Analysis of Clinical Characteristics of Patients with Critical COVID-19

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Research

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Abstract

Background: According to the data from the joint investigative team of the WHO and China, the fatality rate in Wuhan is 5.8%and 0.7% in the rest of China. Most of the patients who have died have had chronic diseases or advanced age, and patients with critical COVID-19 have the highest death rate. Patients with critical COVID-19 are the main focus of research on treatment. However, there are few reports on critical COVID-19 patients in China and worldwide. It will help other researchers and clinicians around the world for similar cases.

Purpose: Coronavirus disease 2019 (COVID-19) is highly infectious and has a high fatality rate.This paper summarizes and analyses the clinical characteristics of patients with critical COVID-19 to improve clinicians' understanding of this disease.

Methods: We selected 16 patients with critical COVID-19 who were treated in the ICU of a grade A hospital in Wuhan from February to March 2020. Then, we collected the clinical data and analysed their general conditions, clinical symptoms, blood tests, CT scans and treatments.

Results: Patients with critical COVID-19 had comorbidities (87.5%), and the main symptoms were low or moderate fever (75%), cough and expectoration (68.75%), and multiple lesions in both lungs (100%). 2. Patients with critical COVID-19 were divided into the non-surviving and surviving groups, and the interleukin-6 (IL-6) level and CD4/CD8 ratio were significantly different ($P<0.05$). 3. On chest CT, multiple patchy lesions were observed in both lungs, mainly as patchy infected lesions, partial consolidation, ground-glass opacities, and interstitial changes. 4. There were 10 patients (62.5%) who survived and 6 (37.5%) who died.

Conclusion: Critical COVID-19 is mainly characterized by low or moderate fever, cough and sputum and often occurs in people with chronic disease.Chest CT showed multiple patchy ground-glass opacities and consolidation. For critically ill patients, it is important to monitor interleukin-6 (IL-6) and CD4/CD8 ratio. Early treatment involves thymalfasin, immunoglobulin and other immune-enhancing treatments, and a large dose of ulinastatin can reduce plasma levels of inflammatory factors.

Background

In December 2019, the first case of pneumonia of unknown cause was found in the South China Seafood Wholesale Market in Wuhan, which was finally confirmed to be an acute respiratory infectious disease caused by a novel coronavirus named SARS-CoV-2. In February 2020, the WHO named the disease coronavirus disease 2019 (COVID-19) [1,2]. COVID-19 quickly spread throughout the country. Through a series of preventive measures, the outbreak in China has been effectively controlled, but the foreign epidemic is still not under control. As of August 28, 2020, 24664109 patients had been confirmed overseas, including a total of 45,068 deaths, and the number of confirmed patients and deaths is still increasing. According to the data from the joint investigative team of the WHO and China, the fatality rate in Wuhan is 5.8%and 0.7% in the rest of China. Most of the patients who have died have had chronic diseases or advanced age, and patients with critical COVID-19 have the highest death rate[3]. Patients with critical COVID-19 are the main focus of research on treatment. However, there are few reports on critical COVID-19 patients in China and worldwide. This paper analyses the clinical characteristics of critical COVID-19 patients admitted to the intensive care unit of a grade A hospital in Wuhan and discusses the changes in levels of indicators and their clinical significance.

Information And Methods

Research objects: According to the Diagnosis and Treatment of Novel Coronavirus Pneumonia (seventh trial version) published by the Chinese government, a suspected case met one of the following criteria: 1. nasopharyngeal swab,

sputum, lower respiratory tract secretion, blood, stool or other specimen tested positive for COVID-19 nucleic acid by real-time fluorescence RT-PCR; 2. viral gene sequencing showed a high degree of homology with SARS-CoV-2. Serum samples tested positive for SARS-CoV-2-specific IgM and IgG antibodies; serum SARS-CoV-2-specific IgG antibody conversion, or a 4-fold reduction in titres. We collected a total of 16 patients with critical COVID-19 admitted to the intensive care unit of a grade A hospital in Wuhan from 1st February to 25th March 2020. The clinical classification of disease severity stipulates that patients with critical COVID-19 meet one of the following conditions: 1. respiratory failure requiring mechanical ventilation; 2. shock; or 3. organ failure requiring ICU care. This study was approved by the Ethics Commission of The Central Hospital of Wuhan. Written informed consent was waived by the Ethics Commission of the designated hospital for emerging infectious diseases.

