Risk Factors of Coronavirus Disease 2019-Related Mortality and Optimal Treatment Regimens: A Retrospective Study

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Background: Coronavirus disease 2019 (COVID-19) is spreading rapidly worldwide, and scientists are trying to find a way to overcome the disease. We explored the risk factors that influence patient outcomes, including treatment regimens, which can provide a reference for further treatment.

Material/Methods: A retrospective cohort study analysis was performed using data from 97 patients with COVID-19 who visited Wuhan Union Hospital from February 2020 to March 2020. We collected data on demographics, comorbidities, clinical manifestations, laboratory tests, treatment methods, outcomes, and complications. Patients were divided into a recovered group and a deceased group. We compared the differences between the 2 groups and analyzed risk factors influencing the treatment effect.

Results: Seventy-six patients recovered and 21 died. The average age and body mass index (BMI) of the deceased group were significantly higher than those of the recovered group (69.81±6.80 years vs 60.79±11.28 years, \( P < 0.001 \) and 24.95±3.14 kg/m\(^2\) vs 23.09±2.97 kg/m\(^2\), \( P = 0.014 \)), respectively. The combination of antiviral drugs and supportive therapy appears to be associated with the lowest mortality (\( P < 0.05 \)). Multivariate Cox regression analysis revealed that age, BMI, H-CRP, shock, and acute respiratory distress syndrome (ARDS) were independent risk factors for patients with COVID-19 (\( P < 0.05 \)).

Conclusions: Elderly patients and those with a high BMI, as well as patients who experience shock and ARDS, may have a higher risk of death from COVID-19. The combination of antiviral drugs and supportive therapy appears to be associated with lower mortality, although further research is needed.

Keywords: Aftercare • COVID-19 • Decision Support Techniques • SARS Virus
Background

Coronavirus disease 19 (COVID-19) is caused by the novel coronavirus severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and has evolved into a global pandemic since its original outbreak in Wuhan, China in 2019. COVID-19 can be transmitted from person to person with high infectivity and has high mortality and a low cure rate, bringing a heavy burden and great challenge to the global public health system. COVID-19 can cause a range of respiratory symptoms, which vary in severity. In some patients, their condition can deteriorate rapidly in a short period of time. It is now believed that inflammation is the main cause of this deterioration, and viral replication affects the inflammatory process [1].

Many factors may affect the prognosis of patients with COVID-19, including clinical characteristics, degree of severity, laboratory test results, and treatment options. Among these, the treatment plan plays a particularly important role in the patient's prognosis. In the face of aggressive COVID-19, countries are striving to explore and optimize treatment options, and a variety of drugs are undergoing clinical trials. A variety of vaccines have entered phase III clinical trials, and the safety and efficacy of the vaccines are being evaluated. Although many are pinning their hopes on a vaccine to fight COVID-19, antiviral treatment is still essential. SARS-CoV-2 invades the host cell using angiotensin-converting enzyme 2 as a receptor; therefore, antiviral drugs are favored. In addition, based on the treatment for SARS, convalescent plasma is used. The technique uses antibodies from the blood plasma or serum of people who have recovered from COVID-19 infection to boost the immunity of newly-infected patients and those at risk of contracting the disease. These antibodies contained in the blood’s serum have the ability to bind to and neutralize SARS-CoV-2, the virus that causes COVID-19. Gamma globulin, the blood’s serum have the ability to bind to and neutralize SARS-CoV-2, the virus that causes COVID-19. Gamma globulin, traditional Chinese medicine, immunomodulatory drugs, and glucocorticoids have also been widely used for the treatment of COVID-19. Although some drugs have shown efficacy, more randomized trials are still needed [2]. Previous studies have found that early intervention in patients with new COVID-19 pneumonia significantly improves the prognosis of patients.

In this study, we aimed to identify factors that affect the mortality of patients with COVID-19 by analyzing the clinical characteristics, laboratory test results, and treatment regimens of patients who either recovered from or died of COVID-19, so as to effectively intervene early and improve the cure rate of patients.

Material and Methods

Patients

A retrospective cohort study analysis was performed on 116 patients with COVID-19 and a positive SARS-CoV-2 test who were admitted to Wuhan Union Hospital from February 2020 to March 2020. All the patients met the diagnostic and typing criteria in the "Diagnosis and Treatment Plan for Novel Coronavirus Pneumonia (trial version 8)" issued by the National Health Commission [3]. Nineteen patients were excluded for the following reasons: (1) age less than 18 years or more than 85 years; (2) pregnant; (3) lack of complete data. The Ethics Committee of the Union Hospital of Tongji Medical College of Huazhong University of Science and Technology approved the study, and it was conducted according to the Helsinki Declaration. Each patient gave informed consent and signed a written informed consent form.

Observation Index and Grouping

Data on patient demographics, comorbidities, clinical manifestations, laboratory tests, treatment methods, outcomes, and complications were collected. According to the outcome after treatment, the patients were divided into the recovered group or the deceased group.

