Clinical Characteristics and Early Intervenational Responses in Patients with Severe COVID-19 Pneumonia

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Progressive acute respiratory distress syndrome (ARDS) is the most lethal cause in patients with severe COVID-19 pneumonia due to uncontrolled inflammatory reaction, for which we found that early intervention of combined treatment with methylprednisolone and human immunoglobulin is a highly effective therapy to improve the prognosis of COVID-19-induced pneumonia patients.

Objective. Herein, we have demonstrated the clinical manifestations, laboratory, and radiological characteristics of patients with severe Coronavirus Disease-2019 (COVID-19) pneumonia, as well as measures to ensure early diagnosis and intervention for improving clinical outcomes of COVID-19 patients.

Summary Background Data. The COVID-19 is a new infection caused by a severe acute respiratory syndrome-(SARS-) like coronavirus that emerged in China in December 2019 and has claimed millions of lives.

Methods. We included 37 severe COVID-19 pneumonia patients who were hospitalized at Taizhou Public Health Medical Center in Zhejiang province from January 17, 2020, to February 18, 2020. Demographic, clinical, and laboratory features; imaging characteristics; treatment history; and clinical outcomes of all patients were collected from electronic medical records.

Results. The patients’ mean age was 54 years (interquartile range, 43–64), with a slightly higher male preponderance (57%). The most common clinical features of COVID-19 pneumonia were fever (29 (78%)), dry cough (28 (76%)), dyspnea (9 (24%)), and fatigue (9 (24%)). Serum interleukin (IL)-6 and IL-10 were elevated in 35 (95%) and 19 (51%) patients, respectively. Chest computed tomography scan revealed bilateral pneumonia in 35 (95%) patients. Early intervention with a combination of methylprednisolone and human immunoglobulin was highly effective in improving the prognosis of these patients.

Conclusions. Progressive acute respiratory distress syndrome is the most common cause of death in patients with severe COVID-19 pneumonia owing to an uncontrolled inflammatory response. Early intervention with methylprednisolone and human immunoglobulin was highly effective in improving their prognosis.

1. Introduction

In December 2019, a novel coronavirus was identified in patients with viral pneumonia in Wuhan, which was later named Coronavirus Disease-2019 (COVID-19) by the World Health Organization (WHO) on January 11, 2020 [1, 2]. Given the possibility of airborne transmission in humans, the virus has infected more than 100 million people and spread worldwide into hundreds of countries [3–5]. Most coronaviruses usually cause mild illness, but there are two β-coronaviruses, severe acute respiratory syndrome (SARS)-coronavirus and Middle-East respiratory syndrome (MERS)-coronavirus, which can lead to severe acute respiratory syndrome with a mortality rate of 10% and 37%,
respectively [6, 7]. Recent studies have revealed that COVID-19 causes severe pneumonia, respiratory distress syndrome, and multiple organ failure, leading to a high mortality rate [8–10].

This study is aimed at describing the clinical, laboratory, and radiological characteristics of critically ill patients with COVID-19, as well as the effective outcomes after early detection and intervention. These findings could provide a useful medicinal strategy for the treatment of severely ill patients with COVID-19 pneumonia.

2. Materials and Methods

2.1. Ethics. This study was approved by the ethics committee of the Enze Hospital of the Zhejiang Enze Medical Center (group). Data collected from enrolled cases were shared with the WHO. Written informed consent was obtained from all patients before data collection.

2.2. Clinical Records and Data Collection. Thirty-seven adult patients with severe COVID-19 pneumonia, diagnosed following the WHO interim guidelines [1, 11], were hospitalized at Taizhou Public Health Medical Center in Taizhou City, Zhejiang Province from January 17, 2020, to March 11, 2020. The medical records obtained from patients were analyzed by the respiratory research team of Zhejiang Enze Medical Center (group) Taizhou Hospital and Enze Hospital. The clinical features; laboratory investigations; chest imaging characteristics; treatment history, including antiviral therapy, hormone therapy, human immunoglobulin therapy, and respiratory support; and recovery data were retrieved from electronic medical records. The source data included demographic data; symptoms; comorbidities; laboratory results; chest computed tomography (CT) scan; and treatment measures, including laboratory results, such as complete blood count, blood clotting parameters, liver and kidney functions, serum electrolytes, erythrocyte sedimentation rate, C-reactive protein (CRP) level, procalcitonin (PCT) level, creatine kinase level, blood gas analysis, troponin level, and cytokine levels. All data were examined by two physicians.

