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Predictors of Mortality for Patients with COVID-19 Pneumonia Caused by SARS-CoV-2: A Prospective Cohort Study

Short running head: Mortality of COVID-19 pneumonia

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ABSTRACT To identify factors associated with the death for patients with COVID-19 pneumonia caused by a novel coronavirus SARS-CoV-2.

All clinical and laboratory parameters were collected prospectively from a cohort of patients with COVID-19 pneumonia who were hospitalized to Wuhan Pulmonary Hospital, Wuhan City, Hubei Province, China, between December 25, 2019 and February 7, 2020. Univariate and multivariate logistic regression was performed to investigate the relationship between each variable and the risk for death of COVID-19 pneumonia patients.

A total of 179 patients with COVID-19 pneumonia (97 male and 82 female) were included in the present prospective study, of whom 21 died. Univariate and multivariate logistic regression analysis revealed that age ≥ 65 years (odd ratio, 3.765; 95% confidence interval, 1.146–17.394; *P* = 0.023), preexisting concurrent cardiovascular or cerebrovascular diseases (2.464; 0.755–8.044; *P* = 0.007), $CD3^+CD8^+$ T cells ≤ 75 cell/μL (3.982; 1.132–14.006; *P* < 0.001), and cardiac troponin I ≥ 0.05 ng/mL (4.077; 1.166–14.253; *P* < 0.001) were associated with an increase in risk of mortality of COVID-19 pneumonia. In the sex–, age–, and comorbid illness-matched case study, $CD3^+CD8^+$ T cells ≤ 75 cell/μL and cardiac troponin I ≥ 0.05 ng/mL remained to be the predictors for high mortality of COVID-19 pneumonia.

We identified four risk factors, age ≥ 65 years, preexisting concurrent cardiovascular or cerebrovascular diseases, $CD3^+CD8^+$ T cells ≤ 75 cell/μL, and cardiac troponin I ≥ 0.05 ng/mL, especially the latter two factors, were predictors for mortality of COVID-19 pneumonia patients.

Introduction

In December 2019, a new contagious named COVID-19 pneumonia caused by a novel coronavirus (SARS-CoV-2) emerged in Wuhan, Hubei, China, and now spreads across international borders.[1-3] Up to the date of February 12, 2020, 189 medical teams consisting of 21569 doctors and nurses from 29 provinces of China were sent to Hubei to deal with COVID-19 pneumonia.[4] The ongoing COVID-19 pneumonia pandemic is currently not under control, with a high risk of spread in China and globally. As of March 22, 2020, a total of 307,297 confirmed cases had been reported in at least 169 countries.[5] Unfortunately, the effect of the outbreak of COVID-19 pneumonia and ultimate scope is unclear so far as the situation is rapidly evolving.[6, 7] As a matter of fact, the fear of ongoing COVID-19 epidemic was and is playing a major role in the economic and social consequences.

In the first published cohort of 41 patients with COVID-19 pneumonia from Wuhan Jinyintan Hospital, six (14.6%) patients worsened in a short period of time and died of multiple organ failure;[8] when the cohort size expanded to 99 cases, 11 (11.1%) patients died.[9] In another Wuhan cohort of hospitalized patients with COVID-19 pneumonia, the overall mortality was 4.3% (6/138).[10] The findings from these three previous studies suggested that older age and underlying comorbidities was associated with disease severity or death of COVID-19 pneumonia patients.[8-10] Between December 25, 2019 and February 7, 2020, a total of 179 adult patients with COVID-19 pneumonia were hospitalized to Wuhan Pulmonary Hospital, a special hospital for isolating and treating patients with infectious diseases. As of March 24, 2020, 158 patients had been discharged and the remaining 21 had died. In the present study, we sought to identify the clinical and laboratory parameters associated with mortality of patients with COVID-19 pneumonia.

Methods

Patients

This study was conducted in accordance with the approved guidelines of the Institutional Review Board of Wuhan Pulmonary Hospital, Wuhan city, Hubei Province, China (wufeilunli-2020-02). The written informed consent from each patient was waived since we prospectively collected and analyzed all data from each patient according to the policy for public health outbreak investigation of emerging infectious diseases issued by the National Health Commission of the People's Republic of China.

Between December 25, 2019 and February 7, 2020, a single-center case cohort of the 179 consecutive patients with confirmed and probable COVID-19 pneumonia were hospitalized to Wuhan Pulmonary Hospital, and they were all included in the present study. The probable and definite diagnosis of COVID-19 pneumonia was established according to the case definition established by WHO interim guidance.[11]

Data collection and analysis

The information of all patients including demographic data, clinical characteristics, laboratory parameters, and outcomes were collected prospectively. Two researchers independently reviewed the data collection forms to double check the collected data.

Descriptive statistics included frequency analysis (percentages) for categorical variables and means ± standard deviations (SD) or medians and interquartile ranges (IQRs) for continuous variables. Comparisons were determined by Student's *t* test or Mann-Whitney U test for continuous variables as appropriate and by the use of the χ^2 test or Fisher exact test for categorical variables. Univariate and multivariate logistic regression were performed to explore the association of clinical characteristics and laboratory parameters and the risk for death. The backward conditional method was used to select imaging variables entering the scoring system. The statistical significance level

was set at 0.05 (two-tailed). All analyses were conducted with MedCalc and SPSS version 23.0 statistical software.