Definitions

The standard for recovery was disappearance of clinical symptoms and 2 negative nucleic acid tests [4]. The endpoint of this study was overall survival, which was defined as the length of time from the date of diagnosis to the date of death or discharge from the hospital. Acute respiratory distress syndrome (ARDS) and shock were defined in accordance with the WHO interim guidance on the novel coronavirus [5]. Acute kidney injury was determined according to the highest serum creatinine and urea level criteria [6]. Secondary bacterial pneumonia was defined in accordance with the clinical symptoms or signs of nosocomial pneumonia or bacteremia, using lung imaging studies and bacterial culture results of respiratory secretions. Acute cardiac injury was diagnosed if the serum levels of cardiac biomarkers were higher than the 99th percentile reference limit or if ECG and echocardiography showed new abnormalities [7].

Data Analysis

Continuous variables that conformed to a normal distribution were expressed as mean±standard deviation; otherwise, variables were expressed as the median and interquartile range. We used the t test or Wilcoxon test to compare intergroup differences in continuous variables. Categorical variables were
presented as the number of cases (percentage), and the chi-square or Fisher’s exact tests were used to evaluate categorical variables. Kaplan-Meier survival curves and log-rank test were used to compare survival differences between groups. A Cox proportional hazard regression model was used for univariate and multivariate regression analysis to estimate hazard ratios (HRs) and 95% confidence intervals (CIs). Statistically significant variables (P < 0.05) in the univariate analysis were included in the multivariate analysis. Statistical analyses were performed using SAS 9.4 (SAS Institute, Inc, Cary, NC, USA) and R 3.5.1 (R Foundation for Statistical Computing, Vienna, Austria). All analyses were two-sided, and P values < 0.05 were considered statistically significant.

Results

Comparison of Demographic Information Between the 2 Groups

There were 76 patients in the recovery group and 21 patients in the deceased group, and the detailed flow diagram of the patient selection process is shown in Figure 1. Both groups had a history of living in Wuhan’s epidemic area before the onset of disease, and there was no statistically significant difference in contact with COVID-19-positive patients. The average age and BMI of the patients in the deceased group were significantly higher than those in the recovered group (69.81±6.80 years vs 60.79±11.28 years, P=0.001 and 24.95±3.14 kg/m² vs 23.09±2.97 kg/m², P=0.014, respectively). No significant differences were found in sex, smoking status, alcohol consumption, or comorbidities (hypertension, cardiovascular disease, lung disease, chronic hepatorenal diseases, and tumor history) between the 2 groups (P>0.05 for all) (Table 1).

Table 1. Demographic and comorbidity characteristics of the COVID-19 patients in the recovered and deceased groups.

| Total n=97 (%) | Recovered n=76 (%) | Deceased n=21 (%) | P* |
|---------------|--------------------|-------------------|----|
| Age (year)    | 62.74±11.09        | 60.79±11.28       | 69.81±6.80 | <0.001 |
| Sex           |                    |                   |               |        |
| Male          | 51 (52.58)         | 37 (48.68)        | 14 (66.67)    | 0.217  |
| Female        | 46 (47.42)         | 39 (51.32)        | 17 (33.33)    |        |
| BMI           | 23.49±3.09         | 23.09±2.97        | 24.95±3.14    | 0.014  |
| Pressure      |                    |                   |               |        |
| Systolic pressure | 125 (115-140) | 124.5 (114.4-133.5) | 131 (116-148) | 0.183  |
| Diastolic pressure | 76 (69-84)   | 76.5 (70-84.5)    | 71 (62-84)    | 0.163  |
| Normal        | 91 (93.81)         | 73 (95.05)        | 18 (85.71)    | 0.114  |
| Hypertension  | 6 (6.19)           | 3 (3.95)          | 3 (14.29)     |        |
| Smoke         |                    |                   |               | 0.999  |
| No            | 93 (95.88)         | 73 (96.05)        | 20 (95.24)    |        |
| Yes           | 4 (4.12)           | 3 (3.95)          | 1 (4.76)      |        |
| Drink         |                    |                   |               |        |
| No            | 88 (90.72)         | 67 (88.16)        | 21 (100.0)    | 0.198  |
| Yes           | 9 (9.28)           | 9 (11.84)         | 0 (0.0)       |        |
Table 1 continued. Demographic and comorbidity characteristics of the COVID-19 patients in the recovered and deceased groups.