2.3. Laboratory Investigations. Real-time fluorescent polymerase chain reaction (RT-PCR) was used to confirm novel coronavirus infection by detecting viral nucleic acid from respiratory tract specimens. Diagnosing severe respiratory symptoms requires fulfilling an oxygenation index criterion (\( \text{PaO}_2/\text{FiO}_2 \) of <300 mmHg). Clinical stability was defined as an oxygenation index of ≥300 mmHg with stable clinical symptoms. The time of symptom remission was defined as the time from the diagnosis of severe illness to the time of symptom relief. The time of oxygenation improvement was the time of diagnosis of severe disease to the time of oxygenation index of ≥300 mmHg. The apparent absorption time of the internal lesion was regarded as the time from the diagnosis of severe disease till obvious absorption of the pulmonary lesion on CT. The discharge criteria were defined as normal body temperature for more than 3 days, significant improvement of respiratory symptoms, pulmonary imaging showing significant inflammatory absorption, and two consecutive negative respiratory nucleic acid test results (sampling interval of at least >24 h).

2.4. Medical Treatment. Laboratory tests and chest CT were performed on the patients on admission. Next, 5 million units of aerosolized α-interferon in combination with oral lopinavir/ritonavir (500 mg) were administered twice daily to reduce viral activity. During hospitalization, vital signs and blood oxygen saturation were closely monitored. Blood gas analysis was performed promptly to determine the oxygenation index and the development of severe or new symptoms (chest tightness) were monitored. Respiratory support (high flow oxygen inhalation through a nasal catheter) was immediately administered to severely ill patients along with intravenous methylprednisolone (0.5–1 mg/kg daily), human immunoglobulin (0.3–0.5 g/kg daily), and fluids. Albendazole tablets (200 mg thrice daily) were administered to increase the efficacy of antiviral drugs. Human

### Table 1: Baseline characteristics of patients infected with COVID-19. Data are median (IQR) or n/N (%), where N is the total number of patients with available data.

| Patients (n = 37) |
|-----------------|
| Age, years |
| Median (IQR) | 54 (43-64) |
| Range | 27-86 |
| <40 | 6 (16%) |
| 40-70 | 30 (81%) |
| >70 | 1 (3%) |
| Sex |
| Male | 21 (57%) |
| Female | 16 (43%) |
| Current smoking | 3 (8%) |
| Comorbidity | 9 (24%) |
| Hypertension | 6 (16%) |
| Diabetes | 2 (5%) |
| Chronic obstructive pulmonary disease | 2 (5%) |
| Hypothyroidism | 2 (5%) |
| Signs and symptoms at admission |
| Fever | 29 (78%) |
| Cough | 28 (76%) |
| Sputum production | 6 (16%) |
| Dyspnea | 9 (24%) |
| Myalgia | 3 (8%) |
| Fatigue | 8 (22%) |
| Diarrhea | 3 (8%) |
| Headache | 4 (11%) |
| Dizzy | 5 (14%) |
| Pharyngula | 3 (8%) |
| More than one sign or symptom | 32 (86%) |
| Clinical outcome |
| Discharged | 37 (100%) |
| Died | 0 (0%) |
immunoglobulin was stopped based on the patients’ condition, and the dose of methylprednisolone was gradually reduced accordingly. Empirical antibiotics were administered to patients who showed elevated white blood cell count and/or significantly elevated C-reactive protein (CRP) level. Critically ill patients were evaluated for oxygenation index at least once daily until clinical signs and symptoms were relieved.

2.5. Statistical Analyses. The categorical variables were described as frequency and percentages, and the continuous variables were described using mean, median, and interquartile range (IQR). All statistical analyses were performed using SPSS (version 20.0) software (IBM, Armonk, NY, USA).

3. Results

The study population consisted of 37 critically ill inpatients diagnosed with COVID-19 pneumonia. The mean age of the patients with severe COVID-19 pneumonia was 54 years (IQR, 43–64), with a slightly higher male preponderance (57%). Nine (24%) patients had one or more comorbidities. The most common clinical features of COVID-19 pneumonia were fever (29 (78%)), dry cough (28 (76%)), dyspnea (9 (24%)), and fatigue (9 (24%)). As of March 11, 2020, all patients were discharged (Table 1).

