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Clinical Features and Outcomes of Acute Kidney Injury in Patients Infected with COVID-19 in Xiangyang, China

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Keywords
Coronavirus disease 2019 · Clinical features · Acute kidney injury · Multiple organ damage · Renal replacement therapy

Abstract
Background: In December 2019, pneumonia associated with COVID-19 has spread from Wuhan to other areas in China. In the present study, we aimed to further clarify the clinical features and outcomes of acute kidney injury (AKI) in patients infected with COVID-19 in Xiangyang, Hubei, China. ***Methods:*** All confirmed cases of COVID-19 with AKI in Xiangyang Central Hospital from January 22 to May 31, 2020, were included in this retrospective study. Data of epidemiological, clinical, laboratory, radiological tests, treatment, complication, and outcomes were collected and analyzed. Patients were divided into intensive care unit (ICU) group and isolation ward (non-ICU) group. ***Results:*** Of the total patients, 33.3% in the non-ICU group and 85.7% in the ICU group had chronic diseases. In addition, 85.7% of patients in the ICU group died. The most common symptoms were fever, cough, and fatigue. The lymphocyte count in the ICU group was significantly reduced compared with the non-ICU group. The chest computed tomography (CT) images appeared showed multiple mottles and ground-glass opacity. Strip shadow could be found in chest CT images of some recovered patients. All patients received antiviral treatment. Most patients in the ICU group were given methylprednisolone, immunoglobulin, antibiotics, and mechanical ventilation and 35.7% of patients in the ICU group received continuous renal replacement therapy. ***Conclusions:*** Elderly with chronic comorbidities were more susceptible to COVID-19, showing a higher mortality rate due to multiple organ damage, and 35.7% of patients with AKI in ICU received renal replacement therapy. Moreover, part of the cured patients might need additional time to recover for poor lung function.

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Introduction

Since December 2019, coronavirus disease 2019 (COVID-19) has rapidly spread from Wuhan to other areas in China. Several studies have described the clinical features of patients with COVID-19 [1–3]. Multiple organ damage, including acute respiratory distress syndrome (ARDS), acute cardiac injury and acute kidney injury

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(AKI), can occur in some patients with COVID-19 [3, 4]. However, specific features and outcomes of AKI patients with COVID-19 remain largely unexplored.

In the present study, we investigated the specific features and outcomes of AKI patients with confirmed COVID-19 who were admitted to Xiangyang Central Hospital, Affiliated Hospital of Hubei University of Arts and Science, about 300 km from Wuhan. Collectively, our findings provide valuable insights into the prevention of COVID-19-related fatality.

Methods

Study Design and Participants

Patients with confirmed COVID-19 from January 22 to May 31, 2020, at Xiangyang Central Hospital (Xiangyang, Hubei, China) were enrolled in this retrospective study according to WHO interim guidance [5]. AKI was diagnosed according to KDIGO Clinical Practice Guideline for Acute Kidney Injury [6]. ARDS was identified according to the Berlin definition [7]. Acute cardiac injury was diagnosed according to serum levels of cardiac biomarkers [8]. Oral consent was obtained from every participant, and written informed consent was waived because of the epidemic. This study was approved by the Ethics Committee of Xiangyang Central Hospital.

Data Collection

Data of epidemiological, clinical, laboratory, radiological tests, treatment, complication, and outcomes were extracted from the electronic medical records of patients. According to the patients' conditions, they were divided into 2 groups as follows: intensive care unit (ICU) group and isolation ward (non-ICU) group. The data of these patients were analyzed by 2 trained physicians.

Laboratory confirmation of COVID-19 was performed in the Chinese Center for Disease Control and Prevention. When the patients went to the hospital, throat swab specimens were obtained from all patients with fever. Information of age, sex, occupation, comorbidities, symptoms, signs, laboratory tests, chest computed tomography (CT) scans, outcomes, and treatment of all patients was collected.

Renal Replacement Therapy

The vascular access was established with central venous catheter via the internal jugular vein or the femoral vein. Continuous renal replacement therapy (CRRT) was performed by using PRISMA hemodialysis machine (Sweden). Bicarbonate-based dialysis solution and synthetic low-flux polysulfone membranes (1.22) were used for hemodialysis. The blood flow rate was 90–150 mL/min, and 4% sodium citrate solution was infused prefilter with an infusion rate of 180 mL/h for anticoagulation, lasting approximately 16–20 h during each session. Calcium substitution via the substitution fluid (0.056 mmol/L calcium chloride solution) was infused postfilter in the venous chamber with an infusion rate of 40 mL/h. Ionized Ca levels (target range 1.0–1.35 mmol/L) were measured with a blood gas analyzer every 2 h. The interval of CRRT was 3 times a week. Standard plasma filters (Gambro PF 2000N, Zurich, Switzerland) were used for plasma exchange (PE).