Results

Clinical data

This report describes a COVID-19 pneumonia cohort of 179 patients who were hospitalized to Wuhan Pulmonary Hospital between December 25, 2019 and February 7, 2020, of whom 136 (76%) were diagnosed definitely as having COVID-19 pneumonia with positive SARS-CoV-2 test result and the remaining 43 (24%) were diagnosed clinically. The mean time between onset of symptoms and hospitalization was 9.7 days (SD, 4.3 days). The mean age was 57.6 years (SD, 13.7 years; range, 18–87 years), and 97 (54.2%) were men (Table 1). Of 179 patients, 21 (11.7%) worsened in a short period of time and died of multiple organ failure, especially respiratory failure and heart failure, and the mean duration from admission to death was 13.7 days (SD, 8.3 day; rang, 3–33 days) (Supplementary Table 1).

As shown in Table 1, the patients in deceased group were much older than those in survivor group (70.2±7.7 years *vs.* 56.0±13.5 years, $P < 0.001$). We noted that more patients in deceased group had hypertension (61.9% *vs.* 28.5%, $P = 0.005$) and cardiovascular or cerebrovascular diseases (57.1% *vs.* 10.8%, $P < 0.001$), and that there was no difference in the incidence of diabetes, chronic digestive disorders, tuberculosis, chronic hepatic or renal insufficiency, peripheral vascular disease, and malignancy between the two groups (all $P > 0.05$).

Very similar to the findings reported in the previous studies,[8-10, 12] we noted that the top five common symptoms included fever (98.9% of the patients), dry cough (81.6%), dyspnea (49.7%), fatigue (39.1%), and sputum production (30.7%), etc. on admission among the total population (Table 1). Except for dyspnea, fatigue, sputum production and headache that were more frequently

present in deceased group than survivor group (85.7% *vs.* 44.9%, *P* < 0.001; 61.9% *vs.*36.7%, *P*=0.033; 57.1% *vs.*27.2%, *P*=0.010; 23.8% *vs*. 7.6%, *P*=0.033), other kinds of symptoms were similar in the two groups. Patients in deceased group had higher respiratory rate than survivor group (*P* = 0.016), there was no difference in heart rate.

Laboratory findings

Might be due to the presence of secondary bacterial infection as suggested by higher concentrations of C-response protein and procalcitonin, the deceased had more white blood cells and neutrophils than the survivors did (Table 2). Actually, lung secondary bacterial infection were documented at late stage of disease in 10 of 21 deceased patients, and the etiological spectrum included *Klebsiella Pneumoniae, Staphylococcus, Acinetobacter Baumannii,* and *Escherichia Coli,* etc. As expected, the deceased had reduced lymphocytes as compared to the survivors. One remarkable finding was that absolute numbers of $CD3^+CD8^+$ T cells, but not $CD3^+CD4^+$ T cells, were significantly reduced in deceased as compared to survivors.

Compared to the patients in survivor group, those in deceased group underwent more frequently and more severe heart injury, as all laboratory parameters reflecting heart function, including cardiac troponin I, myoglobin, and brain natriuretic peptide, were all significantly elevated in the deceased (Table 2 and Table 3). The deceased were more susceptible to hepatic or renal insufficiency, and respiratory failure, indicated by the elevation of aspartate aminotransferase or creatinine, and the reduction of arterial partial pressure of oxygen (PaO_2) and a ratio of PaO_2 to fraction of inspiration O_2 (F_IO_2).

Predictors of mortality

For all demographic data, clinical presentation, and laboratory findings presented in Table 1 and Table 2, we initially evaluated each variable that displayed statistical significance with $p < 0.05$ in difference between non-survivors and survivors using univariate analysis. Our analysis revealed that

age ≥ 65 years, hypertension, cardiovascular or cerebrovascular diseases, dyspnea, fatigue, sputum production, headache, white blood cell counts > 10× 10^9/L, neutrophils > 6.3 × 10^9/L, $CD3^+CD8^+$ T cells ≤ 75 cell/μL, cardiac troponin I ≥ 0.05 ng/mL, myoglobin > 100 ng/L, creatinine ≥ 133 μmol/L, D-dimer ≥ 0.5 mg/L, and < 60 mmHg was associated with the death of patients with COVID-19 pneumonia (Table 3). In all studied variables, PaO_2 ≥ 80 mmHg was the only one factor that was associated with patients' survival (odd ratio, 0.233 [95% CI, 0.065–0.840]; *P* = 0.026). The above 16 variables were further processed using a multivariable logistic regression model which selected four variables that were predictive of mortality, including age group ≥ 65 years, cardiovascular or cerebrovascular diseases, $CD3^+CD8^+$ T cells ≤ 75 cell/μL, and cardiac troponin I ≥ 0.05 ng/mL (Table 4).