Detection method

Patients were divided into the non-surviving group and the surviving group, and their general conditions, clinical symptoms, blood tests, CT imaging characteristics, the changes in each indicator and the relationship between the indicators and critical COVID-19 were compared.

Statistical processing

SPSS 22.0 software was used, and the measurement data with a normal distribution are expressed as the mean ± SD. The t-test was used for the comparison of the mean values of the two groups, and the variance test was used for the comparison of the mean values of more than two samples. $P < 0.05$ was considered statistically significant.

Results

General characteristics

There were 16 patients with critical COVID-19. Their ages ranged from 48 to 93 years, with a median age of 68 years; 11 were male (68.75%), and 5 were female (31.25%). All were local residents in Wuhan with a history of contact with an infected person (100%). There were 14 patients with chronic diseases (87.5%), 5 patients had hypertension (31.25%), 2 patients had diabetes (12.5%), 1 patient had a malignant tumour (6.25%), and 2 patients had chronic kidney disease (12.5%).

Clinical Characteristics

Among the 16 patients critical COVID-19, 12 had fever (75%) (37.4–38 °C, 5 patients; 38.1–39 °C, 6 patients; 39.1 °C, 1 patient), 11 had cough (68.75%), 4 had dyspnoea (25%), 2 had fatigue and muscle aches (12.5%), 3 patients had disordered consciousness (18.75%) and 1 had diarrhoea (6.25%). The main sign was an increased respiratory rate (> 24 breaths/min) in 16 patients (100%).

Laboratory Tests

The total number of peripheral blood white blood cells was elevated in 5 patients (31.25%) and decreased in 4 patients (25%), while 7 patients had normal white blood cell counts (43.75%). The lymphocyte count was reduced in 14 patients (87.5%) and normal in 2 patients (12.5%). The C-reactive protein level was elevated in 5 patients (31.25%), and the procalcitonin level was elevated in 5 patients (31.25%). The 16 patients were divided into the non-surviving group (6 patients, 37.5%) and the surviving group (10 patients, 62.5%). There were statistically significant differences between the non-surviving group and surviving group in the interleukin-6 level and CD4/CD8 ratio ($P < 0.05$), suggesting that the

interleukin-6 level and the CD4/CD8 ratio may affect the prognosis of patients. The results of the statistical analysis suggest that the higher the level of interleukin-6 is, the lower the CD4/CD8 ratio and the worse the prognosis (Table 1).

Table 1
Analysis of patients in the surviving and non-surviving groups (mean ± SD)

Parameters	Surviving group	Non-surviving group	T value	P value
Procalcitonin	0.64 ± 1.26	5.59 ± 12.69	-0.953	0.384
Hs-CRP	5.69 ± 4.10	10.57 ± 5.33	-2.066	0.058
Leucocyte	5.62 ± 3.20	12.51 ± 9.01	-1.806	0.123
Lymphocyte	0.12 ± 0.13	0.08 ± 0.08	0.707	0.491
Interleukin- 6	26.12 ± 26.71	216.00 ± 109.49	-4.174	0.007**
CD4/CD8	1.84 ± 1.02	0.79 ± 0.18	3.165	0.010*
pH	7.46 ± 0.05	7.43 ± 0.05	1.058	0.308
Oxygen partial pressure	119.70 ± 74.68	121.33 ± 48.94	-0.047	0.963
Partial pressure of carbon dioxide	36.80 ± 6.96	35.50 ± 12.47	0.270	0.791
Lactate	0 1.82 ± 1.19	2.85 ± 2.12	-1.255	0.230
NLR	49.41 ± 73.40	23.26 ± 20.81	1.058	0.312
Notice: hs-CRP: high-sensitivity C-reactive protein; * $p < 0.05$; ** $p < 0.01$				

Chest Ct

The 16 critical COVID-19 patients had CT imaging findings indicative of pneumonia, with multiple lesions in the bilateral lungs. The CT characteristics of each group of patients were compared. The findings of the first chest CT after admission in the non-surviving group and surviving group are summarized below (Fig. 1). In the non-surviving group (A-B), CT imaging showed multiple patchy, flaky lesions in the bilateral lungs, with partial consolidation, merging, ground-glass opacities, and interstitial changes. The CT imaging of the surviving group (C-D) were characterized by multiple patchy lesions in both lungs, with ground-glass opacities and interstitial changes but no consolidation.