Table 1. Baseline characteristics and outcomes of patients infected with COVID-19

	Non-ICU (n = 9)	ICU (n = 14)	p value
Age, median (IQR), years	56 (32–78)	73 (51–96)	0.0097
Sex			
Male	4 (44.4)	8 (57.1)	0.68
Female	5 (55.6)	6 (42.9)	
Occupation			
Peasantry	2 (22.2)	1 (7.1)	0.54
Self-employed	3 (33.4)	0	0.047
Employee	2 (22.2)	2 (14.3)	1.0
Retired	2 (22.2)	11 (78.6)	0.13
Comorbidities			
Cardiovascular disease	3 (33.3)	9 (64.3)	0.21
Diabetes	0	4 (28.6)	0.13
Malignant tumor	0	1 (7.1)	1.0
Clinical outcome			
Discharged	9 (100)	2 (14.3)	<0.001
Died	0	12 (85.7)	<0.001

ICU, intensive care unit.

In brief, the patients' plasma was separated and replaced with 2,000–3,000 mL fresh frozen plasma for 2–3 h during each session. The blood flow rate was 90–150 mL/min and PE rate was 20–30 mL/min. The 5,000 U low molecular weight heparin was used for anticoagulation. The interval of PE was a total of 2–3 sessions in 2–3 days.

Statistical Analysis

Continuous variables were expressed as mean (SD) if they were normally distributed or median (IQR). Categorical variables were presented as number (%). All data were analyzed with SPSS 13.0. The differences between non-ICU patients and ICU patients were assessed using Student's t-test or one-way ANOVA. p values <0.05 were considered as statistically significant.

Results

Baseline Characteristics

1,176 COVID-19 patients were admitted in isolation wards of Xiangyang central hospital. A total of 23 AKI patients concomitant with COVID-19 infection were enrolled in the study. The mean age in the non-ICU group was 56 years, while that in the ICU group was 76 years (p = 0.0097). There was no difference in incidence between males and females. Patients with various occupations were found in the non-ICU group. However, most patients were retired in the ICU group. Moreover, 33.3% of patients in the non-ICU group had cardiovascular dis-

Table 2. Clinical characteristics of patients infected with COVID-19

	Non-ICU (n = 9)	ICU (n = 14)	p value
Fever	8 (88.9)	14 (100)	0.39
Fatigue	3 (33.3)	7 (50)	0.67
Anorexia	2 (22.2)	6 (42.9)	0.40
Myalgia	2 (22.2)	1 (7.1)	0.53
Dyspnea	0	7 (50)	0.019
Cough	3 (33.3)	7 (50)	0.67
Expectoration	2 (22.2)	5 (35.7)	0.66
Pharyngalgia	1 (11.1)	4 (28.6)	0.61
Diarrhea	2 (22.2)	1 (7.1)	0.54
Nausea	0	3 (21.4)	0.25
Onset of symptom to, median (IQR), day	7.4 (1–26)	4.8 (1–9)	0.24
Hospital admission			
Heart rate, median (IQR), bpm	82 (69–94)	84 (53–105)	0.67
Respiratory rate, median (IQR)	19 (18–22)	21 (16–28)	0.32
Mean arterial pressure, median (IQR), mm Hg	97 (75–115)	91 (74–132)	0.47
Oxygen saturation, %	96 (94–100)	89 (85–92)	0.012

ICU, intensive care unit.