A vast majority of patients (32 [86%]) showed an increased CRP level (IQR, 10.0–50.8 mg/L). Thirty-one (84%) patients had an increased erythrocyte sedimentation rate (IQR, 29.5–54.5 mm/h). Serum PCT levels were partially increased in 14 (38%) patients, although it was not significant (IQR, 0.03–0.07 ng/mL). Serum interleukin (IL)-6 and IL-10

| Table 2: Laboratory findings of patients infected with COVID-19. |
|---------------------------------------------------------------|
| **Blood routine**                                              | **Patients (n = 37)** |
| Leucocytes (×109 per L; normal range 3.5–9.5)                 | 6 (4.3–7.6) |
| Increased                                                     | 5 (14%) |
| Decreased                                                     | 2 (5%) |
| Neutrophils (×109 per L; normal range 1.8–6.3)                | 4.5 (2.7–6.6) |
| Increased                                                     | 9 (24%) |
| Lymphocytes (×109 per L; normal range 1.1–3.2)                | 0.8 (0.6–1.0) |
| Decreased                                                     | 28 (76%) |
| Platelets (×109 per L; normal range 125.0–350.0)              | 200 (141–258) |
| Increased                                                     | 1 (3%) |
| Decreased                                                     | 7 (19%) |
| Coagulation function                                          | |
| Activated partial thromboplastin time (normal range 23.5–36.0) | 30.2 (28.1–32.7) |
| Increased                                                     | 1 (3%) |
| Decreased                                                     | 0 (0%) |
| Prothrombin time (s; normal range 12.5–14.0)                  | 11.9 (11.3–12.5) |
| Increased                                                     | 2 (5%) |
| Decreased                                                     | 28 (76%) |
| D-dimer (μg/L; normal range 0.0–0.55)                         | 0.32 (0.22–0.71) |
| Increased                                                     | 9 (24%) |
| Blood biochemistry                                            | |
| Alanine aminotransferase (U/L; normal range 9.0–50.0) ALT    | 22 (16.5–36) |
| Increased                                                     | 7 (19%) |
| Aspartate aminotransferase (U/L; normal range 15.0–40.0) AST  | 28 (21.5–39.5) |
| Increased                                                     | 9 (24%) |
| Serum creatinine (μmol/L; normal range 62.0–97.0)             | 42 (29.5–54.5) |
| Increased                                                     | 5 (14%) |
| Creatine kinase (U/L; normal range 38.0–174.0)                 | 88 (66.5–161.5) |
| Increased                                                     | 8 (22%) |
| Troponin (ng/mL; normal range 0.00–0.08)                      | 0.01 (0.01) |
| Increased                                                     | 0 (0%) |
| Infection-related biomarkers                                   | |
| C-reactive protein (mg/L; normal range 0.0–5.0)               | 19.1 (10.0–50.8) |
| Increased                                                     | 32 (86%) |
| Erythrocyte sedimentation rate (mm/h; normal range 0.0–20.0)  | 42 (29.5–54.5) |
| Increased                                                     | 31 (84%) |
| Procalcitonin (ng/mL; normal range 0.0–0.05)                  | 0.05 (0.03–0.07) |

| Table 2: Continued. |
|---------------------|
| **Blood routine**   | **Patients (n = 37)** |
| Increased           | 14 (38%) |
| Interleukin-6 (pg/mL; normal range 0.1–2.9)                  | 12.85 (6.3–27.7) |
| Increased           | 35 (95%) |
| Interleukin-10 (pg/mL; normal range 0.1–5.0)                 | 5.1 (3.4–9.2) |
| Increased           | 19 (51%) |
The median duration from symptom onset to diagnosis of severe illness was 7.5 days (IQR, 4.5–7.5), the median duration for symptom remission was 5 days (IQR, 2.5–11), and the median duration for saturation improvement was 5 days (IQR, 3–9). Significant absorption of pulmonary lesions was observed in 28 (76%) patients within a median duration of 9 days (IQR, 6–11) (Table 5).

