Analysis of the Clinical Characteristics of 77 COVID-19 Deaths

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Abstract

Purpose: For the emerging pandemic Coronavirus Disease 2019 (COVID-19), no clear description on its deaths' clinical characteristics and causes of death is available. Hence, this study analyzed clinical characteristics of 77 COVID-19 deaths, providing data support to further understand this disease.

Method: A retrospective analysis of 77 COVID-19 deaths in East Branch, Renmin Hospital of Wuhan University from February 1 to March 7, 2020 was performed in clinical characteristics, laboratory results, causes of death, and subgroup comparison.

Results: Totally 72.7% of the deaths (male-female ratio: 51:26, average age at death: 71, mean survival time: 17.4 days) had hypertension, heart disease, diabetes, chronic lung disease, and other comorbidities. Acute respiratory distress syndrome (ARDS) and sepsis were the main causes of death. Increases in C-reactive protein (CRP), lactate dehydrogenase (LDH), D-dimer and lactic acid (LAC), and decreases in lymphocyte, cluster of differentiation (CD) 4+ and CD8+ cells were common in laboratory results. Subgroup analysis showed: 1) Most female deaths had cough and diabetes. 2) The male proportion in young and middle-aged deaths was higher; while elderly deaths were more prone to myocardial injury and elevated CRP. 3) There was no statistical difference between short-term and non-short-term survival subgroups. 4) CRP and LDH increased and CD4+ and CD8+ cells decreased significantly in patients with hypertension.

Conclusions: The majority of COVID-19 deaths are males, especially the elderly with underlying diseases. The main causes of death include ARDS and sepsis. Most female deaths have cough and diabetes. Myocardial injury is common in elderly deaths. Patients with hypertension are prone to increased inflammatory index, tissue hypoxia and cellular immune injury.

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Background

In December 2019, the first pneumonia cases of unknown origin was identified in Wuhan, Hubei, China (Citation 1). On January 7, 2020, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was isolated by Chinese scientists from these patients (Citation 2), which was officially named Coronavirus Disease 2019 (COVID-19) by the World Health Organization (WHO) in February 2020. Several articles confirmed that the virus spread from person to person both in hospitals and in family settings (Citation 3). The clinical spectrum of SARS-CoV-2 infection encompasses asymptomatic infection, a mild upper respiratory tract infection, and severe viral pneumonia with respiratory failure and even death. A number of published case studies made summaries on all patients infected with SARS-CoV-2 (Citation 4 and 5), in which some death cases were included (Citation 6). However, no clear description and analysis on the clinical characteristics of patients died of COVID-19 and the causes of death are available. Hence, the detailed clinical data of 77 COVID-19 deaths in RHWU East Branch were included in this study, with a

thorough analysis on their clinical characteristics and laboratory test results, as well as a comparison among different subgroups.

Method

Study Design

The clinical and laboratory data of 77 patients died of COVID-19 in RHWU East Branch from February 1, 2020 to March 7, 2020 were collected. The hospital is a designated hospital for the treatment of severe and critical COVID-19 patients in Wuhan, where all patients are diagnosed with COVID-19 according to the WHO Interim Guidance. Among 79 deaths during this period, two died immediately after admission and were excluded because of lacking of clinical data. Therefore, the clinical and laboratory data of 77 deaths were collected and analyzed in this study after the approval of RHWU Research Ethics Committee (WDRY2020-K068).

Data Collection

The data of epidemiology, demography, clinical characteristics, laboratory tests and treatment plans were extracted from the electronic medical records in accordance with the modified version of WHO/International Severe Acute Respiratory and Emerging Infection Consortium (ISARIC) Case Record Form for Severe Acute Respiratory Infections. All data were reviewed by two doctors, and then a third researcher (LD) determined whether there was a difference in interpretation between the two reviewers.

Laboratory Test Process

The laboratory confirmation method of SARS-CoV-2 infection has been explained in other articles. Real-time RT-PCR assays had been used to detect SARS-CoV-2 in respiratory specimens of patients in other designated hospitals for COVID-19 treatment. Patients with positive results in two assays and pulmonary infection detected by chest CT were confirmed with COVID-19 and admitted to RHWU East Branch. After admission, all patients' respiratory specimens were detected again for further diagnosis of SARS-CoV-2 infection. Laboratory tests such as ECG, arterial blood gas analysis, blood routine (CBC), coagulation function, serum biochemical indexes (incl. liver and kidney functions, creatine kinase and lactate dehydrogenase), myocardial enzyme, brain natriuretic peptide, C-reactive protein and procalcitonin were carried out. In addition, all patients underwent chest X-ray or CT at least once, the examination frequency was determined by their doctors in charge.

Definitions

Young and middle-aged patients refer to patients aged 18-65, and elderly patients refer to patients over 65. An axillary temperature above 37.6°C (99.7°F) is considered a fever. Diagnosis of sepsis and septic shock is based on the Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3) issued in 2016 (Citation 7). Diagnosis of acute kidney injury (AKI) is based on the Kidney Disease Improving Global Outcome (KDIGO) Clinical Practice Guideline for AKI (Citation 8), and diagnosis of acute

respiratory distress syndrome (ARDS) is based on the Berlin Definition of ARDS (Citation 9). Acute myocardial infarction (AMI) is diagnosed by an increase in serum level of cardiac biomarkers (such as high-sensitivity cardiac troponin I), or new abnormalities found in ECG and echocardiography. According to the *Diagnosis and Treatment Plan for Corona Virus Disease 2019* (Tentative Sixth Edition) (Citation 10), the severity of COVID-19 is defined as follows: Ordinary cases: Patients have symptoms like fever, respiratory tract, etc. and pneumonia manifestation can be seen in imaging. Severe cases (meeting any of the following): 1. Respiratory distress, RR ≥ 30 breaths/min; 2. Oxygen saturation ≤ 93% at a rest state; 3. Arterial partial pressure of oxygen (PaO2) / oxygen concentration (FiO2) ≤300mmHg (1mmHg = 0.133kPa). Critical cases (meeting any of the following): 1. Respiratory failure occurs and mechanical ventilation is required; 2. Shock occurs; 3. Complicated with other organ failure that requires monitoring and treatment in ICU. Case of close contact at home refers to the diagnosis of COVID-19 in two or more family members/persons who had close contact within 14 days. Short-term survival case refers to the survival time from disease onset to death ≤ 14 days.