| Demographic and Comorbidity Characteristics | Total n=97 (%) | Recovered n=76 (%) | Deceased n=21 (%) | p*  |
|---------------------------------------------|---------------|-------------------|------------------|-----|
| **Exposure**                                |               |                   |                  |     |
| No                                          | 25 (25.77)    | 19 (25)           | 6 (28.57)        | 0.781 |
| Yes                                         | 72 (74.23)    | 57 (75)           | 15 (71.43)       |     |
| **Comorbidities**                           |               |                   |                  |     |
| No                                          | 34 (35.05)    | 29 (38.16)        | 5 (23.81)        | 0.304 |
| Yes                                         | 63 (64.95)    | 47 (61.84)        | 16 (76.19)       |     |
| **Diabetes**                                |               |                   |                  |     |
| No                                          | 76 (78.35)    | 63 (82.89)        | 13 (61.9)        | 0.069 |
| Yes                                         | 21 (21.65)    | 13 (17.11)        | 8 (38.1)         |     |
| **Hypertension**                            |               |                   |                  |     |
| No                                          | 59 (60.82)    | 49 (64.47)        | 10 (47.62)       | 0.208 |
| Yes                                         | 38 (39.18)    | 27 (35.53)        | 11 (52.38)       |     |
| **Cardiovascular disease**                  |               |                   |                  |     |
| No                                          | 78 (80.41)    | 64 (84.21)        | 14 (66.67)       | 0.116 |
| Yes                                         | 19 (19.59)    | 12 (15.79)        | 7 (33.33)        |     |
| **Lung disease**                            |               |                   |                  |     |
| No                                          | 85 (87.63)    | 66 (86.84)        | 19 (90.48)       | 0.999 |
| Yes                                         | 12 (12.37)    | 10 (13.16)        | 2 (9.52)         |     |
| **Chronic nephropathy**                     |               |                   |                  |     |
| No                                          | 94 (96.91)    | 75 (98.68)        | 19 (90.48)       | 0.117 |
| Yes                                         | 3 (3.09)      | 1 (1.32)          | 2 (9.52)         |     |
| **Chronic liver disease**                   |               |                   |                  |     |
| No                                          | 95 (97.94)    | 74 (97.37)        | 21 (100.0)       | 0.999 |
| Yes                                         | 2 (2.06)      | 2 (2.63)          | 0 (0.00)         |     |
| **Tumor history**                           |               |                   |                  |     |
| No                                          | 96 (98.97)    | 75 (98.68)        | 21 (100.0)       | 0.999 |
| Yes                                         | 1 (1.03)      | 1 (1.32)          | 0 (0.00)         |     |

* P values were calculated by the Student’s t-test or Wilcoxon test for continuous variables. The Chi-square test for categorical variables, and the Fisher exact test was used when the data were limited; BMI – Body mass index.
### Table 2. The Clinical symptoms characteristics of the COVID-19 patients in the recovered and deceased groups.

| Symptom                  | Total n=97 (%) | Recovered n=76 (%) | Deceased n=21 (%) | P* |
|--------------------------|----------------|--------------------|-------------------|----|
| Fever                    |                |                    |                   |    |
| No                       | 36 (37.11)     | 29 (38.16)         | 7 (33.33)         |    |
| Yes                      | 61 (62.89)     | 47 (61.84)         | 14 (66.67)        |    |
| Dry cough                |                |                    |                   |    |
| No                       | 55 (56.7)      | 40 (52.63)         | 15 (71.43)        |    |
| Yes                      | 42 (43.3)      | 36 (47.37)         | 6 (28.57)         |    |
| Expectoration            |                |                    |                   | 0.999 |
| No                       | 80 (82.47)     | 63 (82.89)         | 17 (80.95)        |    |
| Yes                      | 17 (17.53)     | 13 (17.11)         | 4 (19.05)         |    |
| Nasal congestion         |                |                    |                   | 0.999 |
| No                       | 89 (91.75)     | 70 (92.11)         | 19 (90.48)        |    |
| Yes                      | 8 (8.25)       | 6 (7.89)           | 2 (9.52)          |    |
| Headache                 |                |                    |                   | 0.287 |
| No                       | 84 (86.6)      | 64 (84.21)         | 20 (95.24)        |    |
| Yes                      | 13 (13.4)      | 12 (15.79)         | 1 (4.76)          |    |
| Weak                     |                |                    |                   | 0.084 |
| No                       | 47 (48.45)     | 33 (43.42)         | 14 (66.67)        |    |
| Yes                      | 50 (51.55)     | 43 (56.58)         | 7 (33.33)         |    |
| Myalgia                  |                |                    |                   | 0.287 |
| No                       | 68 (70.10)     | 51 (67.11)         | 17 (80.95)        |    |
| Yes                      | 29 (29.90)     | 25 (32.89)         | 4 (19.05)         |    |
| Chest tightness          |                |                    |                   | 0.453 |
| No                       | 85 (87.63)     | 65 (85.53)         | 20 (95.24)        |    |
| Yes                      | 12 (12.37)     | 11 (14.47)         | 1 (4.76)          |    |
| Dyspnea                  |                |                    |                   | 0.643 |
| No                       | 90 (92.78)     | 71 (93.42)         | 19 (90.48)        |    |
| Yes                      | 7 (7.22)       | 5 (6.58)           | 2 (9.52)          |    |
| Gasp                     |                |                    |                   | 0.999 |
| No                       | 89 (91.75)     | 69 (90.79)         | 20 (95.24)        |    |
| Yes                      | 8 (8.25)       | 7 (9.21)           | 1 (4.76)          |    |
| Gastrointestinal symptoms|                |                    |                   | 0.999 |
| No                       | 79 (81.44)     | 62 (81.58)         | 17 (80.95)        |    |
| Yes                      | 18 (18.56)     | 14 (18.42)         | 4 (19.05)         |    |

