Original Article

Diagnosis and treatment of 471 patients with 2019 novel coronavirus disease (COVID-19)

Kebin Cheng[1,2], Weining Xiong[3], Xin Zhou[4], Huiping Li[2], Junhua Zheng[5], Jinfu Xu[2]

[1]Medical College of Soochow University, Suzhou, China; [2]Department of Respiratory and Critical Care Medicine, Shanghai Pulmonary Hospital, Tongji University School of Medicine, Shanghai, China; [3]Department of Respiratory Medicine, Ninth People's Hospital, Shanghai Jiaotong University, Shanghai, China; [4]Department of Respiratory and Critical Care Medicine, Shanghai General Hospital, Shanghai Jiaotong University, Shanghai, China; [5]Department of Urology, Shanghai General Hospital, Shanghai Jiaotong University, Shanghai, China

Contributions: (I) Conception and design: K Cheng, J Xu; (II) Administrative support: H Li, J Zheng; (III) Provision of study materials or patients: W Xiong, X Zhou; (IV) Collection and assembly of data: K Cheng; (V) Data analysis and interpretation: K Cheng, J Xu, J Zheng; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

Correspondence to: Junhua Zheng. Department of Urology, Shanghai General Hospital, Shanghai Jiaotong University, Shanghai 200080, China. Email: zhengjh0471@sina.com; Jinfu Xu. Department of Respiratory and Critical Care Medicine, Shanghai Pulmonary Hospital, Tongji University School of Medicine, Shanghai 200433, China. Email: jfxucn@163.com.

Background: While the 2019 novel coronavirus disease (COVID-19) outbreak has been largely kept under control in China, it remains a global pandemic, and the source, transmission route, and treatments of SARS-COV-2 are still being investigated. Here, we summarized the clinical features, diagnosis, treatment, and prognosis of COVID-19 patients based on our clinical practice.

Methods: The clinical and imaging findings, treatments, and follow-up data of 471 patients with COVID-19 who were discharged from the Wuhan Jinyintan Hospital prior to February 6, 2020, were retrospectively analyzed.

Results: Among these patients, there were 2 mild cases, 282 moderate cases, 181 severe cases, and 6 critical cases. There were 250 males and 221 females aged 17 to 90 years. The median age was 54 years in the severe/critical group, which was significantly older than in the mild/moderate group ($P<0.05$). 44.59% of them had one or more underlying diseases. The most common symptoms were fever, cough, expectoration, and dyspnea. The median body temperature in the severe/critical group was 39℃, which was significantly higher than in the mild/moderate group ($P<0.05$). The incidences of lymphopenia and $CD4^+$ T lymphocytopenia were 53.5% and 41.86%, respectively. Ground-glass opacity and small patchy shadows were the most common findings on chest computed tomography (CT). Compared with the mild/moderate group, the severe/critical group showed higher proportions of severe lymphocytopenia and $CD4^+$ T lymphocytopenia, along with more ground-glass shadows and large-scale consolidation. After anti-infection, oxygen therapy, and symptomatic support, lymphocytes and $CD4^+$ T lymphocytes were markedly increased, all patients were discharged. The median time of nucleic acid conversion and hospital stay were 9 and 12 days, respectively, which were significantly longer in the severe/critical group than in the mild/moderate group. Of the 390 cases followed, only 19 were hospitalized again due to other diseases. All patients recovered well from COVID-19, with negative nucleic acid test results.

Conclusions: Lymphocytopenia and $CD4^+$ T lymphocytopenia were found to be associated with COVID-19 and thus may be important indicators in evaluating the severity and prognosis. Multidisciplinary management including antiviral treatment, immune regulation, and symptomatic support is effective, and yields a low recurrence rate.

Keywords: 2019 novel coronavirus disease (COVID-19); clinical characteristics; treatment; prognosis; lymphocyte

Submitted Dec 02, 2020. Accepted for publication Jan 22, 2021.
doi: 10.21037/atm-21-236
View this article at: http://dx.doi.org/10.21037/atm-21-236

Introduction

The 2019 novel coronavirus disease (COVID-19), as named by the World Health Organization, is a severe infectious disease of the respiratory tract caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2); however, it is quite different from severe acute respiratory syndrome (SARS) and Middle East respiratory syndrome, (MERS) (1,2). According to the statistics of Chinese Center for Disease Control and Prevention (http://2019ncov.chinacdc.cn/nCoV/), as of April 18, 2020, there were 84,201 confirmed COVID-19 cases and 4,642 deaths from the disease in mainland China, including 46,355 confirmed cases and 3,869 deaths in Wuhan, the city where the virus was first identified; meanwhile, more than 2.16 million confirmed COVID-19 cases and over 140,000 deaths had been reported worldwide. While the COVID-19 outbreak has been largely kept under control in China, it remains a global pandemic, and the source, transmission route, and treatments of SARS-COV-2 are still being investigated. Here, we retrospectively analyzed the clinical features and outcomes of 471 COVID-19 patients who were treated in Wuhan Jinyintan Hospital in Wuhan, Hubei Province, China, with an attempt to further inform the clinical diagnosis and treatment of this disease. This is a detailed report in diagnosis, treatment and prognosis of COVID-19 patients at the early stage of the epidemic. We focused on the possible indicators that could predict the severity and prognosis of COVID-19. We present the following article in accordance with the STROBE reporting checklist (available at http://dx.doi.org/10.21037/atm-21-236).