Statistical Method

Data were analyzed by means of SPSS version 19.0. The normally distributed measurements were expressed by Mean ± SD, T-test was used to compare the means of two groups and ANOVA was used to compare the means of more than two groups. The non-normally distributed measurements were expressed by median and analyzed by Wilcoxon rank-sum test. Chi-square test, denoted by $\chi 2$, was used to analyze enumeration data, and a value of $P<0.05$ was considered statistically significant.

Results

Analysis of Clinical Characteristics

From January 31, 2020 to March 7, 2020, 1,179 COVID-19 patients were admitted to and 77 died (incl. 51 males and 26 females) in EHWU East Branch. The average age at death was 71 years old, the number of COVID-19 deaths in males was higher than that in females (66.2% vs 33.8%), and the average age at death in males was lower than that in females (69 vs 75). All patients were permanent residents of Wuhan. Among them, 81.8% were caused by mass gathering, and their initial symptoms include fever (81.8%), dyspnea (32.5%), cough (19.5%), fatigue (15.6%), neurological symptoms (5.2%), and abdominal pain, diarrhea (3.9%); 72.8% had underlying diseases, hypertension (58.9%) was the most common one, followed by diabetes (32.1%), heart disease (32.1%), chronic lung disease (14.3%), nephropathy (13.5%), cerebrovascular disease (12.5%), liver disease (7.1%), cancers (3.6%), etc.; and 33 patients (43.0%) had a history of smoking. (Table 1) According to the assessment results within 24 hours after admission, 71 were critical cases, 4 were severe cases and 2 were ordinary ones. Among the ordinary patients, one patient died of cerebral hemorrhage after kidney transplantation, while the other suffered from massive cerebral infarction and died of cerebral herniation.

Laboratory Tests

Among the 77 deaths, peripheral white blood cell count increased in 36 cases (46.8%) and decreased in 9 cases (11.7%). Fifty cases (64.9%) had increased neutrophil count, 67 cases (87.0%) had decreased lymphocyte count, 43 cases (55.8%) had decreased hemoglobin, and 25 cases (32.5%) had decreased platelet count. C-reactive protein (CRP) increased in 69 cases (89.6%) and procalcitonin increased in 57 cases (74.0%). Troponin increased in 34 cases (44.2%) and brain natriuretic peptide increased in 26 cases (33.8%). Seventeen cases (22.1%) had elevated alanine aminotransferase and 38 cases (49.4%) had elevated aspartate aminotransferase. Creatinine, lactic dehydrogenase and D-dimer increased respectively in 19 cases (24.7%), 68 cases (88.3%) and 59 cases (76.6%). CD4 + cell count decreased in 52 cases (98.1%), CD8+ cell count decreased in 43 cases (81.1%) and lactic acid increased in 68 cases (88.3%). (Table 2)

Imaging Examination

All the 77 patients underwent imaging examination (chest X-ray or CT) from disease onset to death. Diffuse lesions (multiple ground-glass exudation shadows) of both lungs were found in the early stage, and were developed into large areas of lung consolidation on both sides in the later stage, along with bronchiectasis and “white lungs” (asbestosis). Spontaneous pneumothorax and subcutaneous and mediastinal emphysema occurred in 2 patients without mechanical ventilation.

Treatment Plans and Causes of Death

Early treatment with oseltamivir was given to 58 patients, after admission, 75 patients received antiviral treatment with arbidol, 2 patients received lopinavir/ritonavir, and all patients received antibiotic treatment. As for respiratory support, 24 cases (31.2%) were on non-invasive ventilators, 24 (31.2%) received mask oxygen therapy, 16 (20.8%) received high-flow nasal cannula (HFNC) oxygen therapy, and 1 received extracorporeal membrane oxygenation (ECMO). ARDS (87.0%) was the main cause of death, followed by sepsis (18.2%), neurological diseases (3.9%), heart disease (2.6%) and gastrointestinal bleeding (2.6%). The mean survival time (from disease onset to death) was 17.4 days. Only 7 patients (9.1%) underwent endotracheal intubation, and the mean time from admission to endotracheal intubation was 6 days. (Table 1)

Subgroup Analysis

In this study, subgroup analysis was carried out based on a series of baseline characteristics, including gender, age, survival time and whether complicated with hypertension, and the results were shown as follows: (1) Among the initial symptoms of deaths, females were more prone to cough and dyspnea (especially in the early stage), and more likely to be complicated with diabetes; while the incidence of sepsis in males seemed to be higher than that in females. In addition, anemia was more common in females; while elevated CRP, creatinine and creatine kinase, and decreased platelets and CD4 + cells were more common in males (Figure 1). (2) The majority of young and middle-aged deaths (≤ 65 years old) were males. Elderly patients seemed to be more prone to fatigue and myocardial injury, while middle-aged and young patients were more likely to have elevated alanine aminotransferase and creatine kinase

(Figure 2). (3) The majority of short-term survival cases were males. In the short-term survival subgroup, symptoms in abdomen and nervous system were more likely to be found in the early stage, and the proportion of patients complicated with heart disease rather than diabetes or chronic lung disease was higher. The incidence of sepsis was higher in this subgroup, and laboratory tests were characterized by decreased platelets and elevated creatine kinase (Fig. 3). (4) Dyspnea was more common in the deaths complicated with hypertension, while fatigue and neurological symptoms were more common in the deaths without hypertension. Compared with the deaths without hypertension, CRP and LDH increased, and CD4 + cells and CD8 + cells decreased significantly in the deaths complicated with hypertension (Figure 4). (Table 3)

Case Presentation

A 31-year-old male patient, previously healthy, was admitted to hospital on February 5, 2020 due to “fever for 13 days and dyspnea for 2 days”. Before that, he had been exposed to a covid-19 patient. Oral administration of “Oseltamivir 75mg bid and Moxifloxacin 0.5g qd" was given, however the effect was poor. With two positive SARS-CoV nucleic acid assays in throat swab specimens conducted by other hospital, he was transferred to our hospital. Physical examinations: shortness of breath (28 times / min), oxygen saturation (by fingertip pulse oximeter) of 75%, subcutaneous crepitus found in the anterior chest along with low breath sound of both lungs. Auxiliary examinations: blood routine examination: 15.5 × 109/L, neutrophil count: 14.45 ×109/L, lymphocyte count: 0.4 ×109/L; arterial blood gas analysis (oxygen mask at a flow rate of 8L/min): pH:7.48, PO2: 45mmH2O, PCO2: 30mmH2O□Lac: 4mmol/L; CRP: 137.2mg/L; PCT: 0.048ng/L; BNP: 152 pg/ml; creatinine: 52umol/L, creatine kinase: 473u/L, LDH: 894u/L, ALT: 40u/L, AST: 30u/L□ Cell immunity: CD4+ cells: 125/uL, CD8+ cells: 160/uL. Chest CT: bilateral pneumothorax, subcutaneous and mediastinal emphysema in the chest wall and neck; consolidation, exudation and local compressive atelectasis of both lungs. Admission diagnosis: 1. critical case of COVID-19; 2. ARDS; 3. bilateral spontaneous pneumothorax; and 4. subcutaneous and mediastinal emphysema. After admission, the patient was given high-flow nasal oxygen therapy (flow rate: 60L/min, oxygen concentration: 100%), closed chest drainage and subcutaneous emphysema incision and drainage of both lungs, and antiviral therapy with abidol 200mg tid (oral administration) + ribavirin 0.5g bid (intravenous infusion). After the above treatment, the dyspnea was relieved, and oxygen saturation reached 93%. Two days after admission, dyspnea worsened and oxygenation index decreased further. The patient died on February 9. (Figure. 5)