Table 3. Laboratory findings of patients infected with COVID-19

	Normal range	Non-ICU (n = 9)	ICU (n = 14)	p value
White blood cell count, $\times10^9$/L	3.5–9.5	4.3 (3.0–6.9)	5.8 (3.5–9.4)	0.12
Neutrophil count, $\times10^9$/L	1.8–6.3	2.2 (1.9–4.2)	8.1 (3.8–13.1)	0.002
Lymphocyte count, $\times10^9$/L	1.1–3.2	1.0 (0.2–2.1)	0.61 (0.2–1.1)	0.043
Platelet count, $\times10^9$/L	125–350	166 (109–269)	169 (108–296)	0.94
D-dimer, mg/L	<0.55	1.3 (0.2–3.3)	3.2 ((0.6–7.2)	0.038
Fibrinogen, g/L	2–4	5.4 (1.8–8.4)	5.8 (4.1–8.4)	0.69
C-reactive protein, mg/L	<10	40.0 (17.4–121)	133.3 (57.7–293.6)	0.033
Erythrocyte sedimentation rate	0–15	49.8 (26–94)	59.3 (28–102)	0.72
Procalcitonin, ng/mL	<0.05	0.63 (0.12–1.86)	2.43 (1.46–3.49)	0.026
Albumin, g/L	35–50	31.3 (25–37.3)	30.1 (24.5–31.5)	0.67
Alanine aminotransferase, U/L	9–50	28.7 (18–37)	74.9 (26–144)	0.038
Aspartate aminotransferase, U/L	15–40	26.4 (14–42)	58.4 (24–117)	0.019
Lactate dehydrogenase, U/L	120–250	261.0 (124–401)	476.2 (271–749)	0.001
Creatine phosphokinase, U/L	50–310	187.6 (24–426)	249.4 (19–777)	0.61
BUN, mmol/L	3.1–8.0	6.1 (3.6–11.2)	20.6 (9.5–57.4)	0.015
Cr, μmol/L	57–97	120.7 (101.8–157)	164.6 (108.0–292.4)	0.039
Urine protein	Negative	1 (11.1)	5 (35.7)	0.34

ICU, intensive care unit.

eases, while 85.7% of patients in the ICU group had chronic diseases, such as cardiovascular diseases, diabetes, and malignant tumor. By the end of May 31, 2020, all patients in the non-ICU group were discharged. In contrast, 85.7% of patients in the ICU group died, and only 14.3% of patients were discharged (Table 1).

Clinical Characteristics

The most common symptoms in all patients were fever, cough, and fatigue. The other less commonly detected symptoms included anorexia, myalgia, dyspnea, pharyngalgia, diarrhea, and nausea. The mean intervals of symptom onset to clinical presentation were 7.4 and 4.8

days in the non-ICU and ICU groups, respectively. There was no difference in vital signs, including heart rate, respiratory rate, and mean arterial pressure, between the 2 groups. There was a great difference in blood pressure of COVID-19 patients in the ICU group. Because of hematemesis, 1 (7.1%) patient had hypotension and received transfusion of RBCs. In addition, 5 (35.7%) patients with hypertension received antihypertensive agents such as diuretics, calcium antagonists, β-blockers, angiotensin II-converting enzyme inhibitors, and angiotensin II receptor antagonists. Oxygen saturation in the ICU group was significantly lower compared with the non-ICU group (96 vs. 89%, $p = 0.012$) (Table 2).

Laboratory Findings and Chest CT Image

Blood samples of all patients were regularly checked after hospital admission. The mean number of white blood cells in both groups was within the normal range. Compared with the non-ICU group, the mean neutrophil account in the ICU group was significantly elevated (8.1 vs. 2.2, $p = 0.002$). However, the lymphocyte account in both groups was below the normal range, and such number in the ICU group was significantly reduced compared with the non-ICU group (1.0 vs. 0.61, $p = 0.043$). Moreover, the levels of C-reactive protein and procalcitonin in the ICU group were significantly increased compared with the non-ICU group (133.3 vs. 40.0, $p = 0.033$; 2.43 vs. 0.63, $p = 0.026$). Regarding liver function, the levels of alanine aminotransferase and aspartate aminotransferase in the ICU group were significantly increased compared with the non-ICU group (74.9 vs. 28.7, $p = 0.038$; 58.4 vs. 26.4, $p = 0.019$). In addition, the lactate dehydrogenase level in the ICU group was significantly increased compared with the non-ICU group (476.2 vs. 261.0, $p = 0.001$). Furthermore, the levels of BUN and Cr in the ICU group were significantly increased compared with the non-ICU group (20.6 vs. 6.1, $p = 0.015$; 164.6 vs. 120.7, $p = 0.039$) (Table 3). All patients received chest CT scan. The chest CT images showed multiple mottles and ground-glass opacity. Strip shadow could be found in chest CT scans of some recovered patients (Fig. 1).