Methods

Subjects

Patients with confirmed COVID-19 who recovered and were discharged from Wuhan Jinyintan Hospital from January 1 to February 6, 2020, were enrolled in this study. The study was approved by the Ethics Committee of Wuhan Jinyintan Hospital (approval number: KY-2020-34.01). All procedures performed in this study involving human participants were in accordance with the Declaration of Helsinki (as revised in 2013). Individual consent for this retrospective analysis was waived.

Diagnosis and discharge criteria

All the patients had positive nucleic acid test results and met the diagnostic criteria of COVID-19 according to the *Diagnosis and Treatment Protocol for COVID-19 Infection* (Fifth Trial Edition) (3) released by the National Health Commission of China. Clinical typing and discharge criteria were also based on the above document (3).

Study methods

The medical histories of all subjects were collected, and their clinical data including sex, age, occupation, underlying disease, admission date, discharge date, exposure history, symptoms, signs, laboratory tests, imaging, treatments, and prognosis were analyzed. Fever was defined as a body temperature ≥37.3 ℃. COVID-19 patients were followed up via telephone. The last visit was made on March 8, 2020.

Statistical analysis

Data were processed and analyzed using the SPSS v.25.0 software package (IBM Corp., Armonk, NY, USA). Continuous variables are expressed as medians (25^{th} and 75^{th} percentile) and categorical variables as cases (n) and percentages (%). The normally distributed measurement data were compared with independent samples *t*-test and non-normally distributed data with Mann-Whitney U test. The potential correlations of bivariate data were analyzed using Spearman's correlation analysis. A P value of <0.05 was considered to indicate a significant difference.

Results

Clinical features

After patients with incomplete clinical data were excluded, 471 COVID-19 patients who were discharged from Wuhan Jinyintan Hospital from January 1, 2020 to February 6, 2020 were enrolled in our analysis. Among them there were 2 mild cases, 282 moderate cases, 181 severe cases,

and 6 critical cases. These patients included 250 males and 221 females, aged 15–90 years (40–65 years, 64.97%; ≥65 years, 17.20%). The median age was 54 years in the severe/critical group, which was significantly higher than that in the mild/moderate group (P<0.05). The proportion of those ≥65 years was significantly higher in the severe/critical group than in the mild/moderate group (P<0.05). Up to 210 patients had 1 or more underlying diseases including hypertension (n=110), diabetes (n=41), coronary heart disease (n=30), chronic liver disease or cirrhosis (n=22), and chronic obstructive pulmonary disease (COPD) (n=19); other comorbidities included cerebral embolism, chronic kidney disease, and malignancies. Underlying diseases were identified in 95 patients in the severe/critical group and 115 patients in the mild/moderate group; furthermore, the incidences of underlying diseases (especially hypertension, coronary heart disease, and COPD) were higher in the former group than in the latter (*Table 1*).

For the clinical manifestations, the body temperature range was 36.1–40.5 ℃ on admission. Up to 423 patients (89.81%) had a body temperature of ≥37.3 ℃; 176 patients (94.12%) in the severe/critical group had fever, with a median body temperature of 39 ℃; 247 patients (86.97%) in the mild/moderate group had fever, with a median body temperature of 38.4 ℃. The difference was statistically significant between these two groups. The proportion of patients with a maximum body temperature of ≥39 ℃ was 50.27% in the severe/critical group, which was significantly higher than that (30.28%) in the mild/moderate group. In addition to fever, other common symptoms included cough, shortness of breath, sputum, fatigue, muscle aches, and headache in that order. Fewer than 3% of patients presented with diarrhea, sore throat, stuffy nose, runny nose, and hemoptysis (*Table 2*).

Laboratory findings

Anemia (hemoglobin <120 g/L) was detected in 165 patients (40.64% in the severe/critical group *vs.* 31.34% in the mild/moderate group; P<0.05). White blood cell (WBC) count was increased in 58 cases, and the incidence of increased WBC count was significantly higher in the severe/critical group than in the mild/moderate group (P<0.05). WBC count decreased in 76 patients. Reduced lymphocyte count (<1.1×10^9/L) was noted in 252 patients, with the median lymphocyte count being 0.94×10^9/L in the severe/critical group, which was lower than that (1.19×10^9/L) in the mild/moderate group. In addition, the proportion of patients with severely decreased lymphocyte count (<0.5×10^9/L) in the severe/critical group was also significantly higher than that in the mild/moderate group. Thrombocytopenia (<125×10^9/L) occurred in 52 patients, and its incidence was significantly higher in the severe/critical group (15.51%) than that (8.10%) in the mild/moderate group (P<0.05). Erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) level were elevated in most patients, especially in the severe/critical group. Flow cytometry in 172 cases indicated that most patients had varying degrees of decrease in cluster of differentiation 3-positive (CD3+), CD4+, and CD8+ T lymphocyte counts, and the median counts were lower in the severe/critical group than in the mild/moderate group. The CD4+ T lymphocyte count was below 350 in 41.86% of patients, and this proportion was 52.44% in the severe/critical group (*Table 3*). After treatment, the hemoglobin, platelet, and lymphocyte counts were increased in both groups (all P<0.001), while CRP were significantly reduced (P<0.001) (*Table 4*).