Discussion

This study includes a group of 77 COVID-19 deaths who were diagnosed and developed into critical cases in other hospitals from January to February 2020, and then admitted to the temporary infection ICU of RHWU East Branch. The clinical manifestations of this group are very similar to those of SARS-CoV. According to literature, the shortest time from admission to ARDS is 2 days and the mortality rate is 15%-61.5% (Citation 1, 6 and 11). Recent studies have shown that nearly 70% of patients infected with SARS-CoV-2 are males (Citation 1 and 12). In this study, male deaths accounts for 66.2%, which is

consistent with other studies. The majority of deaths are elderly (53/77), which is consistent with the conclusion that risk of death rises with age (Citation 6). The majorities of both young and middle-aged deaths and elderly deaths are males, and the male proportion in the former is comparatively higher. Female deaths are more likely to be complicated with diabetes. About 81.8% of the patients are caused by mass gathering but have no exposure to Huanan Seafood Market, which suggests that most of the deaths may be second-generation infected persons. This study shows that fever and respiratory, neurological and digestive symptoms are the common initial clinical symptoms of the deaths, which is consistent with the previous study (Citation 1). According to Cao Bin's analysis of the first-batch 191 patients admitted to ICU, 48% of the COVID-19 patients have underlying diseases (Citation 6), and that of this study reaches 72.8%. It can be seen that more deaths occurs in patients complicated with underlying diseases. However, there is no relevant research on whether the mortality rate of patients with underlying diseases is higher than that of patients without underlying diseases, or how various underlying diseases affect the deaths. For the first time, a subgroup analysis based on hypertension is conducted in this study.

In terms of laboratory tests, lymphocytopenia occurs in 88% of the patients included in this study, which is a prominent feature of patients with severe SARS-CoV infection, because the targeted invasion of SARS-CoV particles can cause the destruction of lymphocytes by destroying their cytoplasmic components (Citation 13). In addition, lymphocytopenia is also common in patients with severe MERS infection, due to lymphocyte apoptosis (Citation 14 and 15). Most recent studies have confirmed that lymphocytes in patients with critical COVID-19 decrease significantly compared with those in mild patients. Some studies have believed that lymphocytopenia is one of the high-risk factors for death (Citation 6). Others have also pointed out that the neutrophil-to-lymphocyte ratio (NLR) can be used as a risk factor for the early prediction of critical COVID-19 cases, namely patients aged ≥ 50 and NLR ≥ 3.13 are more likely to develop into critical cases (Citation 16). The counts of CD4 + cells and CD8 + cells in most patients of this group decrease significantly, but the specific mechanism of lymphocyte subsets in such diseases needs to be studied. More than 60% of the patients have elevated CRP, LDH and LAC, which may be related to the systemic immune response induced by infection and the early hypoxia in critical patients. However, the correlation between these indicators and death and their predictive value for death risk need to be further investigated. Consistent with other literatures, 77% of the patients have increased D-dimer and are considered to have a hypercoagulable state. Furthermore, the risk of thrombosis is raised because of severe patients' long-term bed rest. Thus anticoagulant therapy should be actively applied. Compared with young and middle-aged deaths, the elderly deaths are more prone to myocardial injury, which may be related to the fact that the elderly patients are more likely to have heart diseases.

ARDS is the main cause of death in this group of deaths, suggesting that SARS-CoV infection mainly affects the respiratory system. A number of literatures have reported that coronavirus invades tissues and organs through a receptor named angiotensin converting enzyme 2 (ACE2), which is abundant in kidney and myocardium; meanwhile, autopsy results also confirmed that coronavirus can invade myocardial cells (Citation 17 and 18). In this study, myocardial injury and acute kidney injury occur in some deaths.

Whether the occurrence is caused by SARS-CoV invasion or secondary changes caused by hypoxia is still uncertain. However, it can be determined that myocardial injury and acute kidney injury are not the main causes of death. At present, there are no effective antiviral drugs, including Kaletra (Citation 19). Therefore, clinicians should focus on correcting hypoxemia caused by ARDS, maintaining stable vital signs and waiting for the body to get rid of the virus. It is reported that the proportion of mechanical ventilation in critical COVID-19 patients is 30:37 (Citation 11). Due to the previous shortage of medical resources, 40.3% of the patients of this group receive mechanical ventilation, and only 9.1% receive endotracheal intubation. The time from admission to endotracheal intubation is so long that some patients cannot recover from ARDS and eventually die of lack of oxygen. There are reports that the incidence of pneumothorax in COVID-19 patients is about 1%-2%, and that in this group reaches about 2.6% (Citation 6 and 12), which is related to that all patients in this group are severely or critically ill. The aforementioned patient rapidly developed ARDS and bilateral spontaneous pneumothorax after onset of the disease. The main cause may be extensively parenchymal injury caused by pneumonia, which results in poor lung compliance and respiratory distress, significantly increases the negative intrapleural pressure and then the trans-pulmonary pressure, leads to the formation of pneumothorax, and further aggravates the disease. Therefore, appropriate respiratory support and adequate sedation and analgesia in the early stage should be given to COVID-19 patients with ARDS. In addition, clinicians should also pay attention to sepsis, the secondary cause of death in this study. Prior studies have believed that bacterial and fungal infections are common in the late stage of virus infection. 30.3% and 16.9% of patients with severe H1N1 flu admitted to the ICU were bacterial or fungal infections, respectively. But the incidence of COVID-19 patients is unclear yet (Citation 12, 20 and 21). In this study, 57 patients (74.0%) have elevated procalcitonin, suggesting the possibility of bacterial infection. All patients are treated with antibiotics. Only 2 patients are diagnosed with complicated fungal infection because of Aspergillus and Candida albicans cultured from their sputum. It is suggested that the incidence of fungal infection may be lower than that of patients with severe H1N1 flu.