Complications and Treatments

Multiple organ damage occurred in most patients, including ARDS, acute cardiac injury, acute liver injury, shock, AKI, and arrhythmia. All patients received antiviral treatment, including lopinavir/ritonavir (500 mg, twice a day, oral administration), oseltamivir (75 mg, twice a day, oral administration), ganciclovir (250 mg, twice a day, intravenous injection), alpha-interferon (5 million U, twice a day, aerosol inhalation), chloroquine (500 mg, twice a day, oral administration), and Abidol (200 mg, 3 times a day, oral administration). The duration of antiviral treatment was 7–10 days. Most patients with high fever were given methylprednisolone (40 mg, twice a day for 3–5 days, intravenous injection), immunoglobulin (10 g, once a day for 5 days, intravenous injection), and antibiotics (cephalosporin, moxifloxacin, meropenem, and linezolid). The duration of antibiotic treatment was uncertain because 3 patients were still in the hospital. Due to renal failure and inflammatory cytokine storm, 5 (35.7%) patients in the ICU group received CRRT, and 2 (14.3%) patients in the ICU group PE. It was worth noting that the convalescent plasma of patients with COVID-19 was transfused to 2 patients in the ICU group, and they were still in the hospital. Due to hypoxia, 5 patients were given high-flow oxygen therapy, and 10 patients were mechanically ventilated. However, the hypoxemia of 2 patients remained unresolved under mechanical ventilation. Hereafter, they received extracorporeal membrane oxygenation (ECMO). By the end of May 31, these 2 patients receiving ECMO were died in the hospital (Table 4).

Table 4. Complications and treatments of patients infected with COVID-19

	Non-ICU ($n = 9$)	ICU ($n = 14$)	p value
Complications			
Shock	0	5 (35.7)	0.12
Acute cardiac injury	1 (11.1)	6 (42.9)	0.18
Acute liver injury	0 (0)	7 (50.0)	0.02
Arrhythmia	0	2 (14.3)	0.50
ARDS	1 (11.1)	10 (71.4)	0.009
Treatment			
Antiviral therapy	9 (100)	14 (100)	–
Antibiotic therapy	4 (44.4)	14 (100)	0.037
Glucocorticoid therapy	1 (11.1)	12 (85.7)	0.0007
Immunoglobulin	1 (11.1)	5 (35.7)	0.34
Convalescent plasma therapy	0	3 (21.4)	0.25
CRRT	0	5 (35.7)	0.12
PE	0	2 (14.3)	0.50
Oxygen inhalation			
Noninvasive	1 (11.1)	4 (28.6)	0.61
Invasive	0	10 (71.4)	0.002
ECMO	0	2 (14.3)	0.50

ICU, intensive care unit; ARDS, acute respiratory distress syndrome; CRRT, continuous renal replacement therapy; ECMO, extracorporeal membrane oxygenation; PE, plasma exchange.