Imaging findings

In this study, 22 patients had only chest radiographic data while 449 cases also had chest computed tomography (CT) scans. Pneumonia was found in all patients except for 2 mild cases. Chest CT revealed ground-glass shadows in 253 cases, small patchy shadows in 228 cases, large-scale consolidations in 95 cases; other findings included pleural thickening and adhesions (n=196) and small amount of pleural effusion (n=29). The incidence of large-scale consolidation was significantly higher in the severe/critical group than in the mild/moderate group (68/175 *vs.* 27/274, P<0.001). Focal lesions affecting a single lung were detected in 67 patients, whereas diffuse lesions involving both lungs were found in 380 patients. The incidence of diffuse distribution of the lesions in both lungs was significantly higher in the severe/critical group than in the mild/moderate group (157/175 *vs.* 223/274, P=0.017).

Treatments and outcomes

At the time of admission, 43 patients in the mild/moderate group did not receive oxygen therapy and 241 patients received oxygen through a nasal catheter; in the severe/critical group, the oxygen therapies applied included conventional nasal cannula oxygen therapy (n=135), high-flow nasal cannula oxygen therapy (n=43), noninvasive ventilator (n=7), and invasive ventilator (n=2). Antivirals

Table 1 The general data of COVID-19 patients

Characteristic	Total (n=471)	Severe/critical group (n=187)	Mild/moderate group (n=284)	P value
Age [years]	51 [43–60]	54 [46–64]	49 [42–58]	<0.001
15–39, n (%)	84 (17.83)	21 (11.23)	63 (22.18)	0.002
40–64, n (%)	306 (64.97)	121 (64.71)	185 (65.14)	0.923
≥65, n (%)	81 (17.20)	45 (24.06)	36 (12.68)	0.001
Gender, n (%)				0.370
Males	250 (53.08)	104 (55.61)	146 (51.41)	
Females	221 (46.92)	83 (44.39)	138 (48.59)	
Hospital stay [days]	12 [9–14]	13 [9–16]	11 [9–14]	0.002
Time to nucleic acid conversion [days]	9 [7–11]	10 [7–13]	9 [6–11]	<0.001
Underlying diseases, n (%)	210 (44.59)	95 (50.80)	115 (40.49)	0.028
Hypertension	110 (23.35)	55 (29.41)	55 (19.37)	0.012
Diabetes	41 (8.71)	21 (11.23)	20 (7.04)	0.115
Coronary heart diseases	30 (6.37)	18 (9.63)	12 (4.23)	0.019
COPD	19 (4.03)	12 (6.42)	7 (2.46)	0.033
Chronic liver diseases	22 (4.67)	5 (2.67)	17 (5.99)	0.096
Chronic kidney diseases	14 (2.97)	7 (3.74)	7 (2.46)	0.424
Cerebral embolism	14 (2.97)	8 (4.28)	6 (2.11)	0.176
Malignant tumors	10 (2.12)	6 (3.21)	4 (1.41)	0.185

COVID-19, 2019 novel coronavirus disease; COPD, chronic obstructive pulmonary disease.

were used in 319 of 471 patients. Lopinavir/ritonavir, (sold under the brand name Kaletra), was used in 95 cases, including 40 cases in the severe/critical group and 55 cases in the mild/moderate group. Combination of interferon alfa by vapor inhalation with other antivirals was applied in 47 cases; arbidol, ribavirin, and oseltamivir were used alone or in combination in 224 patients; 413 patients were treated with empirical antibacterials, such as cefoperazone-sulbactam and levofloxacin; and 22 patients were treated with antifungals. Other treatments included anticoagulation with low-molecular-weight heparin (n=53), traditional Chinese medicine, such as Xuebijing injection and Lianhua Qingfei capsule (n=65); intravenous infusion of gamma globulin (n=55), subcutaneous injection of thymalfasin, or oral administration of thymopolypeptides (n=47); and glucocorticoids (generally methylprednisolone 40–80 mg/d for 5–10 days) (n=100). The administration rates of antimicrobial agents, gamma globulin, thymalfasin/thymopolypeptides, low-molecular–weight heparin, and glucocorticoids were significantly higher in the severe/critical group than in the mild/moderate group (all P<0.05) (*Table 5*). All the patients were discharged according to the *Diagnosis and Treatment Protocol for COVID-19* (The Fifth Trial Edition). The duration of hospitalization ranged from 1 to 48 days (median: 12 days); the median hospital stay was 13 days in the severe/critical group, which was 2 days longer than that in the mild/moderate group (*Table 1*, *Figure 1*). The lymphocyte count and CD4+ T cell count at admission were negatively correlated with the length of hospitalization (r=–0.31, P<0.001; r=–0.35, P=0.026). The time to nucleic acid conversion ranged from 1 to 48 days (median: 12 days), and was 1 day longer in the severe/critical group than in the mild/moderate group (*Table 1*, *Figure 2*). Finally, 390 patients were successfully followed up by telephone, 19 of whom (the disease condition was moderate, severe, and critical in 8, 9, and 2 patients, respectively) were readmitted due the primary underlying lung disease or other conditions. Reexaminations of nucleic acid for SARS-