4. Discussion

Among the 37 laboratory-confirmed severe COVID-19 patients, nine (24%) had underlying diseases, mainly hypertension, but a significant number of previously healthy patients had worsened clinical status during treatment. The main symptoms of patients with severe infection are fever, dry cough, chest tightness, and weakness. A few patients may have muscle pain, pharyngeal pain, dizziness, loss of appetite, etc. COVID-19 patients rarely have gastrointestinal symptoms, such as diarrhea, which is different from the symptoms of SARS-coronavirus and MERS-coronavirus infections [11, 12].

Similar to recent reports [13–15], a reduced absolute lymphocyte count was found in 76% of critically ill patients. Reduced IL-6 and IL-10 levels were found in 95% and 19% of patients, respectively, suggesting that COVID-19 may have a role in cellular immune deficiency. The virus spreads through the mucous membrane along the respiratory tract, which provokes a series of immune reactions leading to cytokine storm, eventually causing a change in the peripheral blood lymphocyte count. IL-6 may play a proinflammatory role in pulmonary inflammation, and a significant increase in IL-6 level was found in the majority of patients, suggesting that severe COVID-19 may cause a significant exudation of IL-6 into the lungs. A decrease in the absolute lymphocyte count and increased IL-6 and IL-10 levels may indicate disease worsening.

In our study, PCT level, D-dimer level, clotting parameters, and troponin level were not much altered or slightly elevated, unlike in previous reports involving patients infected with SARS-CoV and MERS-CoV [16]. We speculate that our patients were not critically ill enough to require intensive care and did not develop coagulation disorders, liver and kidney dysfunctions, and myocardial injuries. Furthermore, it also suggests that PCT level, coagulation parameters, troponin level, and other common indicators cannot predict disease worsening.

Chest CT of patients with severe COVID-19 mainly shows bilateral patchy and frosted glass shadows. In our study, the involvement of multiple lobes was found in most patients, some of them showed consolidations, interstitial changes, and nodule shadows. No patient showed pleural effusion. The oxygenation index is a sensitive indicator of the progress of COVID-19. Patients diagnosed with COVID-19 were closely monitored for vital signs immediately after admission, depending on the clinical condition. Twenty-five (68%) patients were treated with human immunoglobulin (0.3–0.5 g/kg daily), and 24 (65%) of them were treated for 3–11 days (median, 4 days; IQR, 3–5.5) (Table 4).

**Table 3: Radiographic findings of patients infected with COVID-19.**

| Patients (n = 37) |  |
|------------------|---|
| Ground-glass opacity | 27 (73%) |
| Patch shadow | 37 (100%) |
| Interstitial abnormalities | 25 (68%) |
| Consolidation | 22 (59%) |
| Nodule | 10 (27%) |
| Normal | 0 (0%) |
| Local patchy shadowing | 2 (5%) |
| Bilateral patchy shadowing | 35 (95%) |

Data are n/N (%), where N is the total number of patients with available data.

**Table 4: Treatment of patients infected with COVID-19.**

| Treatment | n/N (%) | Median (IQR) |
|-----------|---------|--------------|
| No. of patients | 37 | 37 |
| Oxygen therapy | | |
| Nasal cannula | 32 (86%) | NA |
| High-flow nasal cannula | 5 (14%) | NA |
| Antiviral treatment | | |
| α-Interferon | 37 (100%) | NA |
| Lopinavir/litornavir | 37 (100%) | NA |
| Arbidol | 23 (62%) | NA |
| Glucocorticoids | 30 (81%) | 7 (4.1–11) |
| Intravenous immunoglobulin | 25 (68%) | 4 (3.5–5.5) |
| Antibiotic treatment | 9 (24%) | 7 (4.5–7.5) |

Data are median (IQR) or n/N (%), where N is the total number of patients with available data.

levels were elevated in 35 (95%) and 19 (51%) patients, respectively (Table 2). Abnormal CT findings were detected in all patients. Only two (5%) patients had unilateral lobar lesions, while the remaining 35 (95%) had bilateral lobar lesions. Chest CT in most patients showed multiple manifestations, the most common being a patch shadow, which was found in all patients. The other findings were ground glass shadows (27 (73%)), interstitial changes (25 (68%)), consolidation shadows (22 (59%)), and nodular shadows without pleural effusion (10 (27%)) (Table 3).