To further understand the factors that can affect the survival of COVID-19 pneumonia patients with similar age and underlying diseases, we selected sex–, age–, and underlying disease–matched 42 patients from survivors to perform a case-control study at a ratio of 2 : 1. As shown in Appendix Table 2, there was no difference in all parameters of demography and clinical presentation between deceased and the matched case-control survivors. Given that many survivors were younger people, two survivors whose age was the same or ± one year were matched to each one deceased. As compared to survivors, deceased had significant increased concentrations of procalcitonin, cardiac troponin I, myoglobin, and creatinine and significant reduced numbers of $CD3^+CD8^+$ T cells (Appendix Table 3). After excluded the impact of age and underlying diseases on mortality, univariate analysis indicated that $CD3^+CD8^+$ T cells ≤ 75 cell/μL and cardiac troponin I ≥ 0.05 ng/mL were the only two variables that could be predictors of mortality of patients with COVID-19 pneumonia (Table 5).

Discussion

The ongoing SARS-CoV-2 epidemic was a third time that a zoonotic coronavirus has crossed species to infect human populations during the past 18 years.[13] In November, 2002, severe acute respiratory syndrome (SARS) caused by SARS-CoV were first found in Guangdong province, China, and the number of SARS cases increased substantially in the next year in China and later spread globally,[14] infecting 8098 people in 26 countries and killing 774 of them.[15] Between September 2012 and January 20, 2017, the outbreak of 1879 laboratory-confirmed cases of Middle East respiratory syndrome (MERS) caused by MERS-CoV in 27 countries, resulting in at least 659 related deaths.[16] As of the midnight of March 24, 2020, numbers of Chinese confirmed COVID-19 pneumonia cases and death were 81218 and 3281, respectively, indicating that the overall death rate of COVID-19 pneumonia was 4%.[17]

In Wuhan city, two large-scale special hospitals, Wuhan Pulmonary Hospital and Wuhan Jinyintan Hospital, provide medical service for patients with infectious diseases. Since the outbreak of COVID-19 pneumonia, all patients in the two hospitals have been being COVID-19 pneumonia cases. Usually, only those patients with severe disease from general hospitals were transferred in the especial hospitals for quarantine and treatment. This was why the overall mortality of COVID-19 pneumonia in the special hospitals (11.1% in the cohort of Wuhan Jinyintan Hospital [9] and 11.7% [95% CI, 7.0–16.5%] in our current cohort) seemed to be higher than that in the cohort of a general hospital (4.3%).[10] Unfortunately, no anti-SARS-CoV-2 drugs were available for treating patients with COVID-19 pneumonia. Although none of antibiotic, antifungal drug, corticosteroid, or immune globulin is routinely recommended to be administered for COVID-19 pneumonia, a combination consisting of two or more of the above drugs was given to all critical ill patients in the present study.

It has been documented that although there are some similarities in the clinical features between SARS and MERS, MERS progresses to respiratory failure much more rapidly with much higher mortality than SARS, and that older age and underlying illness is likely related to the mortality

of MERS.[18] In the present study, patients in deceased group were much older than survivors, and univariate and multivariate logistic regression analysis revealed age ≥ 65 years as a strong predictor for death of COVID-19 pneumonia. Actually, in the whole cohort of 179 COVID-19 pneumonia patients, no one died who was younger than 50 years whereas 17 (81%) of deceased patients were older than 65 years. As expected, our analysis also revealed that underlying cardiovascular or cerebrovascular diseases contributed to high mortality of COVID-19 pneumonia.

It has been demonstrated that inactivated SARS-CoV elicits an antigen-specific recall cytotoxic T lymphocyte response in peripheral blood mononuclear cells of recovered SARS patients, but not in the patients with critical SARS or died of SARS, suggesting that the latter apparently cannot generate sufficient protective immunity to eliminate SARS-CoV; their immune responses to this pathogen may have in fact exacerbated their illness.[19] In case of MERS, several inflammatory mediators, including inducible protein-10, monocyte chemoattractant protein-1, and interleukin-6 concentrations, are strongly associated with mortality.[20] Given that COVID-19 pneumonia is an emerging infectious disease, the mechanisms by which SARS-CoV-2 causes severe illness and fatal outcomes in humans are unknown. More recently, $CD8^+$ T cells have been reported to be significantly decreased in peripheral blood in patients with COVID-19 pneumonia.[21] It has been shown that several cytokines and chemokines, such as interleukin-2, interleukin-7, interleukin-10, macrophage colony-stimulating factor, inducible protein-10, monocyte chemoattractant protein-1, macrophage inflammatory protein-1α, and tumor necrosis factor-α concentrations were higher in patients with severe COVID-19 pneumonia than in those with mild disease, suggesting that SARS-CoV-2 infection damages human immune system and results in systematic inflammatory response.[8] One important finding in our study was that $CD3^+CD8^+$ T cells, but not $CD3^+CD4^+$ T cells, in circulation were tremendously reduced in deceased patients compared to either the total survived population or those sex–, age–, and comorbid illness-matched controls. More importantly, $CD3^+CD8^+$ T cells ≤ 75 cell/μL, was a reliable predictor for mortality of patient with COVID-19 pneumonia. These data indicated that

progressive immune-associated injury and inadequate adaptive immune responses could be possible mechanisms by which SARS-CoV-2 causes severe illness and fatal outcomes.