Table 2 Clinical manifestations of COVID-19 patients

Symptoms	Total (n=471)	Severe/critical group (n=187)	Mild/moderate group (n=284)	P value
Fever	38.5 (38–39)	39.0 (38.3–39.2)	38.4 (37.8–39.1)	<0.001
Maximum body temperature (℃), n (%)				
<37.3	48 (10.19)	11 (5.88)	37 (13.03)	0.012
37.3–37.9	46 (9.77)	8 (4.28)	38 (13.38)	0.001
38–38.9	197 (41.83)	74 (39.57)	123 (43.31)	0.420
≥39	180 (38.22)	94 (50.27)	86 (30.28)	<0.001
Cough, n (%)	362 (76.86)	150 (80.21)	212 (74.65)	0.161
Dyspnea, n (%)	198 (42.04)	86 (45.99)	112 (39.43)	0.159
Phlegm production, n (%)	150 (31.85)	67 (35.83)	83 (29.23)	0.132
Fatigue, n (%)	132 (28.03)	50 (26.74)	82 (28.87)	0.613
Muscle aches and pains, n (%)	62 (13.16)	22 (11.76)	40 (14.08)	0.466
Headache, n (%)	26 (5.52)	11 (5.88)	15 (5.28)	0.780
Diarrhea, n (%)	13 (2.76)	4 (2.14)	9 (3.17)	0.504
Sore throat, n (%)	13 (2.76)	3 (1.60)	10 (3.52)	0.214
Runny nose, n (%)	11 (2.33)	3 (1.60)	8 (2.82)	0.394

COVID-19, 2019 novel coronavirus disease.

CoV-2 were negative in all these patients.

Discussion

Similar to SARS-CoV, MERS-CoV, and highly pathogenic avian influenza viruses, SARS-CoV-2 is highly contagious and spreads rapidly from person to person.(4) Droplet transmission and contact transmission are the two main transmission routes of SARS-CoV-2 (5-8). In our current analysis, the median age of patients with COVID-19 was 51 years, and 82.17% of the patients were middle-aged/elderly (>40 years). There were slightly more males than females. These findings were basically consistent with other recent reports (9,10). Chen *et al.* (11) found hypertension, cardiovascular disease, diabetes, and pulmonary disease were triggering or exacerbating factors for COVID-19. Similarly, we also found that patients with co-existing hypertension, coronary heart disease, and/or COPD were more likely to develop severe/critical COVID-19. A possible explanation is that SARS-CoV-2 can enter human cells through the highly expressed angiotensin-converting enzyme 2 (ACE2) in patients with hypertension and/or coronary heart disease (12).

The main clinical symptoms of COVID-19 are fever, dry cough, fatigue, and shortness of breath, and acute respiratory distress syndrome (ARDS) can occur in severe cases. Some patients also have upper respiratory symptoms (e.g., sore throat, stuffy nose, and runny nose) and gastrointestinal symptoms (e.g., nausea, vomiting, and diarrhea) (5,13). Nearly 90% of our patients had fever at admission, and other common symptoms were cough, shortness of breath, sputum, and fatigue; in contrast, upper respiratory symptoms and gastrointestinal symptoms were less common. Thus, febrile patients with a history of COVID-19 exposure should be carefully examined in clinical settings. In our current study, lymphopenia was detected in more than half of the patients, and the incidence of severe lymphopenia was approximately 10%, especially in the severe/critical group, which is consistent with the literature (10,13). Flow cytometry showed varying degrees of decline in CD4+, CD8+, and CD3+ T lymphocytes, and about 40% of the patients showed CD4+ T lymphocytopenia, with a higher incidence in the severe/critical group than in the mild/moderate group, which was basically consistent with a recent report (14). We also found that lymphocyte count and CD4+ T lymphocyte count were negatively correlated with time to nucleic acid conversion and hospital say, suggesting the lymphocyte count and