All patients received oxygen; 32 (86%) and five (14%) patients received high-flow oxygen through a nasal catheter without invasive ventilation. All patients were treated with 5 million units of aerosolized α-interferon and lopinavir/ritonavir therapy (500 mg twice daily). Albendazole tablets (200 mg thrice daily) were administered to 23 (62%) patients. Based on the white blood cell count and CRP level, nine (24%) patients were treated with antibiotics, including penicillin, macrolyclic lipids, and quinolones. The duration of antibiotic treatment was 2–11 days (median, 7 days; IQR, 4.5–7.4). Thirty (81%) patients received intravenous methylprednisolone intravenous infusion (0.5–1 mg/kg daily) for was 3–18 days (median, 7 days; IQR, 4–11 days), depending...
and oxygen saturation was measured twice daily. Blood gas analysis was also performed periodically.

We evaluated the pattern of changes in symptoms. Disease aggravation was reflected by chest tightness. To detect disease progression early, blood gas analysis should be performed immediately to determine the oxygenation index. Because some patients cannot withstand imaging due to advanced disease, and imaging findings may be detected much later (advanced disease), it is not recommended to intervene after the appearance of chest CT features [17, 18].

In patients diagnosed with COVID-19, we immediately administered α-interferon along with lopinavir/ritonavir. However, a considerable number of patients were in the critical stage, suggesting that the antiviral drugs may not be as efficacious as expected. Many patients had diarrhea and other adverse effects; hence, the administration of antiviral drugs remains to be discussed further.

For the diagnosis of severe COVID-19, inflammatory mediators produced by viral infections need to be assessed [19, 20]. Considering cytokine storm, short-term use of a small dose of corticosteroid can reduce the risk of acute respiratory distress syndrome [21]. Therefore, methylprednisolone (0.5–1 mg/kg) was administered to most patients in addition to human immunoglobulin in order to prevent cytokine storm. After patients showed a good response, the oxygenation index returned to ≥300 mmHg. The intervention continued for an average of 9 days after review. Timely administration of glucocorticoids and human immunoglobulin could effectively inhibit the progression of COVID-19 and reverse the condition [22, 23]. However, it needs further study whether glucocorticoids prolong the time of virus excretion from the body. In the treatment of severely ill COVID-19 patients, we added albendazole, whose efficacy against COVID-19 needs further evaluation.

Severe COVID-19 patients were subjected to early intervention under close monitoring. All patients improved and could be discharged alive, which is notably different from previous reports [21, 24]. We believe that the severity of the disease is independent of its prognosis [25, 26], suggesting that symptoms, clinical signs, laboratory results, and chest imaging findings are more reliable for assessing the prognosis of COVID-19 pneumonia.

Progressive acute respiratory distress syndrome is the most common cause of death in patients with severe COVID-19 pneumonia owing to an uncontrolled inflammatory response. Early isolation, early diagnosis, and early treatment with methylprednisolone and human immunoglobulin can reduce the mortality rate of patients with COVID-19 pneumonia.

### Data Availability

The data included in this paper are available without any restriction.

### Conflicts of Interest

The authors declare that they have no conflicts of interest.

### References

1. WHO, Clinical Management of Severe Acute Respiratory Infection when Novel Coronavirus (nCoV) Infection is Suspected: Interim Guidance, 2020, https://apps.who.int/iris/handle/10665/330854.

2. C. Huang, Y. Wang, X. Li et al., “Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China,” The Lancet, vol. 395, no. 10223, pp. 497–506, 2020.

3. S. I. Alsharidah, M. Ayed, R. M. Ameen et al., “COVID-19 convalescent plasma treatment of moderate and severe cases of SARS-CoV-2 infection in Kuwait: a multicenter interventional study,” SSRN Electronic Journal, p. 31, 2020.

4. D. W. Wang, B. Hu, C. Hu et al., “Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus–infected pneumonia in Wuhan, China,” JAMA, vol. 323, no. 11, pp. 1061–1069, 2020.

5. WHO, “Summary of probable SARS cases with onset of illness from 1 November 2002 to 31 July 2003,” 2003, https://www.who.int/csr/sars/country/table2004_04_21/en.

6. WHO, “Middle East respiratory syndrome coronavirus (MERS-CoV),” 2019, http://www.who.int/emergencies/mers-cov/en.

7. L. T. Thanh, T. V. Nguyen, Q. C. Luong et al., “Importation and human-to-human transmission of a novel coronavirus in Vietnam,” The New England Journal of Medicine, vol. 382, no. 9, pp. 872–874, 2020.