On March 24, 2020, China had 4287 current cases with confirmed COVID-19 pneumonia, and 1399 (32.6%) of them were very severe cases.[17] As above mentioned, the overall death rate of COVID-19 pneumonia was 4%,[17] and most deceased patients were older people with underlying illness.[8-10] For a younger cohort of 1716 Chinese medical staff whose age was always < 65 years all over the country, 6 (0.3%) died.[22] These data suggest that the majority of patients with COVID-19 pneumonia would recover from the disease, especially younger people. Our current data demonstrated that patients in deceased group were susceptible to undergo multiple organ failure, especially heart failure and respiratory failure. One of the best laboratory parameters inflecting heart injury for predicting mortality of COVID-19 pneumonia was cardiac troponin I, and this parameter remained to be valid in the sex–, age–, and underlying illness–matched control analysis. Our findings suggest that in the care of critical ill patients with COVID-19 pneumonia, protection strategy of vital organs should be emphasized for their survival. It should be noted that the elevation of cardiac troponin I in COVID-19 patients was just indicative of myocardial injury that was probably secondary to severe hypoxemia. For patients with positive cardiac troponin I result, what we could do was choosing appropriate respiratory support strategy to improve oxygenation and waiting for the recovery of myocardial damage.

In conclusions, we identified four predictors, age ≥ 65 years, preexisting concurrent cardiovascular or cerebrovascular diseases, $CD3^+CD8^+$ T cells ≤ 75 cell/μL, and cardiac troponin I ≥ 0.05 ng/mL, for high mortality among the overall population of COVID-19 pneumonia patients. In the sex–, age–, and comorbid illness-matched case-control study, we further found $CD3^+CD8^+$ T cells ≤ 75 cell/μL and cardiac troponin I ≥ 0.05 ng/mL remained to be the predictors for high mortality of COVID-19 pneumonia patients with similar age and underlying diseases.

Contributors: H.Z.S. and P.P. conceived the idea, designed and supervised the study, had full access to all data and took responsibility for the integrity of the data. R.H.D, C.Q.Y., T.Z.C., M.L., G.Y.G., J.D., C.L.Z., Q.Z., M.H., X.Y.L. were responsible for the diagnosis and treatment patients, and collected the clinical and laboratory data. L.R.L. and W.W. analyzed data and performed statistical analysis. All authors reviewed and approved the final version.

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Table 1. Demography and Clinical Presentation in Patients with COVID-19 pneumonia*.

Characteristic	Total (n = 179)	Deceased (n = 21)	Survivors (n = 158)	*P* value
Age, years	57.6±13.7	70.2±7.7	56.0±13.5	< 0.001
Sex, n (%)				0.642
Male	97 (54.2)	10 (47.6)	87 (55.1)	
Female	82 (45.8)	11 (52.4)	71 (44.9)	
Underlying diseases, n (%)				
Hypertension	58 (32.4)	13 (61.9)	45 (28.5)	0.005
Cardiovascular or cerebrovascular diseases	29 (16.2)	12 (57.1)	17 (10.8)	< 0.001
Diabetes	33 (18.4)	6 (28.6)	27 (17.1)	0.231
Chronic digestive disorders	21 (11.7)	4 (19.0)	17 (10.8)	0.279
Tuberculosis	8 (4.5)	0 (0)	8 (5.1)	0.599
Chronic hepatic or renal insufficiency	4 (2.2)	2 (9.5)	2 (1.3)	0.068
Peripheral vascular disease	4 (2.2)	2 (9.5)	2 (1.3)	0.068
Malignancy	4 (2.2)	1 (4.8)	3 (1.9)	0.396
Symptom, n (%)				
Fever	177 (98.9)	21 (100)	156 (98.7)	1.000
Dry Cough	146 (81.6)	14 (66.7)	132 (83.5)	0.074
Dyspnea	89 (49.7)	18 (85.7)	71 (44.9)	< 0.001
Fatigue	71 (39.7)	13 (61.9)	58 (36.7)	0.033
Sputum production	55 (30.7)	12 (57.1)	43 (27.2)	0.010
Gastrointestinal symptoms	39 (21.8)	8 (38.1)	31 (19.6)	0.087
Myalgia	34 (19.0)	7 (33.3)	27 (17.1)	0.083
Headache	17 (9.5)	5 (23.8)	12 (7.6)	0.033
Hemoptysis	10 (5.6)	0 (0)	10 (6.3)	0.609
Systolic blood pressure, mmHg	–	Not available	122.4±18.6	
Diastolic blood pressure, mmHg	–	Not available	77.9±10.0	
Temperature, □, n (%)				0.156
< 37.3	109 (60.9)	16 (76.2)	93 (58.9)	
≥ 37.3	70 (39.1)	5 (23.8)	65 (41.1)	
Respiratory rate, breath/min	20.0 (20.0–21.0)	20.0 (20.0–34.5)	20.0 (20.0–21.0)	0.016

Heart rate, beat/min	86.0 (78.0–100)	94.0 (78.0–109.5)	85.5 (78.0–99.3)	0.150

* Data are reported as Mean±SD, median interquartile (IQR), or n (%) as appropriate.

Table 2. Laboratory findings in Patients with COVID-19 Pneumonia*.