Table 3 Laboratory findings of COVID-19 patients

Variable	Total	Severe/critical group	Mild/moderate group	P value
White blood cell count (×10^9/L)	5.49 (4.09–7.52)	6.08 (4.15–8.26)	5.30 (4.06–6.88)	0.008
<3.5	76/471 (16.14%)	29/187 (15.51%)	47/284 (16.55%)	0.760
3.5–9.5	337/471 (71.55%)	122/187 (65.24%)	215/284 (75.70%)	0.014
≥9.5	58/471 (12.31%)	36/187 (19.25%)	22/284 (7.75%)	<0.001
Hemoglobin (g/L)	126 (114.75–137)	125 (115–136)	126.5 (114–138)	0.898
<120	165/471 (35.03%)	76/187 (40.64%)	89/284 (31.34%)	0.038
Lymphocytes (×10^9/L)	1.07 (0.76–1.45)	0.94 (0.64–1.28)	1.19 (0.87–1.61)	<0.001
<0.5	48/471 (10.19%)	30/187 (16.04%)	18/284 (6.34%)	<0.001
0.5–1.1	204/471 (43.31%)	87/187 (46.52%)	117/284 (41.20%)	0.254
≥1.1	219/471 (46.50%)	70/187 (37.43%)	149/284 (52.46%)	0.001
Platelets (×10^9/L)	214.5 (155.75–283.5)	204 (141.8–276.3)	217.5 (165.5–287.8)	0.095
<125	52/471 (11.04)	29/187 (15.51%)	23/284 (8.10%)	0.012
≥125	419/471 (88.96%)	158/187 (84.49%)	261/284 (91.90%)	
ESR (434) (mm/H)	49 (39.23–68.00)	53 (43–71.2)	47 (34.6–65)	<0.001
>20	403/434 (92.86%)	172/176 (97.73%)	231/258 (89.53%)	0.001
CRP (mg/dL)	25 (6.1–62.05)	45.40 (16.0–87.98)	15.25 (3.8–39.40)	<0.001
>10	319/471 (67.73%)	148/187 (79.14%)	171/284 (60.21%)	<0.001
$CD4^+$ (/μL)	406.5 (282–648)	357 (266–566)	464 (291.5–790)	0.025
<200	31/172 (18.02%)	17/82 (20.73%)	14/90 (15.56%)	0.378
200–350	41/172 (23.84%)	26/82 (31.71%)	15/90 (16.67)	0.021
≥350	100/172 (58.14%)	39/82 (47.56%)	61/90 (67.78%)	0.007
$CD8^+$ (/μL)	253.5 (163–363.3)	205 (132–305)	292 (220–447.5)	<0.001
$CD3^+$ (/μL)	670.5 (468.8–1,019.5)	620 (433–1,164)	842 (545–1,241)	0.001

COVID-19, 2019 novel coronavirus disease; ESR, erythrocyte sedimentation rate; CRP, C–reactive protein; CD, cluster of differentiation.

CD4+ T lymphocyte count may be important indicators in evaluating the severity and prognosis of COVID-19 (15). The lymphocyte count and $CD4^+$ T lymphocyte count increased significantly after treatment, suggesting that cellular immune function had been gradually restored, which facilitated the eradication of the virus. CRP can be used to identify bacterial and viral infections and is closely related to the systemic inflammatory response (16). A "cytokine storm" in patients with severe/critical COVID-19 can lead to a significant increase in CRP. CRP was remarkably higher in the severe/critical group than in the mild/moderate group and decreased significantly after treatment. In the early stages of COVID-19, patients present with multiple small patchy shadows and interstitial changes, especially in the lung periphery. As the disease progresses, multiple ground-glass opacities and infiltrative shadows are visible in both lungs. Pulmonary consolidation occurs in more severe cases, whereas pleural effusion is less common. In this study, 56.35% of patients presented with ground-glass shadows and 21.16% with diffuse large-scale consolidations, and this phenomenon was more obvious in the severe/critical group than in the mild/moderate group, which was basically consistent with the literature (9,10,17).

In our current study, some of the patients had received antiviral therapy before admission, and therefore antiviral drugs were not applied in about one-third of the patients

Table 4 Changes of blood routine and inflammatory indicators in COVID-19 patients before and after treatment

Group	Severe/critical group				Mild/moderate group			
	Before treatment	After treatment	Z value	P value	Before treatment	After treatment	Z value	P value
White blood cells ($\times10^9$/L)	6.08 (4.15–8.26)	5.60 (4.59–7.19)	–1.731	0.083	5.30 (4.06–6.88)	5.21 (4.56–6.89)	–0.590	0.555
Hemoglobin (g/L)	125 (115–136)	126.5 (111–137)	–5.734	<0.001	126.5 (114–138)	127 (112–140)	–4.562	<0.001
Platelets ($\times10^9$/L)	204 (141.8–276.3)	267 (205.8–336.3)	–5.541	<0.001	217.5 (165.5–287.8)	250 (204–314)	–5.03	<0.001
Lymphocytes ($\times10^9$/L)	0.94 (0.64–1.28)	1.39 (1.04–1.73)	–7.894	<0.001	1.19 (0.87–1.61)	1.46 (1.18–1.77)	–7.847	<0.001
ESR (mm/h)	53 (43–71.2)	49.5 (30.25–61.5)	–3.059	0.002	47 (34.6–65)	46 (38.3–58.8)	–1.564	0.118
CRP (mg/dL)	45.4 (16–87.98)	2.9 (1.1–8.28)	–9.157	<0.001	15.25 (3.8–39.4)	1.5 (0.7–4.23)	–9.047	<0.001

COVID-19, 2019 novel coronavirus disease; ESR, erythrocyte sedimentation rate; CRP, C-reactive protein.

