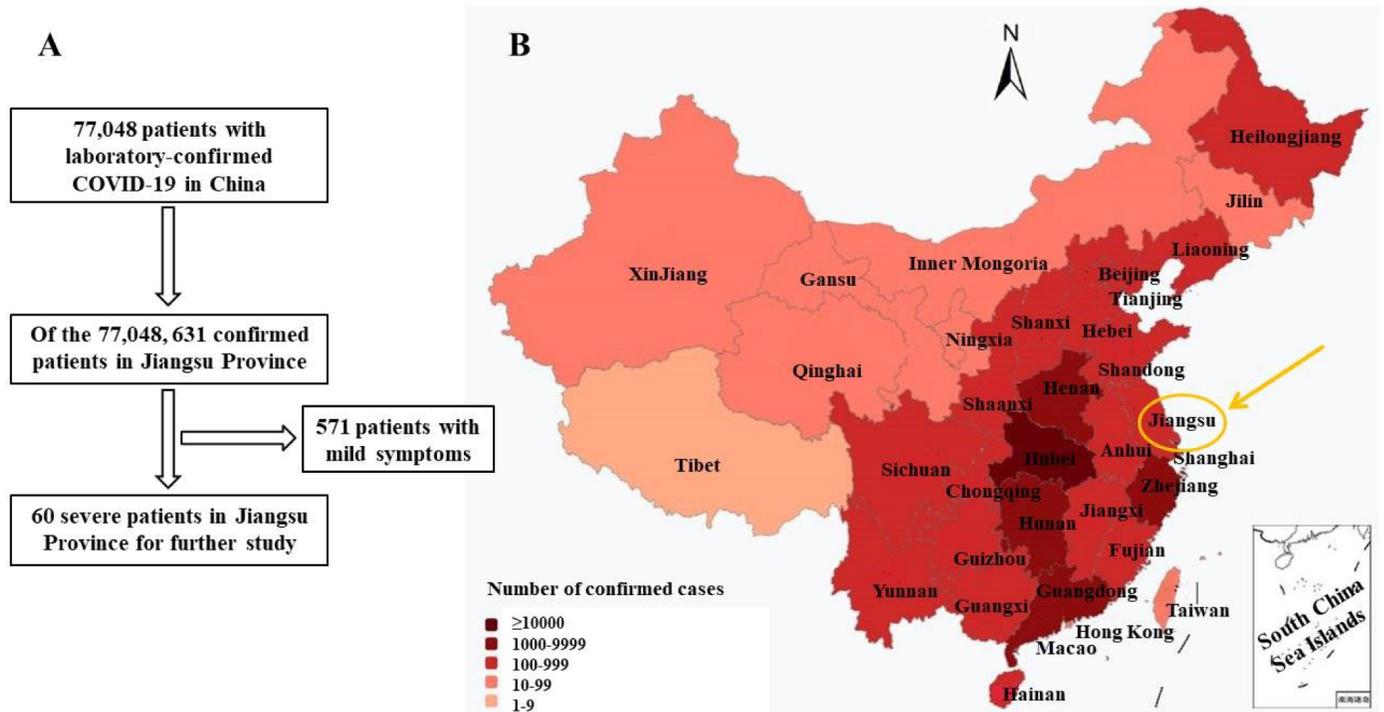
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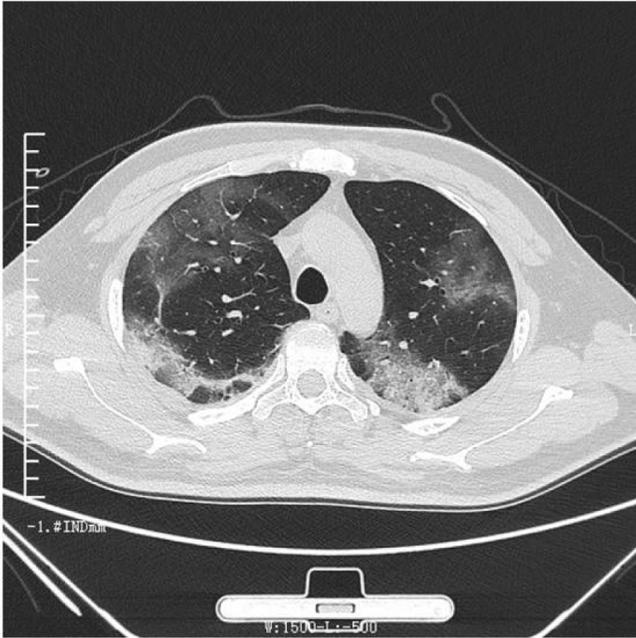
## Figures