Characteristic	Total (n = 179)	Deceased (n = 21)	Survivors (n = 158)	*P* value
White blood cell counts, × 10^9/L	5.3 (3.9–7.8)	8.9 (4.8–13.1)	5.1 (3.8–7.3)	0.003
Neutrophils, × 10^9/L	4.0 (2.7–6.6)	7.7 (3.0–11.5)	3.9 (2.6–6.1)	0.007
Lymphocytes, × 10^9/L	0.8 (0.6–1.1)	0.7 (0.5–0.8)	0.8 (0.6–1.1)	0.046
T cell subsets				
$CD3^+CD4^+$ T cells, cell/μL	114.3 (62.9–195.3)	68.0 (55.1–148.8)	128.3 (73.5–201.7)	0.066
$CD3^+CD8^+$ T cells, cell/μL	75.5 (45.5–125.0)	47.9 (25.4–73.8)	104.5 (58.5–142.7)	0.001
C-reactive protein, mg/L	39.8 (20.6–97.8)	86.4 (37.9–105.5)	36.0 (19.3–91.0)	0.012
Procalcitonin, ng/mL	0.1 (0.0–0.2)	0.1 (0.1–0.5)	0.1 (0.0–0.2)	0.013
Cardiac troponin I, ng/mL	0.0 (0.0–0.1)	0.1 (0.0–0.8)	0.0 (0.0–0.0)	< 0.001
Myoglobin, ng/mL	36.9 (18.4–124.0)	162.0 (48.5–342.8)	32.3 (15.5–60.3)	< 0.001
Brain natriuretic peptide, pg/mL	645.0 (110.0–1504.0)	970.0 (620.5-3531.0)	390.0 (58.0-1118.5)	0.004
Albumin, g/L	33.2 (30.7–36.4)	33.2 (31.2–35.6)	33.0 (30.6–38.1)	0.764
Total bilirubin, μmol/L	8.9 (6.6–12.5)	9.6 (8.3–16.3)	8.7 (6.5–12.3)	0.146
Direct bilirubin, μmol/L	2.5 (1.8–3.9)	3.1 (2.3–6.1)	2.4 (1.8–3.8)	0.101
Alanine aminotransferase, U/L	22.0 (15.0–40.0)	27.0 (20.0–37.0)	22.0 (14.0–40.5)	0.233
Aspartate aminotransferase, U/L	30.0 (19.0–43.0)	40.0 (27.0–61.5)	27.5 (19.0–42.0)	0.010
γ-Glutamyltranspeptidase, U/L	29.0 (17.0–52.5)	23.0 (16.5–42.0)	29.0 (17.0–54.5)	0.518
Creatinine, μmol/L	66.5 (55.8–82.0)	95.0 (63.0–112.0)	65.0 (55.0–80.0)	0.001
D-dimer, mg/L	0.5 (0.3–1.7)	1.1 (0.4–10.5)	0.5 (0.3–1.2)	0.011
Prothrombin time, s	13.7 (12.4–15.4)	13.9 (12.3–16.3)	13.7 (12.4–15.2)	0.758
Activated partial thromboplastin time, s	35.6 (31.0–39.4)	37.8 (30.8–41.5)	35.3 (30.9–39.1)	0.383
PaO_2, mmHg	72.0 (57.0–88.0)	56.0 (49.0 –71.0)	74.5 (59.0–92.0)	0.001
$PaCO_2$, mmHg	37.0 (33.0–	34.0 (29.0–41.0)	37.0 (34.0–41.0)	0.068

	41.0)			
PaO_2:F_IO_2, mmHg	249.6±106.1	185.5±64.8	261.5±108.2	0.002

*Data are reported as median interquartile (IQR).

PaO_2 = arterial partial pressure of oxygen, $PaCO_2$ = arterial partial pressure of carbon dioxide, F_IO_2 = fraction of inspiration O_2.

Table 3. Univariate Analysis of Mortality Risk Factors for Patients with COVID-19 Pneumonia*.