Table 5 Medical treatments in COVID-19 patients

Medicine	Total (n=471)	Severe/critical group (n=187)	Mild/moderate group (n=284)	P value
Antivirals, n (%)	319 (67.73)	160 (85.56)	159 (55.99)	<0.001
Lopinavir/ritonavir	70 (14.86)	25 (13.37)	45 (15.85)	0.460
Lopinavir/ritonavir + interferon	25 (5.31)	15 (8.02)	10 (3.52)	0.033
Arbidol	114 (24.20)	70 (37.43)	44 (15.49)	<0.001
Arbidol + interferon	16 (3.40)	6 (3.21)	10 (3.52)	0.850
Oseltamivir + interferon	6 (1.27)	2 (1.07)	4 (1.41)	0.750
Arbidol + ribavirin	27 (5.73)	12 (6.42)	15 (5.28)	0.600
Arbidol + oseltamivir	61 (12.95)	30 (16.04)	31 (10.92)	0.100
Proprietary Chinese medicines, n (%)	65 (13.80)	21 (11.23)	44 (15.49)	0.190
Antibiotics, n (%)	413 (87.69)	183 (97.86)	230 (80.99)	<0.001
Antifungals, n (%)	22 (4.67)	10 (5.35)	12 (4.23)	0.570
Gamma globulin, n (%)	55 (11.68)	29 (15.51)	26 (9.15)	0.036
Thymalfasin/thymopolypeptides, n (%)	47 (9.98)	25 (13.37)	22 (7.75)	0.046
Low-molecular-weight heparin, n (%)	53 (11.25)	41 (21.93)	12 (4.23)	<0.001
Corticosteroids, n (%)	100 (21.23)	53 (28.34)	47 (16.55)	0.002

COVID-19, 2019 novel coronavirus disease.

after admission. Consequently, 319 cases received antivirals after admission, and the regimens included lopinavir/ritoprevir, alpha interferon, arbidol, oseltamivir, and ribavirin. These drugs were used alone or in combinations, with combinations accounting for 42.32% (135/319) of antivirals treatments, and alpha interferon was used in combinations. Negative conversion of SARS-CoV-2 RNA occurred in all patients after treatment. Based on the available evidence, the World Health Organization (WHO) had listed several priority candidate antiviral drugs for evaluation, which include remdesivir and lopinavir/ritonavir (alone or in combination with alpha interferon). It has been reported that the clinical symptoms in the first patient with severe COVID-19 were remarkably improved after treatment with remdesivir, shedding light on the treatment of this disease (18). Grein *et al.* (19) also

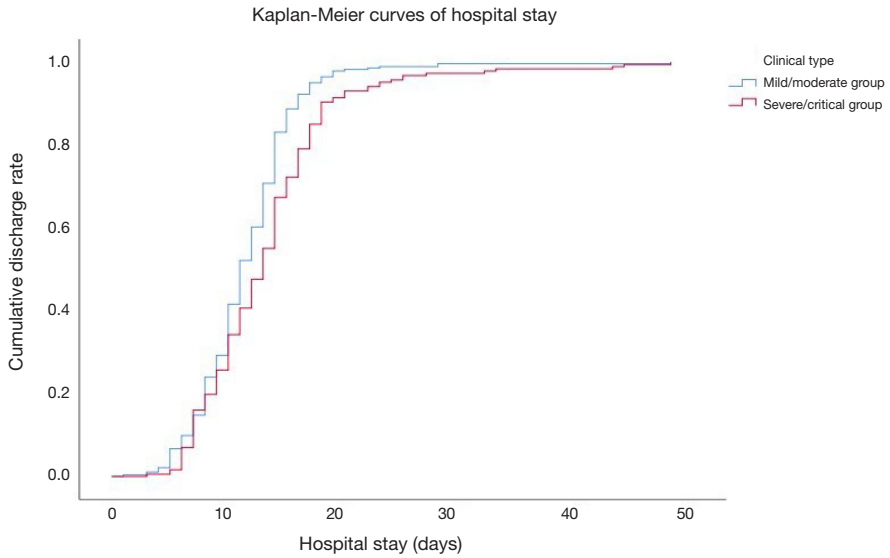

Figure 1 Kaplan-Meier curves of hospital stay (χ^2=16.52, P<0.001).