Conclusions

The majority of COVID-19 deaths are males, especially the elderly with underlying diseases. The disease often starts with cough in female patients who are more likely to be complicated with diabetes. The male proportion in young and middle-aged deaths are higher than that in elderly deaths. Myocardial injury is common in the elderly patients. Dyspnea is likely to occur in the early stage of COVID-19 deaths complicated with hypertension, along with significantly decreased CD4+ cell count. In the short-term survival subgroup, the mortality is not significantly associated with whether patients are complicated with hypertension, the majority of deaths in this subgroup are still males and often have heart diseases, and the main cause of death is ARDS. As for all the 77 deaths, ARDS and sepsis are the main causes of death.

Declarations

For the fulfillment of this retrospective study, written informed consents have been signed by all the Legally Authorized Representatives /next to kin of the subjects. Legally Authorized representatives/next to kin of the subjects provided informed consent for the publication/consent to publish of the data in an online open access publication in the manuscript.

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Tables

Table 1. Clinical Characteristics of COVID-19 Deaths

Clinical characteristics	All cases (N=77)
Gender	
Male	51 (66.2)
Female	26 (33.8)
Average age at death, mean (min-max), years	71 (31-95)
Male	69 (31-95)
Female	75 (52-94)
Mean survival time (from disease onset to death), days	17.4
Permanent residents of Wuhan	77 (100.0)
Mass gathering	63 (81.8)
Initial symptoms	
Fever	63 (81.8)
Cough	15 (19.5)
Dyspnea	25 (32.5)
Fatigue	12 (15.6)
Abdominal pain, diarrhea	3 (3.9)
Neurological symptoms	4 (5.2)
Comorbidities	
Any of comorbidities	56 (72.7)
Hypertension	33 (58.9)
Heart disease	18 (32.1)
Diabetes	18 (32.1)
Chronic lung disease	8 (14.3)
(Chronic obstructive pulmonary disease, Asthma, Bronchiectasis)	
Cerebrovascular disease	7 (12.5)
Nephropathy	7 (13.5)
Liver disease	4 (7.1)
Cancers	2 (3.6)
Surgery	1 (1.8)
Others (Rectal polyps, Gout, Gallstone, Pancreatitis)	4 (7.1)
Smoking history, yes	33 (42.9)
Causes of death	
Acute respiratory distress syndrome[a]	67 (87.0)
Sepsis[a]	14 (18.2)
Nervous system disease[a]	3 (3.9)
Heart disease[a]	2 (2.6)
Gastrointestinal bleeding[a]	2 (2.6)
Others (Pancreatitis, Uremia, Renal insufficiency)[a]	3 (3.9)
Respiratory support	
Invasive mechanical ventilation	7 (9.1)
Non-invasive ventilator	24 (31.2)
Oxygen mask	24 (31.2)
High-flow nasal cannula oxygen therapy	16 (20.8)

Mean time from admission to endotracheal intubation, days	6

Note: [a] Analysis was done in the cases with any comorbidity, so the total number is 56 for all

Table 2. Initial Laboratory Analysis of COVID-19 Deaths

Initial laboratory analysis	All cases (N=77)
Complete blood count	
White blood cell count, >9.5×10^9/L	36 (46.8)
White blood cell count, <3.5×10^9/L	9 (11.7)
Lymphocyte count, <1.1×10^9/L	67 (87.0)
Neutrophil count, >6.3×10^9/L	50 (64.9)
Hemoglobin, <130 g/L	43 (55.8)
Platelet count, <125×10^9/L	25 (32.5)
C-reactive protein, >10 mg/L	69 (89.6)
Procalcitonin, >0.1 ng/mL	57 (74.0)
Myocardial markers	
Creatine kinase-MB, >5 ng/mL	14 (18.2)
Troponin, >0.04 ng/mL	34 (44.2)
Brain natriuretic peptide, >900 pg/mL	26 (33.8)
Blood biochemical analysis	
Alanine aminotransferase, >50 U/L	17 (22.1)
Aspartate aminotransferase, >40 U/L	38 (49.4)
Creatinine, >111 μmol/L	19 (24.7)
Lactic dehydrogenase, >250 U/L	68 (88.3)
Creatine kinase, >310 U/L	8 (10.4)
Coagulation	
Prothrombin time, <9 sec	0 (0.0)
Activated partial prothrombin time, <25 sec	4 (5.2)
D-dimer, >0.55 mg/L	59 (76.6)
Cell immunity [a]	
CD4+ cell count, <404/uL	52 (98.1)
CD4+ cell count, <202/uL	32 (60.4)
CD8+ cell count, <220/uL	43 (81.1)
Lactic acid in blood gas analysis, >1.5 mmol/L	68 (88.3)

Note: [a] The below analysis was done in the cases with the result of Cell immunity, so the total number is 53 for all