A (Non-surviving group**) B (**Non-surviving group**)**

C (Surviving group**) D (**Surviving group**)**

Figure 1. A-B are the results of chest CT examinations of a nonsurviving patient, which show multiple patchy lung lesions, mainly patchy infectious lesions, consolidation of the bilateral lower lungs, and scattered ground-glass opacification indicative of the formation of a hyaline membrane in the bilateral lungs. **C-D** show the results of a patient who survived. The patient was discharged from the hospital. The CT images were characterized by multiple patchy lesions in both lungs, with the majority being patchy infectious lesions, but consolidation was not obvious.

Treatment And Prognosis

All 16 patients (100%) were treated with anti-microbials (meropenem, piperacillin sulbactam, moxifloxacin, etc.), anti-virals (alpha interferon, Arbidol, ribavirin, etc.), and traditional Chinese medicine decoctions. Five patients (31.25%) were

treated with thymalfasin 1.6 mg twice a week for 1 month. Four patients (25%) were given 5% immunoglobulin injections with 100-ml intravenous infusion for 5–7 days. Five patients (31.25%) were given 5% human albumin by intravenous drip (10 mg) daily for 3–7 days. Four (25%) patients with extensive ground-glass opacities in both lungs and fever received methylprednisolone treatment (20 or 40 mg intravenous drip, 2 times/day for 3–10 days). All 16 (100%) patients were treated with high nasal flow humidification due to aggravated shortness of breath and decreased blood oxygen saturation levels. Four patients (25%) were treated with continuous renal replacement therapy (CRRT) due to severe infection and renal dysfunction. Due to poor therapeutic effects, 7 patients were treated with endotracheal intubation and invasive ventilation. One patient was treated with percutaneous tracheotomy due to a long invasive ventilation time. One patient with a concurrent fungal infection was treated with antifungal therapy. There were 10 patients (62.5%) who survived and 6 patients (37.5%) who died. Five of the 6 patients with chronic diseases died of Type I respiratory failure (Table 2).

Table 2
Treatment and prognosis of 16 patients.

Number	Age (years)	Sex	Chronic diseases	Specific treatments	Specific medicines	Complications	Cause of death
1	84	Female	Coronary heart disease, renal insufficiency	HFNC	Albumin, immunoglobulin, thymalfasin	Type I respiratory failure	Respiratory failure
2	62	Male	Hypertension, chronic renal failure	CRRT, HFNC, invasive ventilation	Methylprednisolone, albumin, immunoglobulin	Type I respiratory failure	Respiratory failure
3	43	Male	None	CRRT, HFNC, invasive ventilation	Methylprednisolone, albumin, immunoglobulin	Type I respiratory failure	Respiratory failure
4	70	Male	Rheumatoid arthritis	HFNC	Albumin, thymalfasin	Type I respiratory failure	Respiratory failure
5	90	Male	COPD, lobe placeholder	HFNC, invasive ventilation	Methylprednisolone, albumin, immunoglobulin	Type I respiratory failure	Respiratory failure
6	93	Female	Coronary heart disease, hypertension	HFNC	/	Type I respiratory failure	Respiratory failure
7	59	Male	Diabetes, remote cerebral infarction	HFNC, CRRT, invasive ventilation	Methylprednisolone	Type I respiratory failure	/
8	83	Female	Diabetes, hypertension, coronary heart disease	HFNC	/	Type I respiratory failure	/
9	61	Male	None	HFNC, CRRT	/	Type I respiratory failure	/
10	77	Male	Cerebral infarction	HFNC	Thymalfasin	Type I respiratory failure	/
11	70	Female	Atrial fibrillation	HFNC	/	Type I respiratory failure	/
12	62	Male	Chronic bronchitis	HFNC	Thymalfasin	Type I respiratory failure	/
13	48	Female	Hypertension, coronary heart disease	HFNC	/	Type I respiratory failure	/

Note: 1–6 belong to the non-surviving group; 7–16 belong to the surviving group; HFNC: high-flow nasal cannula oxygen therapy; COPD: chronic obstructive pulmonary disease.