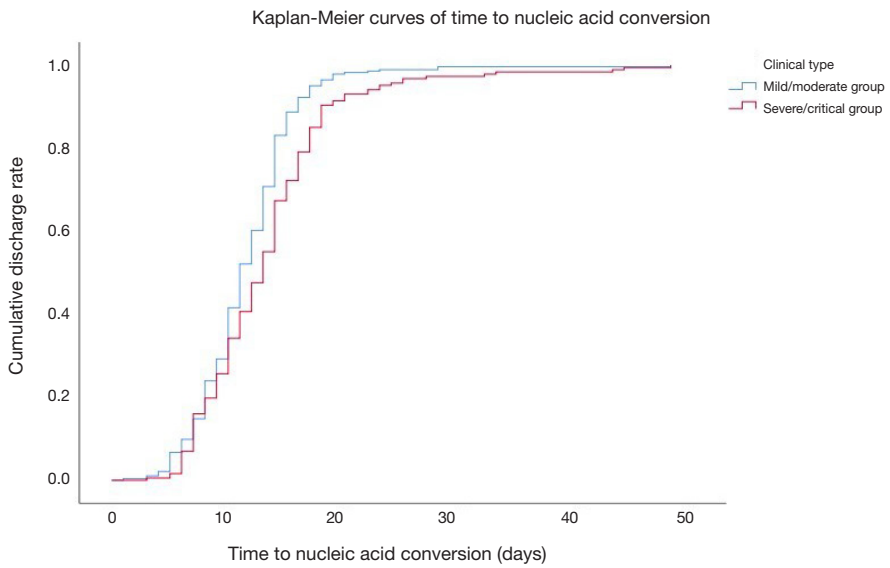

Figure 2 Kaplan-Meier curves of time to nucleic acid conversion (χ^2=23.72, P<0.001).

found that remdesivir improved clinical symptoms in critically ill patients and significantly reduced the case-fatality rate in mechanically ventilated patients. However, the results of a recently published randomized, double-blind, placebo-controlled, multicenter clinical trial showed that, compared with placebo, remdesivir treatment of critically ill inpatients did not accelerate recovery from COVID-19 or lower the case-fatality rate (20).

Both chloroquine and hydroxychloroquine have strong inhibitory effects on SARS-CoV and MERS-CoV, and they can effectively suppress SARS-CoV replication when administered either before or after infection; therefore, they have also gradually been used in the treatment of COVID-19 (21). However, recent studies suggested that a standard dose of hydroxychloroquine sulfate (400 mg, qd) showed no therapeutic effects in terms of improving

symptoms or accelerating virologic suppression in patients with COVID-19; instead, it lowered survival rates and increased the incidence of arrhythmias in inpatients (22,23). According to the *Diagnosis and Treatment Protocol for COVID-19 Infection (7th Trial Edition)* released by the National Health Committee of China, lopinavir/ritoprevir can be used alone or in combination with ribavirin in clinical settings (24). However, the clinical outcomes of patients treated with lopinavir/ritoprevir were found to not be as satisfactory as expected. In a randomized, controlled, open-label clinical trial that included 199 patients with severe COVID-19, a lopinavir/ritonavir treatment group did not demonstrate superiority over the control group in terms of improvement in clinical symptoms and clearance of the virus (25). Acute lung injury and ARDS are mostly caused by immune responses, whereas glucocorticoids can suppress pulmonary inflammation. Research has confirmed that low- and moderate-dose glucocorticoids can reduce the case-fatality rate and shorten hospital stay in patients with severe viral pneumonia without causing secondary infections or other complications (26). In our current study, 21.23% of patients had received glucocorticoids, and the conditions were significantly more severe in the severe/critical group than in the mild/moderate group; notably, these patients had progressive deterioration of oxygenation indicators, rapid imaging progress, and excessive activation of the body's inflammatory response. Low-to-moderate-dose glucocorticoid therapy can control the overactivated inflammatory response without producing strong immunosuppressive effects or delaying the clearance of SARS-CoV-2. Therefore, there is no effective antiviral drugs against SARS-CoV-2, and symptomatic treatment remains the mainstay for COVID-19 patients. However, the novel targeted therapies, including neutralizing antibodies and Fc-fusion proteins, are mainly targeting the SARS-CoV-2 viral entry step. Some of these products may prove to be helpful in preventing the spread of the virus in the body, thereby accelerating recovery after infection or providing a means of prophylaxis (27). In our current study, in addition to the use of antivirals, we also actively controlled secondary infections, restored immunity, and offered symptomatic support in COVID-19 patients. After the treatments, the patients' lymphocyte and CD4+ T lymphocyte counts increased significantly, the clinical symptoms and chest imaging findings were markedly improved, and all the patients were successfully discharged. The median nucleic acid conversion time of SARS-CoV-2 was 9 days and the median length of hospital stay was 12 days. In particular, the median time to conversion and the median length of hospital stay were longer in the severe/critical group than in the mild/moderate group. Of the 390 COVID-19 patients who were regularly followed up, only 19 were hospitalized again due to other diseases; all patients recovered well from COVID-19, with negative nucleic acid test results. Similar findings have been reported in a recent article (28).

In conclusion, middle-aged and elderly people with underlying diseases including hypertension, diabetes, coronary artery disease, and/or COPD are at high risk for COVID-19 and are likely to develop severe forms of this disease. Lymphocytopenia and CD4+ T lymphocytopenia may be associated with COVID-19 and thus may be important indicators in evaluating the severity and prognosis of the disease. If the above patients develop symptoms such as fever, cough, and dyspnea, chest CT and nucleic acid test for SARS-CoV-2 in respiratory specimens must be completed promptly for early diagnosis. Although there is no specific anti-SARS-CoV-2 drug, multidisciplinary management including antiviral treatment, immune regulation, and symptomatic support is effective in treating COVID-19, and both the re-positive rate and the recurrence rate are low after treatment.