*P values were calculated by the Student’s t-test or Wilcoxon test for continuous variables. The Chi-square test for categorical variables, and the Fisher exact test was used when the data were limited.
|                  | Total n=97 (%) | Recovered n=76 (%) | Deceased n=21 (%) | p*  |
|------------------|----------------|--------------------|-------------------|-----|
| WBC (G/L)        | 7.10 (4.46-9.7) | 5.98 (4.28-9.06)   | 9.70 (7.81-13.85) | 0.002 |
| Decreased        | 8 (8.25)       | 7 (9.21)           | 1 (4.76)          | 0.999 |
| Normal           | 89 (91.75)     | 69 (90.79)         | 20 (95.24)        |     |
| LYM (G/L)        | 0.77 (0.54-1.03) | 0.79 (0.55-1.04)   | 0.56 (0.45-0.89)  | 0.146 |
| Decreased        | 76 (78.35)     | 59 (77.63)         | 17 (80.95)        | 0.999 |
| Normal           | 21 (21.65)     | 17 (22.37)         | 4 (19.05)         |     |
| NEU (G/L)        | 6.04 (3.45-8.97) | 4.79 (3.28-7.965)  | 8.92 (7.08-12.73) | 0.001 |
| Decreased        | 5 (5.15)       | 5 (6.58)           | 0 (0)             | 0.582 |
| Normal           | 92 (94.85)     | 71 (93.42)         | 21 (100)          |     |
| MON (G/L)        | 0.33 (0.25-0.5) | 0.32 (0.19-0.48)   | 0.35 (0.29-0.54)  | 0.059 |
| Decreased        | 85 (87.63)     | 69 (90.79)         | 16 (76.19)        | 0.126 |
| Normal           | 12 (12.37)     | 7 (9.21)           | 5 (23.81)         |     |
| HGB (G/L)        | 129 (121-140)  | 128 (121-140.5)    | 132 (118-137)     | 0.976 |
| Decreased        | 51 (52.58)     | 41 (53.95)         | 10 (47.62)        |     |
| Normal           | 46 (47.42)     | 35 (46.05)         | 11 (52.38)        | 0.630 |
| PLT (G/L)        | 187 (149-233)  | 192 (155-231.5)    | 163 (131-237)     | 0.160 |
| Decreased        | 11 (11.34)     | 6 (7.89)           | 5 (23.81)         |     |
| Normal           | 83 (85.57)     | 67 (88.16)         | 16 (76.19)        | 0.091 |
| Increased        | 3 (3.09)       | 3 (3.95)           | 0 (0)             |     |
| PT (s)           | 13.5 (12.5-15) | 13.15 (12.4-14.55) | 15.6 (13-17.4)    | 0.005 |
| Normal           | 83 (85.57)     | 70 (92.11)         | 13 (61.9)         | 0.002 |
| Increased        | 14 (14.43)     | 6 (7.89)           | 8 (38.1)          | 0.001 |
| APTT (s)         | 34.8 (32.4-40.1)| 34.05 (32.25-38.45)| 41.5 (37.7-43.9)  |     |
| Decreased        | 3 (3.09)       | 3 (3.95)           | 0 (0)             | 0.005 |
| Normal           | 78 (80.41)     | 63 (82.89)         | 15 (71.43)        | 0.176 |
| Increased        | 16 (16.49)     | 10 (13.16)         | 6 (28.57)         |     |
| ALT (U/L)        | 25 (15-44)     | 24.0 (14-44.5)     | 26 (20-39)        | 0.534 |
| Decreased        | 38 (39.18)     | 32 (42.11)         | 6 (28.57)         |     |
| Normal           | 53 (54.64)     | 40 (52.63)         | 13 (61.9)         | 0.469 |
| Increased        | 6 (6.19)       | 4 (5.26)           | 2 (9.52)          |     |
| AST (U/L)        | 29 (20-47)     | 27 (20-43.5)       | 42 (25-66)        | 0.048 |
| Decreased        | 11 (11.34)     | 10 (13.16)         | 1 (4.76)          |     |
| Normal           | 68 (70.1)      | 56 (73.68)         | 12 (57.14)        | 0.028 |
| Increased        | 18 (18.56)     | 10 (13.16)         | 8 (38.1)          |     |
Table 3 continued. The laboratory characteristics of the COVID-19 patients in the recovered and deceased groups.