Number	Age (years)	Sex	Chronic diseases	Specific treatments	Specific medicines	Complications	Cause of death
14	65	Male	Hypertension, coronary heart disease	HFNC	/	Type I respiratory failure	/
15	53	Male	Right renal tumour resection, duodenal ulcer	HFNC	/	Type I respiratory failure	/
16	68	Female	Hypertension	HFNC	Thymalfasin	Type I respiratory failure	/

Note: 1–6 belong to the non-surviving group; 7–16 belong to the surviving group; HFNC: high-flow nasal cannula oxygen therapy; COPD: chronic obstructive pulmonary disease.

Discussion

Coronaviruses are enveloped positive-stranded RNA viruses that are named for their characteristic crown-like appearance on electron micrographs[4]. According to the Diagnosis and Treatment of Novel Coronavirus Pneumonia (seventh trial version) published by the Chinese government, COVID-19 can be classified as mild, moderate, severe and critical [5]. Of the approximately 44,500 confirmed infections with estimates disease severity, 81% have been mild and moderate, 14% have been severe and 5% have been critical, according to a report by the Chinese Center for Disease Control and Prevention[6]. Since COVID-19 is highly infectious, spreads rapidly, and has a high fatality rate, and since there is no effective vaccine and drug to prevent or cure it, a small number of patients rapidly progress to the critical type or even die. Therefore, it is very important to study the clinical characteristics of patients with critical COVID-19 in depth.

At present, there are few clinical studies on patients with critical COVID-19. Studies show that compared with mild COVID-19 patients, severe or critical COVID-19 patients are older, have more complications and have higher incidences of cough, sputum, chest pain and dyspnoea[7,8]. The results of this study are similar to those of previous studies, but there are some differences. We analysed the clinical characteristics of 16 patients with critical COVID-19: 1. The clinical characteristics are mainly fever, cough, dyspnoea, and chest CT abnormalities[7,9–12]. There were 12 patients with fever among the 16 patients with critical COVID-19, including 5 patients with low fevers, 6 patients with moderate fevers, and 1 patient with a high fever. Patients with critical COVID-19 generally had a fever, but it was usually a low- or moderate-grade fever, which may be related to their reduced immunity. 2. The chest CT manifestations of patients with critical COVID-19 are multiple patchy ground-glass opacities; multiple patchy, flaky infectious lesions; partial consolidation; merging; and interstitial changes. The results of this study suggest that consolidation indicates a relatively worse prognosis, but this need to be confirmed in a large sample. Patients with critical COVID-19 may exhibit leucopenia, leucocytosis and lymphocytopenia[13]; a reduced lymphocyte count and elevated levels of inflammatory markers are risk factors for a poor prognosis [8]. In the 6 patients who died in this study, the lymphocyte counts were significantly reduced, the levels of IL-6 reached more than 140 pg/ml, and the CD4/CD8 ratios were significantly reduced. Even when immunoglobulin, thymalfasin and other treatments that regulate the immune system are adopted, the mortality of the patients is still high, which may be related to the late initiation of immunoregulatory therapy. In addition, large doses of a broad-spectrum protease inhibitor (ulinastatin) have been shown to reduce the plasma levels of the inflammatory factor IL-6 and increase the levels of the anti-inflammatory factor IL-10[14]; therefore, large doses can be considered for critical COVID-19 patients.

At present, there are no specific antiviral drugs for COVID-19, and treatment is mainly nutritional support, immune regulation and other symptomatic support therapies. Previous studies have shown that dot-interferon can be tried (5 million U or the equivalent dose for adults, atomized inhalation twice a day). Chloroquine phosphate (referred to as 'chloroquine') has a wide range of general antiviral and specific anti-coronavirus effects and can improve the treatment success rate of patients with COVID-19, shorten the length of hospital stay and improve the prognosis[5,15,16]. Remdesivir is a novel nucleotide analogue, and its anti-coronavirus activity has been demonstrated in vitro[17,18]. Lopinavir/ritonavir also has anti-coronavirus activity in vitro[19]. Plasma from recovering patients may contain antibodies that neutralize the virus, and there is evidence of that treating patients with antibodies from recovering patients is effective [20,21]. Tian et al. found that a specific human monoclonal antibody against SARS-CoV is a potential candidate for the treatment of COVID-19[22]. Based on the latest clinical standards[5], two types of antiviral drugs can be used at the same time. The patients in the study mainly received Arbidol and interferon; chloroquine, remdesivir, lopinavir/ritonavir, antibodies, monoclonal antibodies and dual antiviral therapy were less frequently used. Even these treatments are insufficient, and their efficacy and safety need to be determined in further clinical trials. Previous studies have linked glucocorticoids to an increased risk of mortality in influenza patients, and although they have been widely used to treat SARS, there is insufficient evidence of their efficiency against COVID-19; some results have shown that patients have short-term and long-term adverse reactions[23]. The WHO and the CDC in the US do not recommend glucocorticoid treatment for COVID-19, except for in patients with other indications such as the acute exacerbation of chronic obstructive pulmonary disease[13,24]. For patients with critical COVID-19, glucocorticoids can be used in the short term based on the individual patient's condition[5]. In this study, 4 patients took methylprednisolone, but no obvious treatment effect was observed, so it is not recommended to use the hormone routinely. Chinese medicine has always played an important role in the treatment of infectious diseases, and the National Health Commission recommended it for the treatment of COVID-19[5]. All 16 patients in this study were routinely treated with Chinese medicine.