Table 3. Comparison of Clinical Characteristics among Different Subgroups

Characteristics	All	Gender			Age at death			Survival Time, days			Complicated with Hypertension[d]		
	(N=77)	Male (n=51)	Female (n=26)	*P* value*	≤ 65y (n=24)	> 65y (n=53)	*P* value*	<14 days (n=29)	≥14 days (n=48)	*P* value*	Yes (n=32)	No (n=24)	*P* value*
Age at death, mean (min-max), years	71 (31-95)	69 (31-95)	75 (52-94)	0.057[b]	NA	NA	NA	71 (39-95)	71 (31-94)	0.906[b]	74 (51-94)	74 (42-95)	0.962[b]
Male	51(66.2)	NA	NA	NA	20 (83.3)	31 (58.5)	0.033	22 (75.9)	29 (60.4)	0.165	24 (75.0)	14 (58.3)	0.186
Mean survival time (from disease onset to death), days	17.4	16.9	18.5	0.418[b]	17.0	17.6	0.774[b]	NA	NA	NA	17.1	17.8	0.773[b]
Initial symptoms													
Fever	63 (81.8)	40 (78.4)	23 (88.5)	0.360[a]	20 (83.3)	43 (81.1)	1.000[a]	24 (82.8)	39 (81.3)	0.868	27 (84.4)	17 (70.8)	0.222
Cough	15 (19.5)	6 (11.8)	9 (34.6)	0.017	5 (20.8)	10 (18.9)	1.000[a]	7 (24.1)	8 (16.7)	0.423	9 (28.1)	6 (25.0)	0.794
Dyspnea	25 (32.5)	14 (27.5)	11 (42.3)	0.188	7 (29.2)	18 (34.0)	0.677	9 (31.0)	16 (33.3)	0.835	13 (40.6)	5 (20.8)	0.117
Fatigue	12 (15.6)	10 (19.6)	2 (7.7)	0.318[a]	1 (4.2)	11 (20.8)	0.091[a]	3 (10.3)	9 (18.8)	0.518[a]	3 (9.4)	4 (16.7)	0.447[a]
Abdominal pain, diarrhea	3 (3.9)	3 (5.9)	0 (0.0)	0.547[a]	1 (4.2)	2 (3.8)	1.000[a]	2 (6.9)	1 (2.1)	0.553[a]	1 (3.1)	1 (4.2)	1.000[a]
Neurological symptoms	4 (5.2)	4 (7.8)	0 (0.0)	0.294[a]	1 (4.2)	3 (5.7)	1.000[a]	3 (10.3)	1 (2.1)	0.147[a]	1 (3.1)	1 (4.2)	1.000[a]
Comorbidities													
Any of comorbidities	56 (72.7)	38 (74.5)	18 (69.2)	0.623	15 (62.5)	41 (77.4)	0.175	21 (72.4)	35 (72.9)	0.962	NA	NA	NA
Hypertension[c]	33 (58.9)	24 (63.2)	9 (50.0)	0.350	8 (53.3)	25 (61.0)	0.607	12 (57.1)	21 (60.0)	0.833	NA	NA	NA
Heart disease[c]	18 (32.1)	12 (31.6)	6 (33.3)	0.896	4 (26.7)	14 (34.1)	0.751[a]	9 (42.9)	9 (25.7)	0.184	NA	NA	NA
Diabetes[c]	18 (32.1)	7 (18.4)	11 (61.1)	0.001	3 (20.0)	15 (36.6)	0.338[a]	4 (19.0)	14 (40.0)	0.104	NA	NA	NA
Chronic lung disease[c]	8 (14.3	5 (13.2)	3 (16.7)	0.703[a]	4 (26.7)	4 (9.8)	0.190[a]	1 (4.8)	7 (20.0)	0.235[a]	NA	NA	NA
Cerebrovascular disease[c]	7 (12.5)	5 (13%)	2 (11.1)	1.000[a]	0 ((0.0))	7 (17.1)	0.171[a]	3 (14.3)	4 (11.4)	1.000[a]	NA	NA	NA
Nephropathy[c]	7 (13.5)	4 (10.5)	3 (16.7)	0.669[a]	2 (13.3)	5 (12.2)	1.000[a]	2 (9.5)	5 (14.3)	0.700[a]	NA	NA	NA
Liver disease[c]	4 (7.1)	2 (5.3)	2 (11.1)	0.587[a]	1 (6.7)	3 (7.3)	1.000[a]	1 (4.8)	3 (8.6)	1.000[a]	NA	NA	NA
Cancers[c]	2 (3.6)	2 (5.3)	0 (0.0)	1.000[a]	0 (0.0)	2 (4.9)	1.000[a]	2 (9.5)	0 (0.0)	0.136[a]	NA	NA	NA
Surgery[c]	1 (1.8)	1 (2.6)	0 (0.0)	1.000[a]	1 (6.7)	0 ((0.0))	0.268[a]	0 (0.0)	1 (2.9)	1.000[a]	NA	NA	NA
Others[c]	4 (7.1)	3 (7.9)	1 (5.6)	1.000[a]	1 (6.7)	3 (7.3)	1.000[a]	3 (14.3)	1 (2.9)	0.143[a]	NA	NA	NA
Causes of death													
Acute respiratory distress syndrome	67 (87.0)	43 (84.3)	24 (92.3)	0.480[a]	19 (79.2)	48 (90.6)	0.270[a]	23 (79.3)	43 (89.6)	0.314[a]	29 (90.6)	18 (75.0)	0.151[a]
Sepsis	14 (18.2)	12 (23.5)	2 (7.7)	0.122[a]	4 (16.7)	8 (15.1)	1.000[a]	8 (27.6)	6 (12.5)	0.096	8 (27.6)	4 (22.2)	0.452
Nervous system disease	3 (3.9)	2 (3.9)	1(3.8)	1.000[a]	2 (8.3)	1 (1.9)	0.228[a]	1 (3.4)	2 (4.2)	1.000[a]	0 (0.0)	3 (12.5)	0.073[a]
Heart disease	2 (2.6)	2 (3.9)	0 (0.0)	0.547[a]	0 (0.0)	2 (3.9)	1.000[a]	2 (6.9)	0 (0.0)	0.139[a]	1 (3.4)	1 (4.2)	1.000[a]
Gastrointestinal bleeding	2 (2.6)	2 (3.9)	0 (0.0)	0.547[a]	0 (0.0)	2 (3.9)	1.000[a]	1 (3.4)	1 (2.1)	1.000[a]	1 (3.4)	1 (4.2)	1.000[a]
Others	3 (3.9)	2 (3.9)	1 (3.8)	1.000[a]	2 (8.3)	1 (1.9)	0.228[a]	2 (6.9)	1 (2.1)	0.553[a]	0 (0.0)	3 (12.5)	0.073[a]
Mean time from admission to endotracheal intubation, days	6	5	8		5	7		6	9		8	1	

Notes: NA means "Not Applicated"

* Chi-square test is used except for special denote.

[a] Fisher's exact test;

[b] T test;

[c] Analysis was done in the cases with any comorbidity, so the total number is 56 for all cases; 38 for male and 18 for female among the gender subgroup; 15 for cases aged at 65 and below and 41 for cases aged beyond 65; 21 for cases with dead time less than 14 days and below and 35 for cases with dead time no less than 14;

[d] The patients including in this analysis was with at least one of comorbidities, so the total number of this analysis was 56 (32 for cases with hypertension, 24 for cases without hypertension).