|                      | Total n=97 (%) | Recovered n=76 (%) | Deceased n=21 (%) | p*  |
|----------------------|----------------|--------------------|-------------------|-----|
| **TBIL (umol/L)**    |                |                    |                   |     |
| Normal               | 9.14 (6.76-13.98) | 8.63 (6.67-12.37) | 9.62 (8.06-23.75) | 0.057 |
| Increased            | 11 (11.34)     | 5 (6.58)           | 6 (28.57)         | 0.012 |
| **DBIL (umol/L)**    |                |                    |                   |     |
| Normal               | 3.04 (1.94-5.00) | 2.69 (1.88-4.13)   | 5.16 (3.04-8.15)  | 0.002 |
| Increased            | 72 (74.23)     | 62 (81.58)         | 10 (47.62)        | 0.004 |
| **ALB (G/L)**        |                |                    |                   |     |
| Normal               | 35.1 (32.6-38)/35.24±3.43 | 35.59±3.51       | 33.98±2.94        | 0.056 |
| Decreased            | 46 (47.42)     | 32 (42.11)         | 14 (66.67)        | 0.053 |
| **CRE (umol/L)**     |                |                    |                   |     |
| Normal               | 66 (56-83)     | 65.5 (54.5-75.5)   | 83 (64-95)        | 0.004 |
| Decreased            | 29 (29.9)      | 25 (32.89)         | 4 (19.05)         | 0.005 |
| **BUN (mmol/L)**     |                |                    |                   |     |
| Normal               | 6.08 (4.78-7.72) | 5.88 (4.61-7.45)   | 7.37 (6.12-9.69)  | 0.005 |
| Increased            | 9 (9.28)       | 8 (10.53)          | 1 (4.76)          | 0.021 |
| **H-CRP (mg/L)**     |                |                    |                   |     |
| Normal               | 45.51 (23.89-89.02) | 35.6 (21.53-82.39) | 88.88 (59.63-99.67) | 0.004 |
| Increased            | 7 (7.22)       | 6 (7.89)           | 1 (4.76)          | 0.624 |
| **CK (umol/L)**      |                |                    |                   |     |
| Normal               | 67.2 (43.1-139.1) | 64.15 (39.95-100.85) | 93.7 (50.4-185.0) | 0.121 |
| Increased            | 2 (2.06)       | 1 (1.32)           | 1 (4.76)          | 0.279 |
| **CKMB (umol/L)**    |                |                    |                   |     |
| Normal               | 17.2 (14.0-22.0) | 16.5 (13.15-19.80) | 21 (17.2-25.0)    | 0.005 |
| Increased            | 82 (84.54)     | 68 (89.47)         | 14 (66.67)        | 0.018 |

* P values were calculated by the Student's t-test or Wilcoxon test for continuous variables. The Chi-square test for categorical variables, and the Fisher exact test was used when the data were limited. WBC – white blood cell; LYM – lymphocyte; NEU – neutrophil; MON – monocyte; ALB – albumin; ALP – alkaline phosphatase; HGB – hemoglobin; PLT – platelet; PT – prothrombin; APTT – activated partial thromboplastin time; ALT – alanine aminotransferase; AST – glutamic oxaloacetylase; TBIL – total bilirubin; DBIL – direct bilirubin; ALB – albumin; CRE – creatinine; BUN – urea nitrogen; H-CRP – hypersensitive C-reactive protein; CK – creatine kinase; CKMB – creatine Kinase isomer-MB.
Comparison of Clinical Symptoms and Laboratory Test Results Between the 2 Groups

The proportion of patients with fever in the recovered group was lower than that in the deceased group (61.84% vs 66.67%), but the difference was not statistically significant ($P=0.801$). No significant differences were found in the incidence or disease severity of other common clinical symptoms between the 2 groups, including dry cough, expectoration, nasal congestion, headache, weakness, myalgia, chest tightness, dyspnea, grasp, and gastrointestinal symptoms ($P>0.05$ for all) (Table 2). The disease severity in this study was defined as mild, normal, severe, or critical, according to “Diagnosis and Treatment Plan for Novel Coronavirus Pneumonia (trial version 8)” [3].
Figure 2. Kaplan-Meier survival curves of patients with COVID-19. (A) Survival curve of patients receiving single-agent antiviral therapy and those receiving combination antiviral therapy (*P*=0.004). (B) Survival curve of patients receiving single-agent anti-infection therapy and those receiving combination anti-infection therapy (*P*<0.001). (C) Overall survival for all patients based on administration of gamma globulin therapy (*P*<0.001). (D) Overall survival for all patients based on receiving other supportive treatment (Chinese medicine or other) (*P*=0.048).
Compared with patients in the recovered group, patients in the deceased group were more likely to have different degrees of increase in white blood cell counts (97.0 [7.81-13.85]×10^9/L vs 5.98 [4.28-9.06]×10^9/L, \( P < 0.001 \)), neutrophil counts (8.92 [7.08-12.73]×10^9/L vs 4.79 [3.28-7.965]×10^9/L, \( P < 0.002 \)), prothrombin time (15.6 [13-17.4] s vs 13.15 [12.4-15.5] s), activated partial thromboplastin time (41.5 [37.7-43.9] s vs 34.05 [32.25-38.45] s), glutamic-oxaloacetic transaminase (42 [25-66] u/L vs 27 [20-43.5] u/L), direct bilirubin (5.16 [3.04-8.15] umol/L vs 2.69 [1.88-4.13] umol/L), creatinine (83 [64-95] umol/L vs 65.5 [54.5-75.5] umol/L), blood urea nitrogen (7.37 [6.12-9.69] mmol/L vs 5.88 [4.61-7.45] mmol/L), and hypersensitive C-reactive protein (88.88 [59.63-99.67] mg/L vs 35.6 [21.53-82.39] mg/L) (\( P < 0.05 \) for all). There was no significant difference in other laboratory indexes between the 2 groups (\( P > 0.05 \) for all) (Table 3).