Due to the critical condition of patients in the ICU, their ability to cough up phlegm is reduced, resulting in airway obstruction, impaired breathing, aggravation of the pulmonary infection, atelectasis and other complications. In addition, due to the influence and limitation of various monitoring channels, it is challenging to routinely turn patients over and actively assist the patient to produce phlegm; instead, it is necessary to rely on passive sputum aspiration to remove secretions in a timely manner. On 28th February, Gross Examination Report of a Covid-19 Death Autopsy suggested that a large number of viscous secretions could be seen in the lung tissue, and there were fibrous cords. COVID-19 mainly causes inflammatory responses characterized by deep airway and alveolar injury[25]. In this study, 6 patients with critical COVID-19 did not survive, and they all had serious Type I respiratory failure. Based on the current pathological and anatomical data and given the possibility of airway obstruction by mucus and the later fibrotic changes in the lung tissue, the management of airway humidity and sputum drainage should be strengthened. In this study, 6 of the 16 patients with critical COVID-19 died, and 5 of them had chronic diseases, with a mortality rate of 37.5%. In addition to chronic diseases and complications of COVID-19, mortality may be related to the lack of human resources, airway humidification and sputum drainage. We modified the treatment of our patients based on these clinical observations, and the mortality rate was significantly reduced, suggesting that strengthening airway humidification and sputum drainage, facilitating expectoration, and reducing the exudation of airway secretions could reduce the mortality rate of COVID-19 patients.

Conclusion

This novel coronavirus is different from HCoV-229E, HCoV-NL63, HCoV-HKU1, HCoV-OC43, MERS-CoV and SARS-CoV, and there are no specific antiviral treatments. Critical COVID-19 is characterized by low and moderate fever. Chest CT indicated multiple patchy lesions in both lungs, mainly characterized by patchy infectious lesions, partial consolidation,

ground-glass opacities and interstitial changes. Consolidation on imaging may indicate a poor prognosis. Currently, treatment involves supportive therapies, antiviral treatments, antibodies from surviving patients, monoclonal antibodies, and traditional Chinese medicine treatment. The routine use of hormone therapy is not recommended. It is important to monitor IL-6 level and CD4/CD8 ratio. Early treatment with thymalfasin, immunomodulatory treatment with immunoglobulin, and treatment with a large dose of ulinastatin to reduce the plasma levels of inflammatory factors should be considered. Attention should be paid to ensuring airway humidification and drainage, enhancing expectoration, and reducing airway secretions. Although the sample size is very small for this study, authors explained the clinical symptom in critical patient. It will help other researchers and clinicians around the world for similar cases.

Declarations

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Ethics approval and consent to participate

The study was approved by local Ethics Committee, and informed consent was obtained by enrolled patients according to committee recommendation.

Consent for publication

Not applicable

Availability of data and materials

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

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

Qiquan Zhao, Li Jian and Yuguo Zhou equally to this article as Co-first authors. Fengying Peng and Bei Jia equally to this article as Co-coressponding authors. Qiquan Zhao designed the study, gathered and analyzed data, performed statistical analysis, wrote the manuscript, and are responsible for the integrity of the work as a whole. Li Jian and Yuguo Zhou gathered data and revised the manuscript for critical intellectual content. Fengying Peng and Bei Jia analyzed data and revised the manuscript for critical intellectual content. All authors read and approved the final manuscript.