Figures

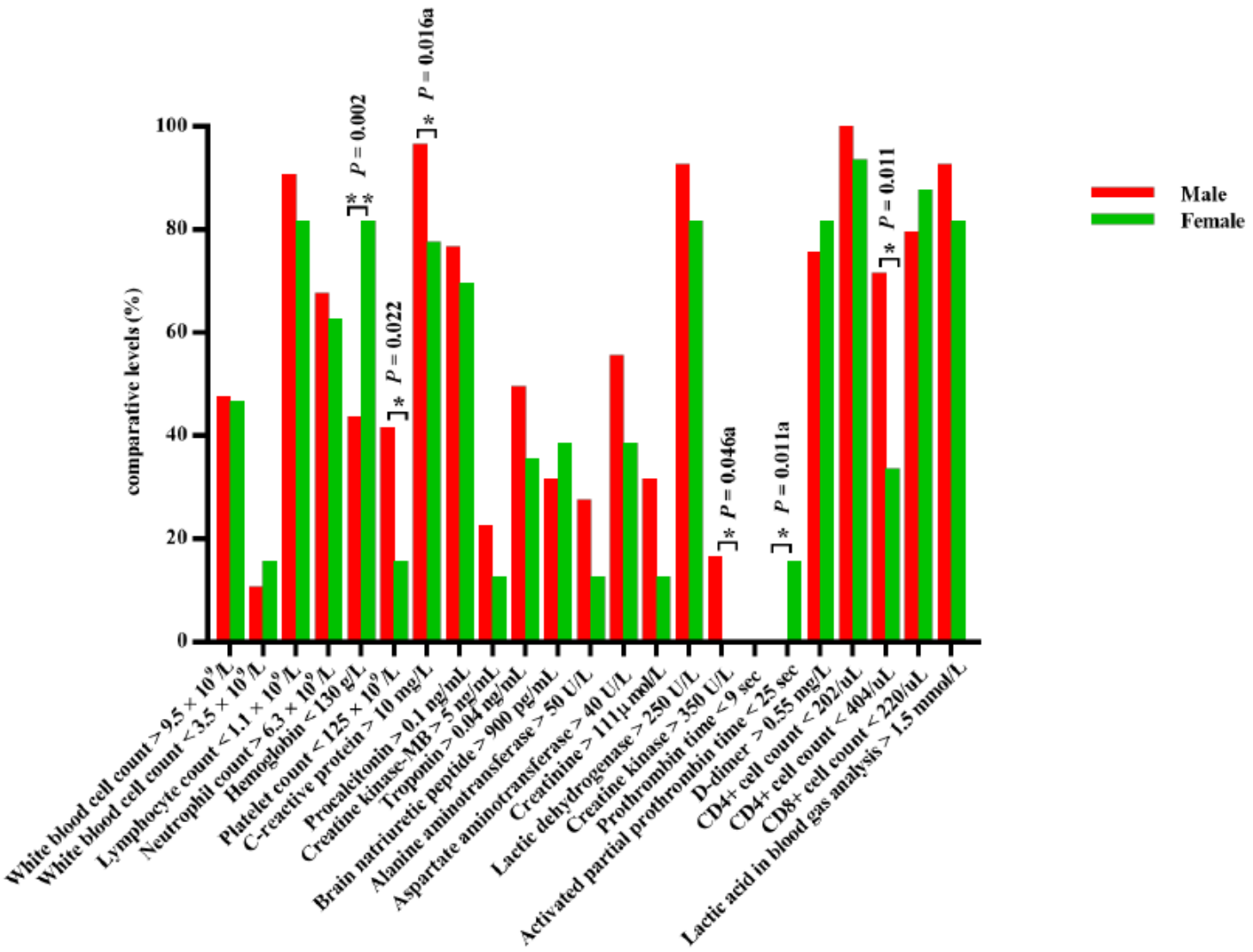

Figure 1 Comparison of clinical characteristics of COVID-19 patients with different gender

Figure 1

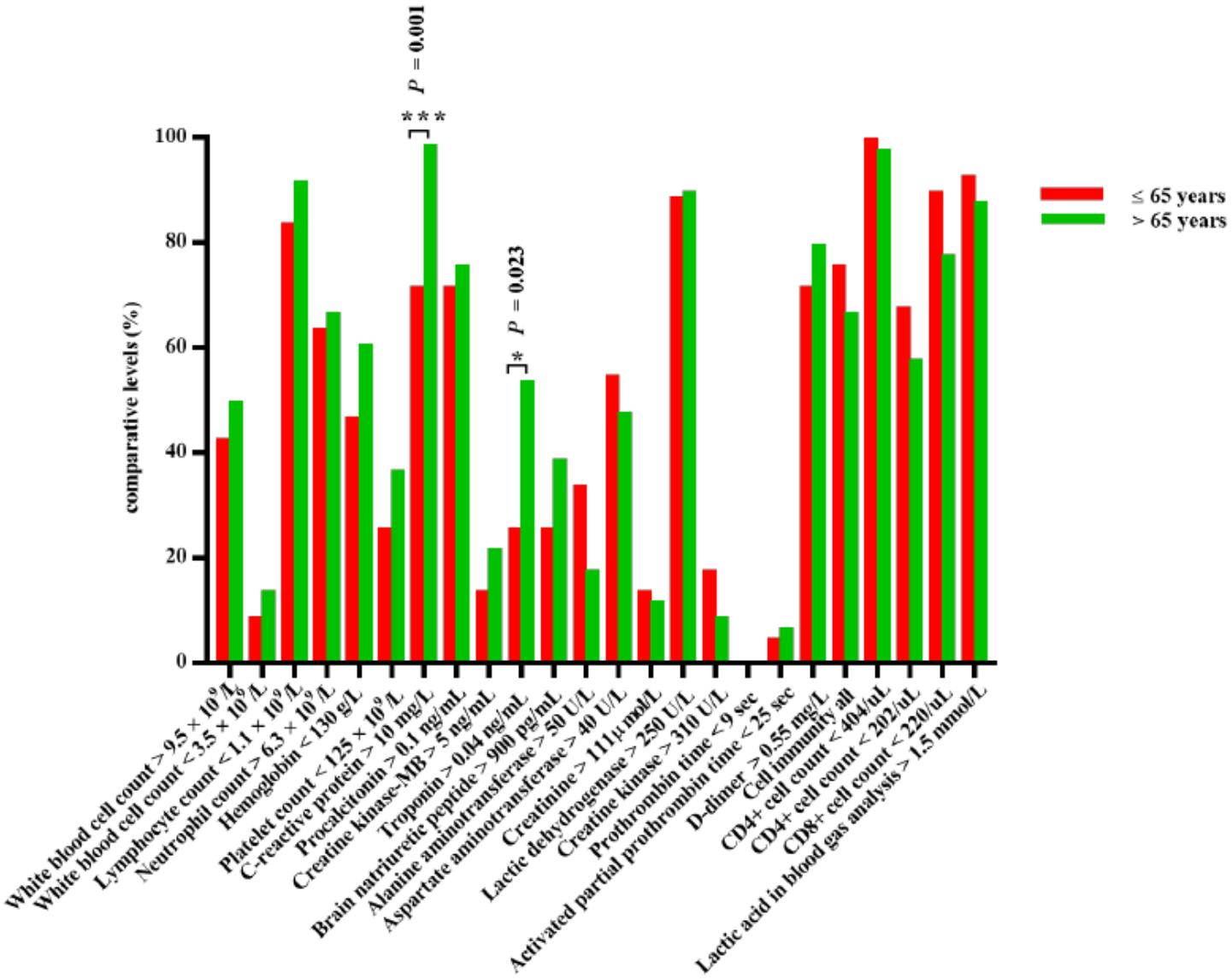

Figure 2 Comparison of clinical characteristics of COVID-19 patients with different age