Comparison of Treatment Between the 2 Groups

The rate of combination antiviral therapy was lower in the deceased group than in the recovered group (47.62% vs 81.58%, \( P = 0.004 \)). Additionally, the rate of other supportive treatment in the recovered group was significantly higher than that in the deceased group (63.16% vs 38.1%, \( P = 0.048 \)). However, the rates of anti-infection therapy and gamma globulin therapy were significantly higher in the deceased group (90.48% vs 28.95, \( P < 0.001 \) and 90.48% vs 39.72, \( P < 0.001 \), respectively). There was no statistically significant difference in the administration of hormone therapy or single-agent antiviral therapy between the 2 groups (\( P > 0.05 \)) (Table 4).

Figure 1 depicts the Kaplan-Meier survival curves of the patients. The survival rates of patients who received more than 1 antiviral therapy and other supportive therapy were higher than those of patients who received single-agent antiviral therapy and no other supportive therapy (\( P < 0.05 \)) (Figure 2A, 2D). By contrast, the survival rates of patients who received gamma globulin therapy and more than 1 anti-infection therapy were lower than those of patients who received no gamma globulin therapy and only a single anti-infection therapy (\( P < 0.05 \)) (Figure 2B, 2C).

Comparison of Complications Between the 2 Groups

The rate of extremely severe cases in the deceased group was higher than that in the recovered group (76.19% vs 13.16%, \( P < 0.001 \)). Compared with patients in the recovered group, patients in the deceased group were more likely to develop shock (0% vs 19.05%, \( P = 0.002 \)), ARDS (19.74% vs 90.48%, \( P < 0.001 \)), kidney injury (3.95% vs 90.48, \( P < 0.001 \)), acute heart injury (3.95% vs 76.19%, \( P < 0.001 \), and secondary bacterial pneumonia (17.11% vs 66.67%, \( P < 0.001 \)) (Table 5).

Risk Factors Affecting the Outcome of Treatment

The univariate Cox analysis showed that age (HR: 1.092, 95% CI: 1.036-1.150, \( P = 0.001 \)), BMI (HR: 1.336, 95% CI: 1.132-1.607, \( P = 0.002 \)), prothrombin count (HR: 1.141, 95% CI: 1.068-1.219, \( P < 0.001 \)), prothrombin time (HR: 1.213, 95% CI: 1.045-1.407, \( P = 0.011 \)), total bilirubin (HR: 1.044, 95% CI: 1.015-1.073, \( P = 0.002 \)), direct bilirubin (HR: 1.125, 95% CI: 1.050-1.206, \( P = 0.001 \)), blood urea nitrogen (HR: 1.074, 95% CI: 1.025-1.125, \( P = 0.003 \)), hypersensitive C-reactive protein (HR: 1.008, 95% CI: 1.002-1.013, \( P = 0.004 \)); extremely severe disease (HR: 13.395, 95% CI: 1.773-101.175, \( P = 0.012 \)), shock (HR: 11.726, 95% CI: 3.373-30.760, \( P = 0.001 \)), ARDS (HR: 11.22, 95% CI: 2.573-48.915, \( P = 0.013 \), kidney injury (HR: 5.233, 95% CI: 1.823-15.016, \( P = 0.002 \), and acute heart injury (HR: 4.533, 95% CI: 1.600-12.840, \( P = 0.004 \)) were the risk factors affecting the clinical outcome. Multivariate Cox regression analysis showed that age (HR: 1.319, 95% CI: 1.115-1.561, \( P = 0.001 \)), BMI (HR: 1.344, 95% CI: 1.014-1.783, \( P = 0.008 \)), prothrombin time (HR: 0.489, 95% CI: 0.271-0.884, \( P = 0.018 \), H-CRP (HR: 1.014, 95% CI: 1.003-1.025, \( P = 0.001 \)), shock (HR: 34.713, 95% CI: 2.596-464.133, \( P = 0.007 \), and ARDS (HR: 46.252, 95% CI: 1.504-1422.171, \( P = 0.028 \)) were independent risk factors affecting the treatment effect of patients with COVID-19 (Table 6).

Discussion

In this study, we analyzed the risk factors of mortality in patients with COVID-19. We found no significant difference in clinical symptoms such as cough, fever, fatigue, chest tightness, diarrhea, and dyspnea between patients who died and those who recovered. However, a variety of factors affected the mortality of patients with COVID-19, especially older age, higher BMI, lower prothrombin time, higher bilirubin, higher H-CRP, disease severity, comorbidities, and treatment options. Further, the mortality rate was lower in patients receiving combined antiviral therapies than in those receiving single-agent therapies. Patients who received supportive treatment had a lower mortality rate than those who did not receive supportive treatment. However, gamma globulin or antibiotics did not significantly improve the mortality rate of patients with COVID-19.