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References

1. World Health Organization. Director-General's remarks at the media briefing on 2019-nCoV on 11 February 2020.https://www.who.int/dg/speeches/detail/who-director-general-s-remarks-at-the-media-briefing-on-2019-ncov-on-11-february-2020 (Accessed on February 12, 2020).
2. Zhu Naiwei ZP, Zhongtian Q. Current status of treatment for 2019 novel coronavirus pneumonia. *Chin J Microbiol Immunol*. 2020;40(1):7–10.
3. Report of the WHO-China Joint Mission on Coronavirus DIsease 2019 (COVID-2019). February 16–24, 2020. http://www.who.int/docs/default-source/coronaviruse/who-china-joint-mission-on-covid-19-final-report.pdf (Accessed on March 04, 2020).
4. International Committee on Taxonomy of Viruses. http://ictvonline.org/virusTaxonomy.asp (Accessed on May 21, 2015).
5. The Diagnosis and Treatment of Novel Coronavirus Pneumonia (seventh trial version) published by the Chinese government. 2020.
6. Lauer SA, Grantz KH, Bi Q, et al. The Incubation Period of Coronavirus Disease 2019 (COVID-19) From Publicly Reported Confirmed Cases: Estimation and Application. *Ann Intern Med*. 2020.
7. Guan WJ, Ni ZY, Hu Y, et al. Clinical Characteristics of Coronavirus Disease 2019 in China. *N Engl J Med*. 2020.
8. Li K, Wu J, Wu F, et al. The Clinical and Chest CT Features Associated with Severe and Critical COVID-19 Pneumonia. *Invest Radiol*. 2020.
9. Chen N, Zhou M, Dong X, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. *Lancet*. 2020;395(10223):507–513.
10. Huang C, Wang Y, Li X, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *Lancet*. 2020;395(10223):497–506.
11. McIntosh K, Dees JH, Becker WB, Kapikian AZ, Chanock RM. Recovery in tracheal organ cultures of novel viruses from patients with respiratory disease. *Proc Natl Acad Sci U S A*. 1967;57(4):933–940.
12. Wang D, Hu B, Hu C, et al. Clinical Characteristics of 138 Hospitalized Patients With 2019 Novel Coronavirus-Infected Pneumonia in Wuhan, China. *JAMA*. 2020.

13. Centers for Disease Control and Prevention. Interim Clinical Guidance for Management of Patients with Confirmed 2019 Novel Coronavirus (2019-nCoV) Infection, Updated February 12, 2020.https://www.cdc.gov/coronavirus/2019-ncov/hcp/clinical-guidance-management-patients.html (Accessed on February 14, 2020).
14. Karnad DR, Bhadade R, Verma PK, et al. Intravenous administration of ulinastatin (human urinary trypsin inhibitor) in severe sepsis: a multicenter randomized controlled study. *Intensive Care Med*. 2014;40(6):830–838.
15. Colson P, Rolain JM, Lagier JC, Brouqui P, Raoult D. Chloroquine and hydroxychloroquine as available weapons to fight COVID-19. *Int J Antimicrob Agents*. 2020:105932.
16. Gao J, Tian Z, Yang X. Breakthrough: Chloroquine phosphate has shown apparent efficacy in treatment of COVID-19 associated pneumonia in clinical studies. *Biosci Trends*. 2020;14(1):72–73.
17. Wang M, Cao R, Zhang L, et al. Remdesivir and chloroquine effectively inhibit the recently emerged novel coronavirus (2019-nCoV) in vitro. *Cell Res*. 2020;30(3):269–271.
18. Wang Y, Liu Y, Liu L, Wang X, Luo N, Ling L. Clinical outcome of 55 asymptomatic cases at the time of hospital admission infected with SARS-Coronavirus-2 in Shenzhen, China. *J Infect Dis*. 2020.
19. Chang, Lin M, Wei L, et al. Epidemiologic and Clinical Characteristics of Novel Coronavirus Infections Involving 13 Patients Outside Wuhan, China. *JAMA*. 2020.
20. Mair-Jenkins J, Saavedra-Campos M, Baillie JK, et al. The effectiveness of convalescent plasma and hyperimmune immunoglobulin for the treatment of severe acute respiratory infections of viral etiology: a systematic review and exploratory meta-analysis. J Infect Dis. 2015;211(1):80–90.
21. Marano G, Vaglio S, Pupella S, et al. Convalescent plasma: new evidence for an old therapeutic tool. *Blood Transfus*. 2016;14(2):152–157.
22. Tian X, Li C, Huang A, et al. Potent binding of 2019 novel coronavirus spike protein by a SARS coronavirus-specific human monoclonal antibody. *Emerg Microbes Infect*. 2020;9(1):382–385.
23. Russell CD, Millar JE, Baillie JK. Clinical evidence does not support corticosteroid treatment for 2019-nCoV lung injury. *Lancet*. 2020;395(10223):473–475.
24. World Health Organization. Novel Coronavirus (2019-nCoV) technical guidance: Patient management. https://www.who.int/emergencies/diseases/novel-coronavirus-2019/technical-guidance/patient-management (Accessed on February 02, 2020).
25. Qian Liu RW, Guoqiang Qu ea. Autopsy report of Patients with COVID-19. *Journal of Forensic Medcine*. 2020.