Figure 2

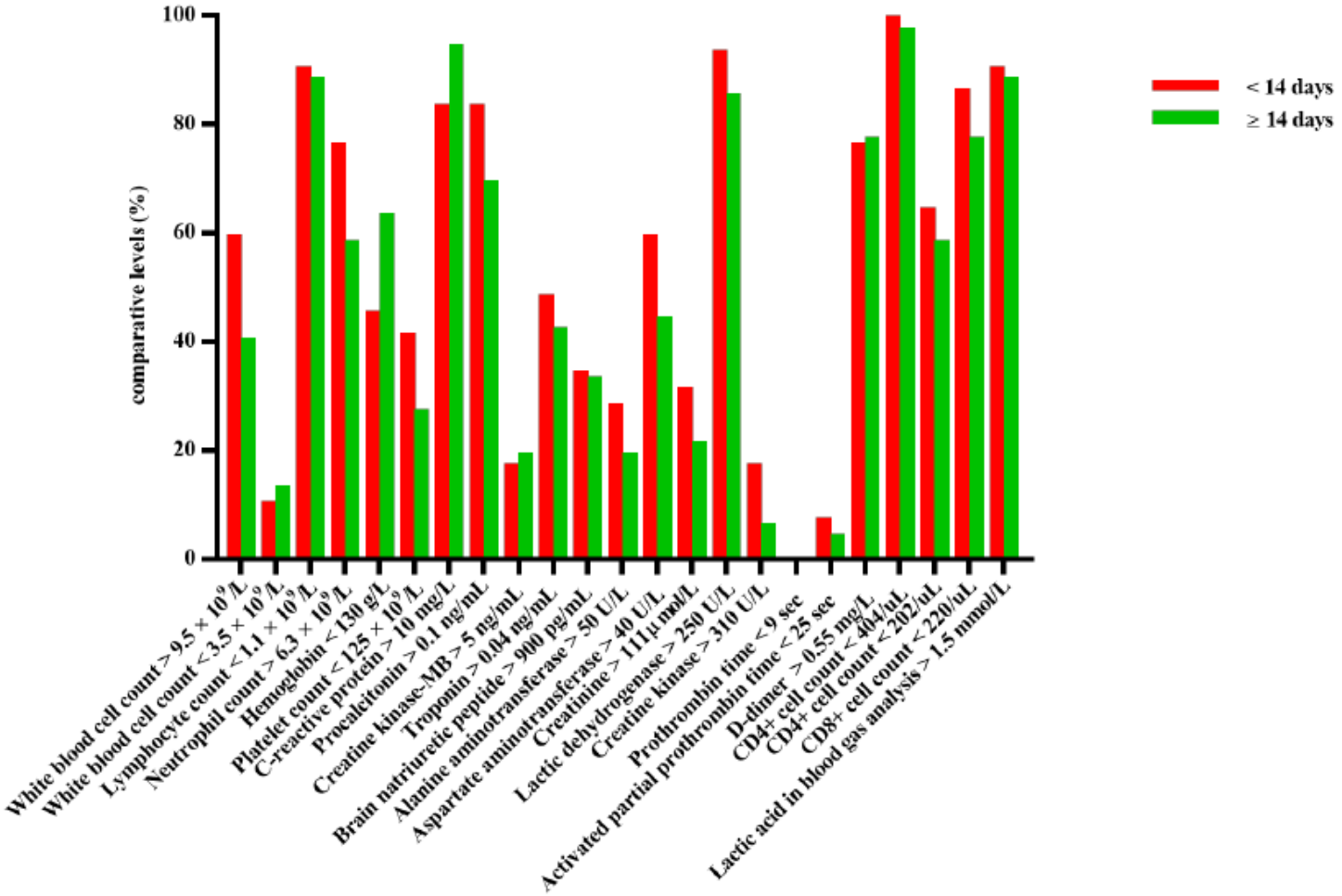

Figure 3 Comparison of clinical characteristics of COVID-19 patients with different survival time