Characteristic	Deceased (n = 21)	Survivors (n = 158)	OR (95%CI)	*P* value
Age group, %				
0–49 years	0	31.0	0.000 (0.000–)	0.997
50 – 64 years	19.0	38.6	2.673(0.859–8.318)	0.090
≥ 65 years	81.0	30.4	9.740 (3.113–30.476)	< 0.001
Underlying diseases, %				
Hypertension	61.9	28.5	4.081 (1.584–10.510)	0.004
Cardiovascular or cerebrovascular diseases	57.1	10.8	11.059 (4.068–30.063)	< 0.001
Symptom, %				
Dyspnea	85.7	44.9	7.352 (2.082–25.966)	0.002
Fatigue	61.9	36.7	2.802(1.096–7.160)	0.031
Sputum production	57.1	27.2	3.566 (1.403–9.061)	0.008
Headache	23.8	7.6	3.802 (1.187–12.177)	0.025
Respiratory rate > 20 breath/min, %	47.6	31.0	2.022(0.806–5.076)	0.134
White blood cell counts, %				
> 10×10^9/L	33.3	12.7	3.450 (1.242–9.580)	0.017
4–10×10^9/L	52.4	60.1	1.371 (0.550–3.418)	0.499
< 4×10^9/L	14.3	27.2	0.446 (0.125–1.590)	0.213
Neutrophil counts, %				
> 6.3×10^9/L	57.1	24.7	4.068 (1.594–10.382)	0.003
1.8–6.3×10^9/L	33.3	65.2	0.267 (0.102–0.700)	0.071
< 1.8×10^9/L	9.5	10.1	0.934 (0.199–4.384)	0.931
Lymphocyte counts < 1.1×10^9/L, %	90.5	72.2	3.667(0.820–16.400)	0.089
$CD3^+CD8^+$ T cells ≤ 75 cell/μL, %	78.9	40.0	5.625 (1.664–19.013)	0.005
C-response protein ≥ 10 mg/L, %	95.2	87.3	2.901 (0.368–22.878)	0.312
Procalcitonin ≥ 0.5 ng/mL, %	21.1	9.9	2.438 (0.631–9.414)	0.196
Cardiac troponin I ≥ 0.05 ng/mL, %	61.5	17.9	7.314 (1.832–29.210)	0.005
Myoglobin > 100 ng/mL, %	64.3	18.4	8.000 (2.157–29.671)	0.002
Brain natriuretic peptide > 100 pg/mL, %	94.1	67.6	7.680 (0.909–64.906)	0.061
Aspartate aminotransferase > 40	47.6	29.9	2.134 (0.848–5.373)	0.108

U/L, %				
Creatinine ≥ 133 µmol/L, %	19.0	2.1	11.137 (2.296–54.028)	0.003
D-dimer ≥ 0.5 mg/L, %	76.2	47.9	3.474 (1.152–10.481)	0.027
PaO_2, %				
≥ 80 mmHg	14.3	41.7	0.233 (0.065–0.840)	0.026
60–79 mmHg	28.6	32.4	0.834 (0.298–2.334)	0.730
< 60 mmHg	57.1	25.9	3.810 (1.451–10.004)	0.007
PaO_2:F_IO_2 < 200 mmHg	47.6	29.2	2.204 (0.854−5.684)	0.102

* Data are reported as median interquartile (IQR).

CI = confidence interval, OR = odd ratio, PaO_2 = Arterial partial pressure of oxygen, F_IO_2 = fraction of inspiration O_2.

Table 4. Multivariate Logistic Regression Analysis of Mortality Risk Factors for Patients with COVID-19 Pneumonia.

Variables	OR (95% CI)	*P* value
Age ≥ 65 years	3.765 (1.146–17.394)	0.023
Cardiovascular or cerebrovascular diseases	2.464 (0.755–8.044)	0.007
$CD3^+CD8^+$ T cells ≤ 75 cell/μL	3.982 (1.132–14.006)	< 0.001
Cardiac troponin I ≥ 0.05 ng/mL	4.077 (1.166–14.253)	< 0.001

CI = confidence interval, OR = odd ratio.

Table 5. Univariate Analysis of Mortality Risk Factors for Patients with COVID-19 Pneumonia in Matched Case-Control Study.

Variables	Deceased (n = 21)	Survivors (n = 42)	OR (95% CI)	*P* value
$CD3^+CD8^+$ T cells ≤ 75 cell/μL, %	78.9	42.9	5.000 (1.319–18.960)	0.018
Cardiac troponin I ≥ 0.05 ng/mL, %	61.5	18.2	7.200 (1.518–34.139)	0.013
Myoglobin > 100 ng/mL, %	60.0	28.6	3.750 (0.924–15.226)	0.064
Procalcitonin ≥ 0.5 ng/mL, %	21.1	9.1	2.667 (0.528–13.477)	0.235
Creatinine ≥ 133 μmol/L, %	19.0	4.8	4.706 (0.786–28.178)	0.090

CI = confidence interval, OR = odd ratio.

Supplementary Table 1. Characteristics of 21 Patients Who Died from COVID-19 Pneumonia.

Patient No.	Sex	Age (years)	Underlying disease	Treatment	SOFA score	Admission date	Death date
1	Male	82	Hypertension, cardiovascular or cerebrovascular diseases	Oxygen therapy, antibiotics, antiviral drug, glucocorticoids, γ-globulin, mechanical ventilation	14	Jan 24	Jan 26
2	Male	71	Hypertension, cardiovascular or cerebrovascular diseases, diabetes	Oxygen therapy, antibiotics, antiviral drug, glucocorticoids, γ-globulin, mechanical ventilation	3	Jan 15	Jan 26
3	Female	66	Hypertension	Oxygen therapy, antibiotics, antiviral drug, glucocorticoids, γ-globulin, mechanical ventilation	3	Jan 9	Jan 28
4	Male	72	Hypertension, cardiovascular or cerebrovascular diseases, diabetes	Oxygen therapy, antibiotics, antiviral drug, glucocorticoids, γ-globulin, mechanical ventilation	8	Jan 7	Jan 28
5	Male	77	Prostatitis	Oxygen therapy, antibiotics, antiviral drug, glucocorticoids, mechanical ventilation	2	Jan 23	Jan 29
6	Female	51	Hyperlipidemia	Oxygen therapy, antibiotics, antiviral drug, glucocorticoids, γ-globulin, mechanical ventilation	3	Jan 26	Jan 30
7	Female	79	Hypertension, cardiovascular or cerebrovascular diseases, diabetes, chronic digestive disorders, peripheral vascular disease, chronic renal insufficiency	Oxygen therapy, antibiotics, glucocorticoids, mechanical ventilation	7	Jan 20	Jan 26
8	Male	80	Hypertension, cardiovascular or cerebrovascular diseases, diabetes	Oxygen therapy, antibiotics, antiviral drug, mechanical ventilation	4	Jan 22	Jan 27
9	Female	62	Cardiovascular or cerebrovascular diseases, chronic digestive disorders	Oxygen therapy, antibiotics, antiviral drug, glucocorticoids, γ-globulin, mechanical ventilation, ECMO	3	Jan 6	Feb 7
10	Female	68	No	Oxygen therapy, antibiotics, antiviral drug, glucocorticoids, γ-globulin, mechanical ventilation, ECMO	3	Jan 12	Feb 1