8. D. Ray, M. Salvatore, R. Bhattacharyya et al., “Predictions, role of interventions and effects of a historic national lockdown in India’s response to the COVID-19 pandemic: data science call to arms,” 2020.

9. S. Marchini, E. Zaurino, J. Bouziotis, N. Brondino, V. Delvenne, and M. Delhaye, “Study of resilience and loneliness in youth (18–25 years old) during the COVID-19 epidemic: a systematic review,” European Journal of Pediatrics, 2020.
pandemic lockdown measures,” *Journal of Community Psychology*, vol. 49, no. 2, pp. 468–480, 2021.

[10] W. K. Leung, K. F. To, P. K. S. Chan et al., “Enteric involvement of severe acute respiratory syndrome-associated coronavirus infection,” *Gastroenterology*, vol. 125, no. 4, pp. 1011–1017, 2003.

[11] M. H. Jang, M. J. Shin, and Y. B. Shin, “Pulmonary and physical rehabilitation in critically ill patients,” *Acute and Critical Care*, vol. 34, no. 1, pp. 1–13, 2019.

[12] D. Wu, D. Ellis, and S. Datta, “COVID-19, reduced lung function, and increased psycho-emotional stress,” *Bioinformation*, vol. 16, no. 4, pp. 293–296, 2020.

[13] A. Assiri, A. McGeer, T. M. Perl et al., “Hospital outbreak of Middle East respiratory syndrome coronavirus,” *The New England Journal of Medicine*, vol. 369, no. 5, pp. 407–416, 2013.

[14] S. Wan, Q. Yi, S. Fan et al., “Characteristics of lymphocyte subsets and cytokines in peripheral blood of 123 hospitalized patients with 2019 novel coronavirus pneumonia (NCP),” *MedRxiv*, 2020.

[15] J. H. Wu, X. Li, B. Huang et al., “Pathological changes of fatal coronavirus disease 2019 (COVID-19) in the lungs: report of 10 cases by postmortem needle autopsy,” *Zhonghua Bing Li Xue Za Zhi = Chinese Journal of Pathology*, vol. 49, no. 6, pp. 568–575, 2020.

[16] J. C. Leemans, M. J. B. M. Vervoordeldonk, S. Florquin, K. P. van Kessel, and T. van der Poll, “Differential role of interleukin-6 in lung inflammation induced by lipoteichoic acid and peptidoglycan from *Staphylococcus aureus*,” *American Journal of Respiratory and Critical Care Medicine*, vol. 165, no. 10, pp. 1445–1450, 2002.

[17] Z. Xu, L. Shi, Y. Wang et al., “Pathological findings of COVID-19 associated with acute respiratory distress syndrome,” *The Lancet Respiratory Medicine*, vol. 8, no. 4, pp. 420–422, 2020.

[18] P. Zhang, J. Li, H. Liu et al., “Long-term bone and lung consequences associated with hospital-acquired severe acute respiratory syndrome: a 15-year follow-up from a prospective cohort study,” *Bone Res.*, vol. 8, no. 1, p. 8, 2020.

[19] J. T. Wu, K. Leung, and G. M. Leung, “Nowcasting and forecasting the potential domestic and international spread of the 2019-nCoV outbreak originating in Wuhan, China: a modelling study,” *The Lancet*, vol. 395, no. 10225, pp. 689–697, 2020.

[20] N. Chen, M. Zhou, X. Dong et al., “Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study,” *Lancet*, vol. 395, no. 10223, pp. 507–513, 2020.

[21] J.-Y. Wang, S.-Y. Chang, Y.-W. Huang, and S. C. Chang, “Serology-positive but minimally symptomatic COVID-19 may still cause lung injury and lung function impairment,” *The International Journal of Tuberculosis and Lung Disease*, vol. 24, no. 6, pp. 568–569, 2020.

[22] Y. D. Wan, T. W. Sun, Z. Q. Liu, S. G. Zhang, L. X. Wang, and Q. C. Kan, “Efficacy and safety of corticosteroids for community-acquired pneumonia: a systematic review and meta-analysis,” *Chest*, vol. 149, no. 1, pp. 209–219, 2016.

[23] X. Li, C. Wang, S. Kou, P. Luo, M. Zhao, and K. Yu, “Lung ventilation function characteristics of survivors from severe COVID-19: a prospective study,” *Critical Care*, vol. 24, no. 1, p. 300, 2020.