It has been reported that MERS and SARS are important independent predictors of death in old age, and recent studies have also shown that patients over the age of 65 years and with complications such as hypertension have a higher risk of death [8]. Previous studies have shown that the risk factors related to the development of ARDS and progression from ARDS to death included neutrophilia and organ and coagulation dysfunction [9].
In addition, previous studies have shown that total bilirubin, prothrombin time, and H-CRP were significantly higher in COVID-19 patients who died than in those who recovered, and the increase in these indicators may be related to acute lung injury [10]. Our research findings are consistent with this. According to previous reports, older patients have higher COVID-19-related mortality rates. Older patients may have a stronger innate response to viral infection than younger patients, resulting in insufficient inhibition of viral replication and longer proinflammatory responses, which may lead to poor prognosis [11, 12]. Obesity was an important factor that causes significant changes in bronchoalveolar lavage fluid and blood. Higher BMI results in higher expression levels of CD147-related genes in immune cells, but lower expression levels in barrier cells, which may affect the development and progression of COVID-19 [13]. In our study, the average age and BMI in the deceased group were significantly higher than those in the recovered group, which suggests that a high BMI and older age may be risk factors for mortality. Shock and ARDS are serious complications in COVID-19 patients that may be directly caused by SARS-CoV-2 infection or by the low immune response in elderly patients [14]. This is consistent with our finding that patients in the deceased group were older and the incidence of complications was higher. However, further studies are needed to investigate the pathogenesis of sudden shock and ARDS caused by COVID-19.

### Table 5. The complications characteristics of the COVID-19 patients in the recovered and deceased groups.

|                          | Total n=97 (%) | Recovered n=76 (%) | Deceased n=21 (%) | P*  |
|--------------------------|---------------|--------------------|-------------------|-----|
| Disease severity         |               |                    |                   |     |
| Light                    | 30 (30.93)    | 29 (38.16)         | 1 (4.76)          | <0.001 |
| Severe                   | 41 (42.27)    | 37 (48.68)         | 4 (19.05)         |     |
| Extremely severe         | 26 (26.80)    | 10 (13.16)         | 16 (76.19)        |     |
| Shock                    |               |                    |                   | 0.002 |
| No                       | 93 (95.88)    | 76 (100)           | 17 (80.95)        |     |
| Yes                      | 4 (4.12)      | 0 (0)              | 4 (19.05)         |     |
| ARDS                     |               |                    |                   | <0.001 |
| No                       | 63 (64.95)    | 61 (80.26)         | 2 (9.52)          |     |
| Yes                      | 34 (35.05)    | 15 (19.74)         | 19 (90.48)        |     |
| Kidney injury            |               |                    |                   | <0.001 |
| No                       | 78 (80.41)    | 73 (96.05)         | 5 (23.81)         |     |
| Yes                      | 19 (19.59)    | 3 (3.95)           | 16 (76.19)        |     |
| Acute heart injury       |               |                    |                   | <0.001 |
| No                       | 71 (73.2)     | 66 (86.84)         | 5 (23.81)         |     |
| Yes                      | 26 (26.8)     | 10 (13.16)         | 16 (76.19)        |     |
| Arrhythmia               |               |                    |                   | 0.204 |
| No                       | 93 (95.88)    | 74 (97.37)         | 19 (90.48)        |     |
| Yes                      | 4 (4.12)      | 2 (2.63)           | 2 (9.52)          |     |
| Secondary bacterial pneumonia |         |                    |                   | <0.001 |
| No                       | 70 (72.16)    | 63 (82.89)         | 7 (33.33)         |     |
| Yes                      | 27 (27.84)    | 13 (17.11)         | 14 (66.67)        |     |

*P* values were calculated by the Student’s t-test or Wilcoxon test for continuous variables. The Chi-square test for categorical variables, and the Fisher exact test was used when the data were limited; ARDS: acute respiratory distress syndrome.
### Table 6. The factors associated with survival of COVID-19 patients by univariate and multivariate cox regression analysis.