11	Male	69	Hypertension, cardiovascular or cerebrovascular diseases, diabetes	Oxygen therapy, antibiotics, antiviral drug, glucocorticoids, γ-globulin, mechanical ventilation	6	Jan 20	Feb 3
12	Female	71	Hypertension, cardiovascular or cerebrovascular diseases, peripheral vascular disease, chronic renal insufficiency, malignancy	Oxygen therapy, antibiotics, antiviral drug, glucocorticoids, γ-globulin, mechanical ventilation	5	Feb 3	Feb 7
13	Male	77	Hypertension, benign prostatic hyperplasia	Oxygen therapy, antibiotics, antiviral drug, glucocorticoids, γ-globulin, mechanical ventilation	4	Jan 28	Feb 6
14	Female	66	Rheumatoid arthritis	Oxygen therapy, antibiotics, antiviral drug, γ-globulin, mechanical ventilation	–	Jan 25	Feb 3
15	Female	62	No	Oxygen therapy, antibiotics, antiviral drug, γ-globulin, mechanical ventilation	–	Jan 24	Feb 2
16	Male	68	Cardiovascular or cerebrovascular diseases	Oxygen therapy, antibiotics, antiviral drug, glucocorticoids, γ-globulin, mechanical ventilation	3	Jan 11	Feb 1
17	Male	72	Hypertension	Oxygen therapy, antibiotics, antiviral drug, glucocorticoids, γ-globulin, mechanical ventilation	5	Jan 28	Feb 7
18	Female	60	No	Oxygen therapy, antibiotics, antiviral drug, glucocorticoids, γ-globulin, mechanical ventilation	3	Jan 10	Feb 9
19	Female	69	Hypertension, cardiovascular or cerebrovascular diseases, chronic digestive disorders	Oxygen therapy, antibiotics, antiviral drug, glucocorticoids, γ-globulin, mechanical ventilation	3	Jan 26	Feb 8
20	Female	71	Hypertension, cardiovascular or cerebrovascular diseases	Oxygen therapy, antibiotics, antiviral drug, glucocorticoids, γ-globulin, mechanical ventilation	3	Jan 30	Feb 10
21	Male	81	Hypertension, cardiovascular or cerebrovascular diseases, diabetes, chronic digestive disorders	Oxygen therapy, antibiotics, antiviral drug, glucocorticoids, γ-globulin, mechanical ventilation	3	Jan 30	Feb 10

ECMO, extracorporeal membrane oxygenation. SOFA score, sequential organ failure assessment include oxygenation index, platelet count, cardiovascular system drug dose, glasgow coma score and creatinine.

Supplementary Table 2. Comparison of Demography and Clinical Presentation between Deceased and Gender–, Age–, and Underlying disease–Matched Case-Control Survivors*.

Characteristic	Total (n = 63)	Deceased (n = 21)	Survivors (n = 42)	*P* value
Age, years	69.7±7.7	70.2±7.7	69.5±7.8	0.741
Sex, n (%)				1.000
Male	30 (47.6)	10 (47.6)	20 (47.6)	
Female	33 (52.4)	11 (52.4)	22 (52.4)	
Underlying diseases, n (%)				
Hypertension	36 (57.1)	13 (61.9)	23 (54.8)	0.788
Cardiovascular or cerebrovascular diseases	25 (39.7)	12 (57.1)	13 (31.0)	0.059
Diabetes	20 (31.7)	6 (28.6)	14 (33.3)	0.780
Chronic digestive disorders	8 (12.7)	4 (19.0)	4 (9.5)	0.423
Tuberculosis	3 (4.8)	0 (0)	3 (7.1)	0.545
Peripheral vascular disease	4 (6.3)	2 (9.5)	2 (4.8)	0.595
Chronic hepatic or renal insufficiency	2 (3.2)	2 (9.5)	0 (0)	0.108
Malignancy	2 (3.2)	1 (4.8)	1 (2.4)	1.000
Symptom, n (%)				
Fever	63 (100)	21 (100)	42 (100)	–
Dry Cough	51 (81.0)	14 (66.7)	37 (88.1)	0.085
Dyspnea	45 (71.4)	18 (85.7)	27 (64.3)	0.137
Fatigue	42 (66.7)	13 (61.9)	29 (69.0)	0.584
Sputum production	31 (49.2)	12 (57.1)	19 (45.2)	0.430
Gastrointestinal symptoms	24 (38.1)	8 (38.1)	16 (38.1)	1.000
Myalgia	21 (33.3)	7 (33.3)	14 (33.3)	1.000
Headache	12 (19.0)	5 (23.8)	7 (16.7)	0.513
Hemoptysis	3 (4.8)	0 (0)	3 (7.1)	0.545
Systolic blood pressure, mmHg	–	Not available	121±21	
Diastolic blood pressure, mmHg	–	Not available	76±11	
Temperature, ℃, n (%)				0.053
< 37.3	40 (63.5)	16 (76.2)	24 (57.1)	
≥ 37.3	23 (36.5)	5 (23.8)	18 (42.9)	