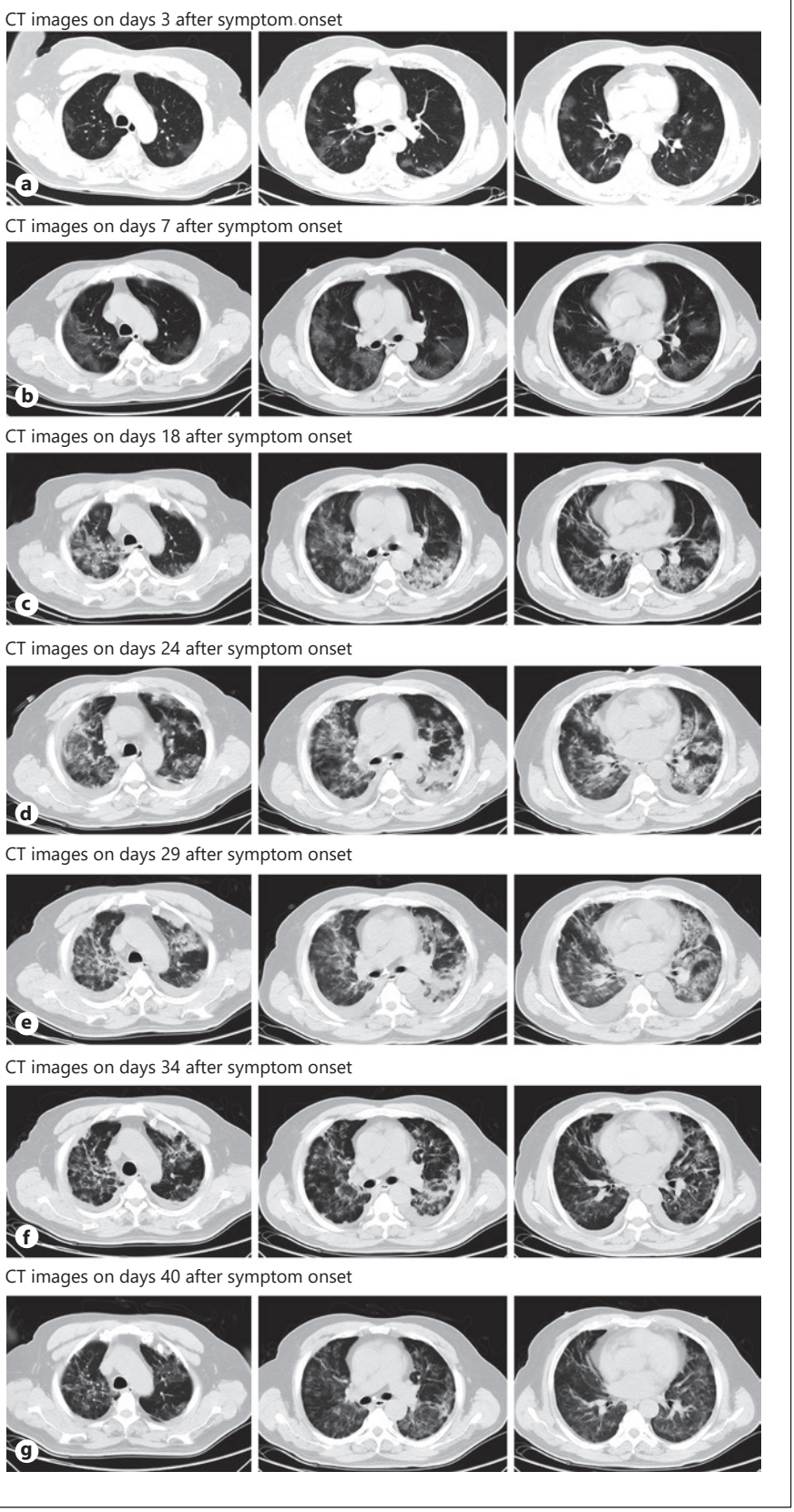

Fig. 1. Chest CT images of a 58-year-old male patient. Chest CT images obtained on February 3, 2020, show ground-glass opacity in both lungs on day 3 after symptom onset (**a**); chest CT images show the changes after the treatment from February 5 to March 3 in ICU (**b–f**); chest CT images obtained on March 9, 2020, show bilateral ground-glass opacity, and the remaining strip shadow can be seen in the lung tissue (**g**). CT, computed tomography.

Discussion

This was a retrospective study on clinical features and outcomes of AKI patients infected with COVID-19 in Xiangyang, China. It presented characteristics, outcomes, laboratory findings, complications, treatments, and chest CT images of AKI patients infected with COVID-19.

Recent studies have reported that the incidence of AKI in patients with COVID-19 is 3–7%, and 7–9% of the patients with COVID-19 receive CRRT. Furthermore, 23% of the patients with COVID-19 in ICU are treated with CRRT [4]. The latest research [9] shows that the key receptor of COVID-19 ACE2 is highly expressed in human kidneys (almost 100 times higher than the lungs), and the kidney may be one of the main targets of COVID-19. Virus-induced renal injury may be one of the main causes of disease and may eventually lead to multiple organ dysfunction or death. Li has reported that 63% of patients with COVID-19 have proteinuria. The incidence of abnormal serum Cr and BUN is 13 and 29%, respectively. The chest CT scan has shown that 100% (27/27) of the patients have radiographic abnormalities of the kidneys [10].

In the present study, the mortality of the patients with COVID-19 in the ICU group was 64.3%. However, more deaths might occur for patients still in the hospital. There was no difference in the incidence of COVID-19 between males and females. In addition, the elderly with chronic comorbidities were more susceptible to COVID-19, exhibiting a higher mortality rate due to their weaker immune functions. In terms of laboratory tests, the lymphocyte account in patients with COVID-19 was significantly decreased. However, the levels of C-reactive protein and erythrocyte sedimentation rate were significantly increased. Most patients in the ICU group rapidly progressed to ARDS and had multiple complications, including acute cardiac injury, acute liver injury, shock, arrhythmia, and AKI. These results suggested that cytokine storm syndrome was an important pathophysiological basis for multiple organ dysfunction caused by COVID-19. Coronavirus could severely impair the immune system of patients, and then inflammatory cytokines were excessively released, leading to diffuse alveolar damage, transparent membrane formation, and fibrin exudation [11]. In critically ill patients, the levels of interleukin-6, interleukin-10, and tumor necrosis factor-α are significantly increased [12]. Therefore, early identification and timely treatment are very important for critically ill patients.