|                      | Univariate analysis |                     | Multivariate analysis |                     |
|----------------------|---------------------|---------------------|-----------------------|---------------------|
|                      | HR                  | (95% CI)            | P                     | HR                  | (95% CI)            | P                     |
| Age                  | 1.092               | 1.036-1.150         | 0.001                 | 1.319               | 1.115-1.561         | 0.001                 |
| BMI                  | 1.336               | 1.112-1.607         | 0.002                 | 1.344               | 1.014-1.783         | 0.040                 |
| WBC                  | 1.019               | 0.999-1.039         | 0.061                 |                     |                     |                      |
| NEU                  | 1.141               | 1.068-1.219         | <0.001                | 0.910               | 0.748-1.107         | 0.346                 |
| PT                   | 1.213               | 1.054-1.407         | 0.011                 | 0.489               | 0.271-0.884         | 0.018                 |
| APTT                 | 1.051               | 0.983-1.125         | 0.147                 |                     |                     |                      |
| AST                  | 1.008               | 0.989-1.026         | 0.414                 |                     |                     |                      |
| TBIL                 | 1.044               | 1.015-1.073         | 0.002                 | 1.063               | 1.006-1.124         | 0.031                 |
| DBIL                 | 1.125               | 1.050-1.206         | 0.001                 | 0.869               | 0.693-1.091         | 0.226                 |
| CRE                  | 1.005               | 1.000-1.010         | 0.071                 |                     |                     |                      |
| BUN                  | 1.074               | 1.025-1.125         | 0.003                 | 1.123               | 0.978-1.289         | 0.099                 |
| H-CRP                | 1.008               | 1.002-1.013         | 0.004                 | 1.014               | 1.003-1.025         | 0.013                 |
| Disease severity     |                     |                     |                       |                     |                     |                      |
| Severe               | 2.438               | 0.253-23.516        | 0.441                 | 2.19                | 0.056-86.278        | 0.676                 |
| Extremely severe     | 13.395              | 1.773-101.175       | 0.012                 | 40.8                | 0.551-3023.150      | 0.091                 |
| Shock                | 11.726              | 3.373-40.760        | 0.001                 | 34.713              | 2.596-464.133       | 0.007                 |
| ARDS                 | 11.220              | 2.573-48.915        | 0.013                 | 46.252              | 1.504-1422.171      | 0.028                 |
| Kidney injury        | 5.233               | 1.823-15.016        | 0.002                 | 4.380               | 0.052-366.380       | 0.513                 |
| Acute heart injury   | 4.533               | 1.600-12.840        | 0.004                 | 0.201               | 0.004-11.385        | 0.436                 |
| Secondary bacterial pneumonia | 2.120 | 0.901-5.976 | 0.081 |
| Antiviral therapy    | 0.211               | 0.084-0.577         | 0.002                 | 6.753               | 0.449-101.645       | 0.167                 |
| Oseltamivir          | 0.283               | 0.088-0.913         | 0.055                 |                     |                     |                      |
| Arbidol hydrochloride| 0.297               | 0.040-2.227         | 0.238                 |                     |                     |                      |
| Anti-HIV drugs       | –                   | –                   | 0.992                 |                     |                     |                      |
| CK                   |                     |                     |                       |                     |                     |                      |
| Decreased            | 1.198               | 0.154-9.323         | 0.863                 |                     |                     |                      |
| Increased            | 1.271               | 0.413-3.910         | 0.675                 |                     |                     |                      |
| CKMB                 | 2.303               | 0.907-5.848         | 0.079                 |                     |                     |                      |
| Other treatment      | 0.264               | 0.104-0.674         | 0.005                 | 0.053               | 0.003-0.890         | 0.041                 |
| Anti-infection therapy| 5.442              | 1.227-24.142        | 0.026                 | 0.842               | 0.037-19.383        | 0.914                 |
| Gammaglobulin therapy| 0.173               | 0.040-0.748         | 0.019                 | 1.736               | 0.202-14.894        | 0.615                 |

HR – hazard ratio; CI – confidence interval; BMI – body mass index; WBC – white blood cell; NEU – neutrophil; PT – prothrombin; APTT – activated partial thromboplastin time; AST – glutamic oxaloacetylase; TBIL – total bilirubin; DBIL – direct bilirubin; CRE – creatinine; BUN – urea nitrogen; H-CRP – hypersensitive C-reactive protein; ARDS – acute respiratory distress syndrome; CK – creatine kinase; CKMB – creatine kinase isomer-MB.
The level and duration of viral replication are significant factors in assessing the risk of transmission and making patient isolation decisions. Therefore, the rational use of antiviral drugs is vital. However, there is no clear treatment for COVID-19 at present. Previous studies have shown that arbidol monotherapy is superior to lopinavir/ritonavir for COVID-19 [3]. Further, Deng et al reported that the combination of arbidol and lopinavir/ritonavir led to faster viral clearance than lopinavir/ritonavir alone [15]. In addition to antiviral drugs, some antibiotics have also been shown to be effective for the treatment of COVID-19. Azithromycin is a broad-spectrum macrolide antibiotic. In vitro studies have suggested that azithromycin has antiviral activity, and its mechanism is similar to that of chloroquine or hydroxychloroquine [16]. In clinical studies, azithromycin combined with chloroquine or hydroxychloroquine reduced the viral load of patients with COVID-19 and increased the recovery rate [17,18]. In severe influenza, prolonged viral shedding is associated with mortality, and delayed antiviral treatment is an independent risk factor for prolonged viral shedding [19,20]. Similarly, effective antiviral treatment may improve the prognosis of COVID-19. To improve the recovery rate, the focus should be on starting antiviral therapy early, which would reduce the peak viral load and thus reduce the degree of associated immunopathological damage [21].

There are some limitations in our study. First, the sample size was not large enough because this study was performed in a single center, which may have led to selection bias. Therefore, the mortality rate in our study may not reflect the true mortality rate of COVID-19. Second, the analysis indexes included in this study were not comprehensive enough, and there may be information bias. Third, it was a retrospective design with inherent limitations in study design, and some missing variables may have affected the results of our study. Finally, the lack of effective antiviral drugs in the early stage of the disease may also have led to poor clinical outcomes in some patients. Large-scale clinical studies with more clinical features and treatment performed in multiple centers are needed to validate our conclusions.

Conclusions

Age, BMI, prothrombin, H-CRP, shock, and ARDS are independent risk factors affecting the treatment effect of patients with COVID-19. The combination of antiviral drugs and supportive therapy appears to be associated with lower mortality, but further research is needed.

Conflict of Interest

None.

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