Figure 3

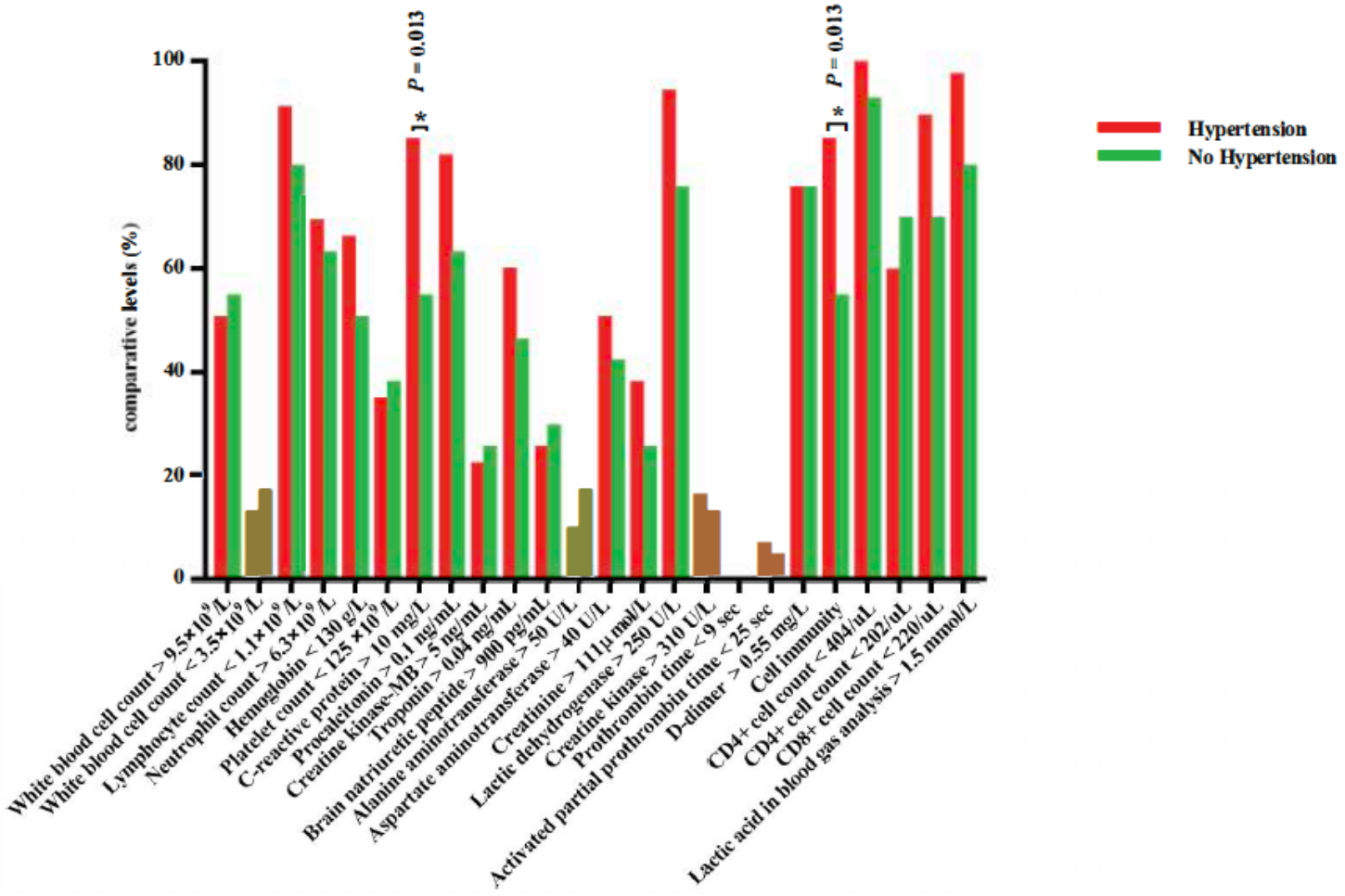

Figure 4 Comparison of clinical characteristics of COVID-19 patients with hypertension and without hypertension

Figure 4

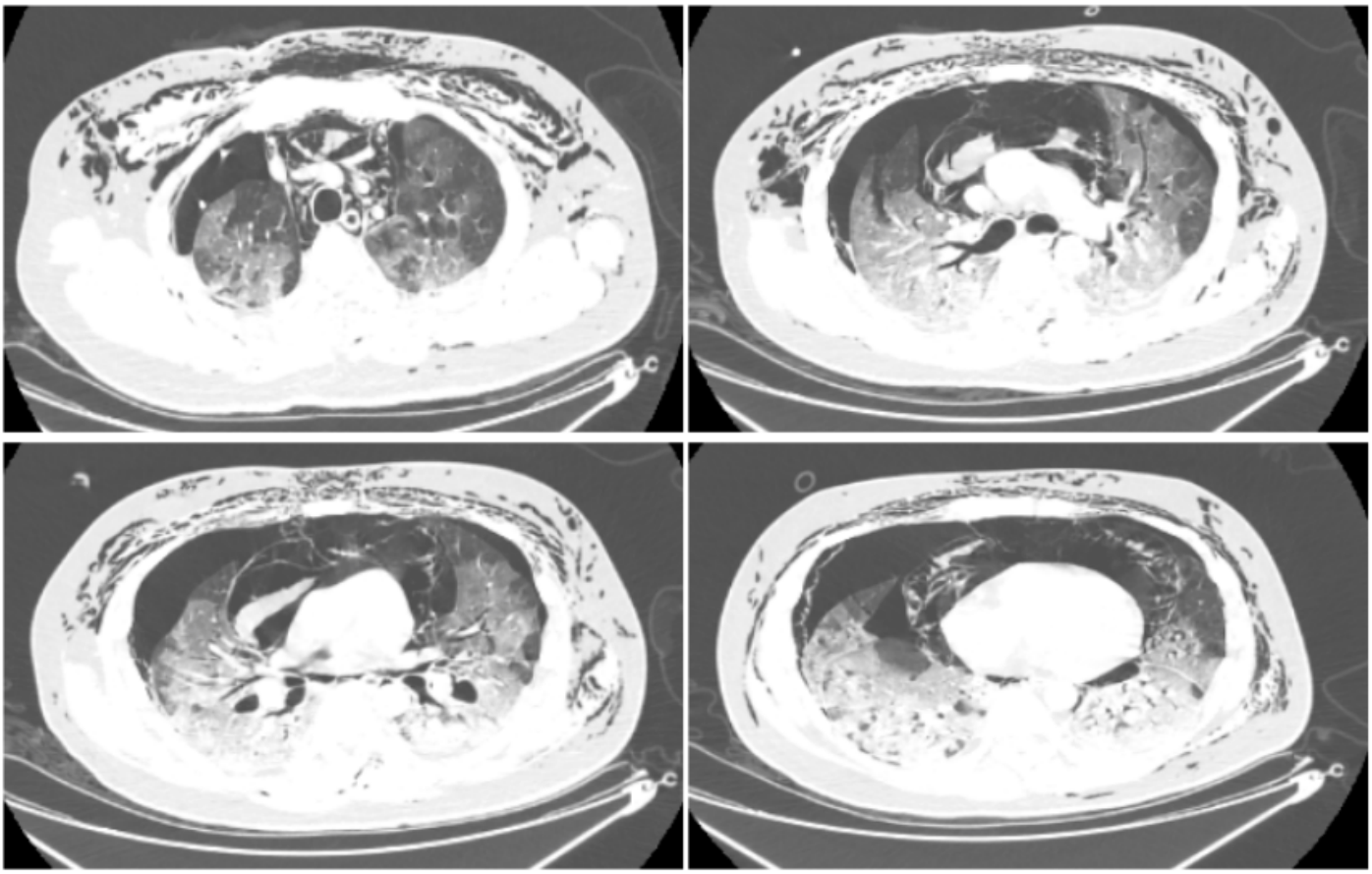

Figure 5 A 31-year-old male patient rapidly progressed to ARDS after onset and developed bilateral spontaneous pneumothorax

Figure 5