Respiratory rate, breath/min	21.0 (20.0–30.0)	20.0(20.0–34.5)	21.0(20.0–26.3)	0.534
Heart rate, beat/min	88.0 (76.5–102.5)	94.0(78.0–109.5)	86.5(72.5–98.0)	0.083

*Data are reported as Mean±SD, median interquartile (IQR), or n (%) as appropriate.

Supplementary Table 3. Comparison of Laboratory Findings between Deceased and Age-Gender Matched Case-Control Survivors *.

Characteristic	Total (n = 63)	Deceased (n = 21)	Survivors (n = 42)	*P* value
White blood cell counts, × 10^9/L	6.6 (4.1–9.7)	8.9 (4.8–13.1)	5.8 (3.8–8.8)	0.052
Neutrophils, × 10^9/L	5.6 (2.9–8.3)	7.7 (3.0–11.5)	4.8 (2.8–7.4)	0.085
Lymphocytes, × 10^9/L	0.7 (0.5–0.9)	0.7 (0.5–0.8)	0.6 (0.5–1.0)	0.873
T cell subsets				
$CD3^+CD4^+$ T cells, cell/μL	92.6 (62.8–185.6)	68.0 (55.1–148.8)	114.6 (75.0–195.2)	0.068
$CD3^+CD8^+$ T cells, cell/μL	70.1 (33.3–113.6)	47.9 (25.4–73.8)	97.2 (55.4–132.1)	0.005
C-reactive protein, mg/L	65.8 (27.8–101.4)	86.4 (37.9–105.5)	58.1 (26.3–95.2)	0.124
Procalcitonin, ng/mL	0.1 (0.0–0.3)	0.1 (0.1–0.5)	0.1 (0.0–0.2)	0.032
Cardiac troponin I, ng/mL	0.0 (0.0–0.1)	0.1 (0.0–0.8)	0.0 (0.0–0.1)	0.001
Myoglobin, ng/mL	60.3 (34.3–190.5)	162.0 (48.5–342.8)	47.5 (28.0–142.0)	0.027
Brain natriuretic peptide, pg/mL	946.5 (444.0-1700.0)	970.0 (620.5-3531.0)	882.0 (399.5-1393.0)	0.212
Albumin, g/L	33.0 (30.6–35.7)	33.2 (31.2–35.6)	31.6 (30.0–36.1)	0.473
Total bilirubin, μmol/L	9.6 (8.2–15.4)	9.6 (8.3–16.3)	9.4 (8.1–15.5)	0.729
Direct bilirubin, μmol/L	3.4 (2.2–6.1)	3.1 (2.3–6.1)	3.6 (2.2–6.1)	0.808
Alanine aminotransferase, U/L	29.0 (20.0–43.0)	27.0 (20.0–37.0)	31.0 (18.5–44.8)	0.855
Aspartate aminotransferase, U/L	40.0 (24.0–57.0)	40.0 (27.0–61.5)	39.5 (20.8–52.5)	0.362
γ-Glutamyltranspeptidase, U/L	30.0 (19.0–43.0)	23.0 (16.5–42.0)	32.0 (19.8–54.0)	0.290
Creatinine, μmol/L	64.0 (56.0–87.0)	95.0 (63.0–112.0)	60.0 (54.8–74.3)	0.001
D-dimer, mg/L	0.6 (0.4–2.9)	1.1 (0.4–10.5)	0.6 (0.4–1.2)	0.075
Prothrombin time, s	13.3 (12.3–15.3)	13.9 (12.3–16.3)	13.2 (12.3–14.5)	0.420
Activated partial thromboplastin time, s	35.0 (32.1–39.7)	37.8 (30.8–41.5)	34.6 (32.4–39.0)	0.385
PaO_2, mmHg	59.0 (49.0 – 74.0)	56.0 (49.0 – 71.0)	64.5 (49.0–80.5)	0.358

$PaCO_2$, mmHg	36.0 (31.5–41.0)	34.0 (29.0–41.0)	36.5 (33.0–41.0)	0.169
PaO_2:F_IO_2 < 200 mmHg	47.6	29.2	2.204 (0.854–5.684)	0.102

*Data are reported as median interquartile (IQR).

PaO_2 = Arterial partial pressure of oxygen, $PaCO_2$ = Arterial partial pressure of carbon dioxide, F_IO_2 = fraction of inspiration O_2.