Although all confirmed patients received antiviral therapy, the mortality rate of patients in the ICU group remained very high, indicating that there was no specific medications to cure COVID-19 at present. According to patients' symptoms and CT images, some patients received antibiotics to prevent secondary infections. Immunoglobulin and methylprednisolone were used to inhibit excessive inflammation for a short duration (usually no more than 5 days). Moreover, 35.7% of the patients in the ICU group received CRRT to treat renal failure and clear inflammatory factors. Due to ARDS, 2 patients received ECMO. In addition, the convalescent plasma of patients with COVID-19 was transfused to 2 patients. Unfortunately, the prognosis for patients in the ICU group remained poor despite extensive supportive care. It was worth noting that chest CT images of cured patients showed chronic manifestations. Therefore, those patients might need additional time to recover in the future.

This study has several limitations. First, few patients with COVID-19 were included in the study. It would be better to include more patients from other medical institutions in Xiangyang, China. Second, the recovered patients were not followed up. Long-term prognosis of curing patients was important for us to better treat COVID-19.

Conclusion

Collectively, elderly with chronic comorbidities were more susceptible to COVID-19, exhibiting a higher mortality rate due to multiple organ damage. Part of the cured patients might need additional time to recover due to poor lung function.

Statement of Ethics

This study was conducted in accordance with the 1964 Helsinki Declaration. Ethical approval was waived in view of the retrospective nature of the study.

Conflict of Interests Statement

We declare no competing interests.

Funding Sources

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Author Contributions

H.Y. and J.L. collected the epidemiological and clinical data and processed statistical data. J.L. drafted the manuscript. F.H. revised the final manuscript. Z.G. was responsible for summarizing all data related to the virus. Z.G. was responsible for summarizing all epidemiological and clinical data.

References

1 Guan WJ, Ni ZY, Hu Y, Liang WH, Ou CQ, He JX, et al. Clinical characteristics of coronavirus disease 2019 in China. N Engl J Med. 2020;382(18):1708–20.

2 Wang D, Hu B, Hu C, Zhu F, Liu X, Zhang J, et al. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected pneumonia in Wuhan, China. JAMA. 2020;323(11):1061–9.

3 Chen N, Zhou M, Dong X, Qu J, Gong F, Han Y, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. Lancet. 2020;395(10223):507–13.

4 Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet. 2020;395(10223):497–506.

5 World Health Organization. Clinical management of severe acute respiratory infection when novel coronavirus (nCoV) infection is suspected: interim guidance. Published March 13, 2020.

6 Kidney Disease: Improving Global Outcomes (KDIGO) Acute Kidney Injury Work Group. KDIGO clinical practice guideline for acute kidney injury. Kidney Int Suppl. 2012;2:1.

7 ARDS Definition Task Force; Ranieri VM, Ranieri VM, Rubenfeld GD, Thompson BT, Ferguson ND, Caldwell E, et al. Acute respiratory distress syndrome: the Berlin definition. JAMA. 2012;307(23):2526–33.

8 Gao C, Wang YM, Gu XY, Shen XH, Zhou DM, Zhou SJ, et al. Association between cardiac injury and mortality in hospitalized patients infected with avian influenza A (H7N9). Virus. Crit Care Med. 2020;48:451–8.

9 Zhou P, Yang XL, Wang XG, Hu B, Zhang L, Zhang W, et al. A pneumonia outbreak associated with a new coronavirus of probable bat origin. Nature. 2020;579(7798):270–3.

10 Anti-2019 n-Cov-Volunteers; Li Z, Wu M, Guo J, Yao JW, Liao X, Song SJ, et al. Caution kidney dysfunctions of 2019-nCoV patients. medRxiv. 2020 Feb 8.

11 Guo XJ, Thomas PG. New fronts emerge in the influenza cytokine storm. Semin Immunopathol. 2017;39(5):541–50.

12 Gong J, Dong H, Xia SQ, Huang YZ, Wang DK, Zhao Y, et al. Correlation analysis between disease severity and inflammation-related parameters in patients with COVID-19 pneumonia. medRxiv. 2020 Feb 25.