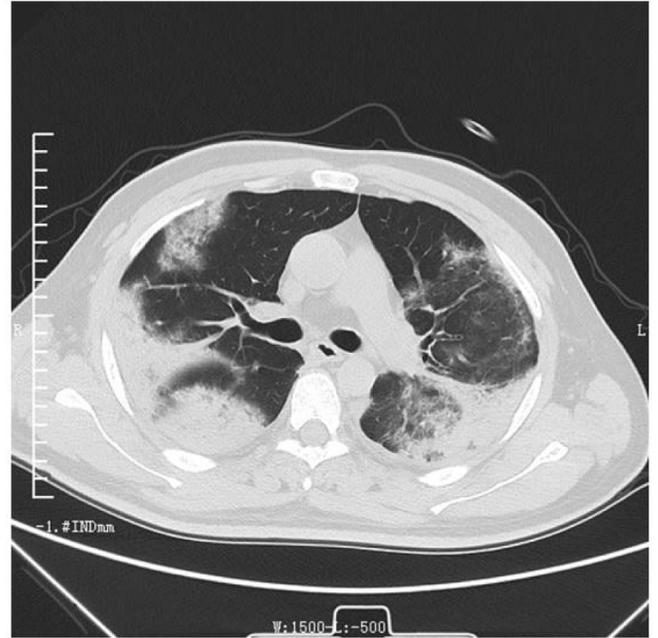
**Figure 1**

Patient recruitment flow chart and patient distribution across China A: Patient recruitment flowchart; B: The distribution of laboratory-confirmed cases throughout China; Shown are the official statistics of all documented laboratory-confirmed cases throughout China according to the National Health Commission (as of February 23, 2020). Note: The designations employed and the presentation of the material on this map do not imply the expression of any opinion whatsoever on the part of Research Square concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. This map has been provided by the authors.

**A**      **The early stage**

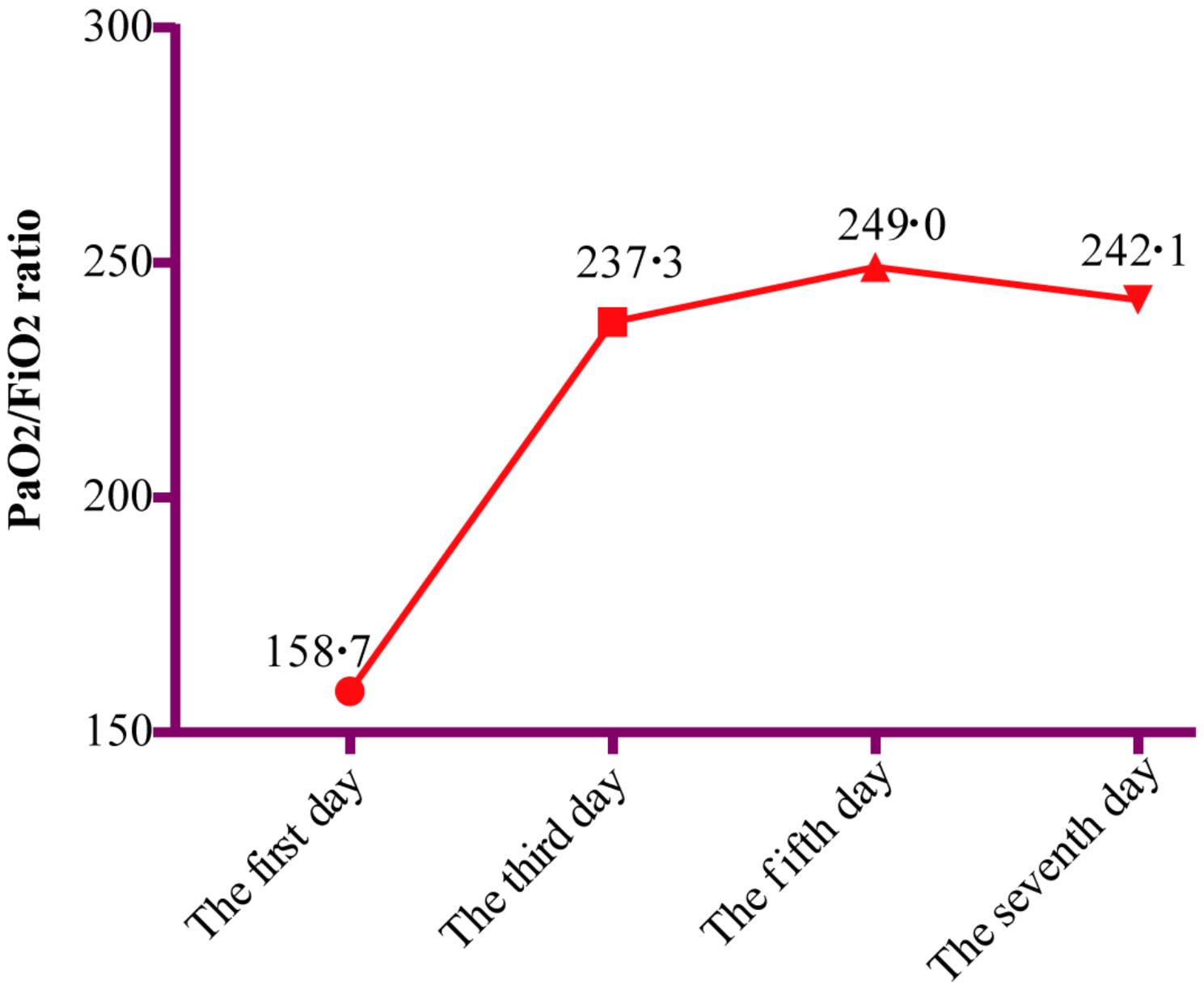


**B**      **The deterioration stage**



**Figure 2**

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



**Figure 3**

The tendency chart of patients' oxygenation index on the 1st, 3rd, 5th, and 7th days after the prone ventilation. PaO<sub>2</sub>, partial pressure of arterial oxygen; FiO<sub>2</sub>, fraction of inspiration O<sub>2</sub>