Figures

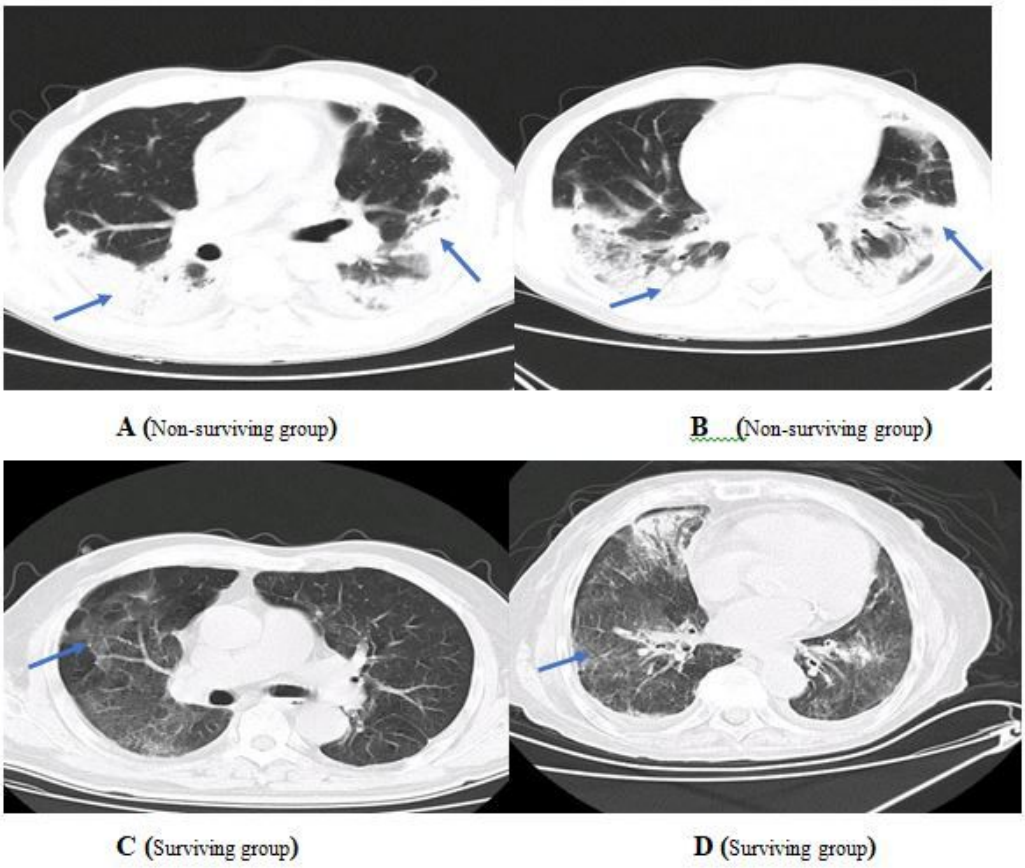

Figure 1

A-B are the results of chest CT examinations of a nonsurviving patient, which show multiple patchy lung lesions, mainly patchy infectious lesions, consolidation of the bilateral lower lungs, and scattered ground-glass opacification indicative of the formation of a hyaline membrane in the bilateral lungs. C-D show the results of a patient who survived. The patient was discharged from the hospital. The CT images were characterized by multiple patchy lesions in both lungs, with the majority being patchy infectious lesions, but consolidation was not obvious.