Acknowledgments

We are thankful for the support and help from all the members of the first wave of the Shanghai Medical Assistance Team Aiding Hubei Province in writing this article.
Funding: None.

Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at http://dx.doi.org/10.21037/atm-21-236

Data Sharing Statement: Available at http://dx.doi.org/10.21037/atm-21-236

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at http://dx.doi.org/10.21037/atm-21-236). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all

aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was approved by the Ethics Committee of Wuhan Jinyintan Hospital (approval number: KY-2020-34.01). All procedures performed in this study involving human participants were in accordance with the Declaration of Helsinki (as revised in 2013). Individual consent for this retrospective analysis was waived.

References

1. Coronaviridae Study Group of the International Committee on Taxonomy of V. The species Severe acute respiratory syndrome-related coronavirus: classifying 2019-nCoV and naming it SARS-CoV-2. Nat Microbiol 2020;5:536-44.
2. Lu R, Zhao X, Li J, et al. Genomic characterisation and epidemiology of 2019 novel coronavirus: implications for virus origins and receptor binding. Lancet 2020;395:565-74.
3. National Health Commission of the People's Republic of China Notice on printing and distributing the diagnosis and treatment plan of pneumonia with new coronavirus infection (trial version 5). 20200204.
4. Li Q, Guan X, Wu P, et al. Early Transmission Dynamics in Wuhan, China, of Novel Coronavirus-Infected Pneumonia. N Engl J Med 2020;382:1199-207.
5. Chan JF, Yuan S, Kok KH, et al. A familial cluster of pneumonia associated with the 2019 novel coronavirus indicating person-to-person transmission: a study of a family cluster. Lancet 2020;395:514-23.
6. Lei H, Li Y, Xiao S, et al. Routes of transmission of influenza A H1N1, SARS CoV, and norovirus in air cabin: Comparative analyses. Indoor Air 2018;28:394-403.
7. Otter JA, Donskey C, Yezli S, et al. Transmission of SARS and MERS coronaviruses and influenza virus in healthcare settings: the possible role of dry surface contamination. J Hosp Infect 2016;92:235-50.
8. Zumla A, Hui DS, Perlman S. Middle East respiratory syndrome. Lancet 2015;386:995-1007.
9. Feng Y, Ling Y, Bai T, et al. COVID-19 with Different Severities: A Multicenter Study of Clinical Features. Am J Respir Crit Care Med 2020;201:1380-8.
10. Guan WJ, Ni ZY, Hu Y, et al. Clinical Characteristics of Coronavirus Disease 2019 in China. N Engl J Med 2020;382:1708-20.
11. Chen N, Zhou M, Dong X, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. Lancet 2020;395:507-13.
12. Letko M, Marzi A, Munster V. Functional assessment of cell entry and receptor usage for SARS-CoV-2 and other lineage B betacoronaviruses. Nat Microbiol 2020;5:562-9.
13. Huang C, Wang Y, Li X, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet 2020;395:497-506.
14. Guo L, Wei D, Zhang X, et al. Clinical Features Predicting Mortality Risk in Patients With Viral Pneumonia: The MuLBSTA Score. Front Microbiol 2019;10:2752.
15. Wang D, Hu B, Hu C, et al. Clinical Characteristics of 138 Hospitalized Patients With 2019 Novel Coronavirus-Infected Pneumonia in Wuhan, China. JAMA 2020;323:1061-9.
16. Munoz JL, Alvarez MO, Cuquerella V, et al. Procalcitonin and C-reactive protein as early markers of anastomotic leak after laparoscopic colorectal surgery within an enhanced recovery after surgery (ERAS) program. Surg Endosc 2018;32:4003-10.
17. Song F, Shi N, Shan F, et al. Emerging 2019 Novel Coronavirus (2019-nCoV) Pneumonia. Radiology 2020;295:210-7.
18. Holshue ML, DeBolt C, Lindquist S, et al. First Case of 2019 Novel Coronavirus in the United States. N Engl J Med 2020;382:929-36.
19. Grein J, Ohmagari N, Shin D, et al. Compassionate Use of Remdesivir for Patients with Severe Covid-19. N Engl J Med 2020;382:2327-36.
20. Wang Y, Zhang D, Du G, et al. Remdesivir in adults with severe COVID-19: a randomised, double-blind, placebo-controlled, multicentre trial. Lancet 2020;395:1569-78.
21. Dyall J, Coleman CM, Hart BJ, et al. Repurposing of clinically developed drugs for treatment of Middle East respiratory syndrome coronavirus infection. Antimicrob

Agents Chemother 2014;58:4885-93.
22. Chen J, Liu D, Liu P, et al. A pilot study of hydroxychloroquine in treatment of patients with moderate COVID-19. Journal of Zhejiang University (Medical Sciences) 2020;49:215-9.
23. Mehra MR, Desai SS, Ruschitzka F, et al. RETRACTED: Hydroxychloroquine or chloroquine with or without a macrolide for treatment of COVID-19: a multinational registry analysis. Lancet 2020. [Epub ahead of print]. doi: 10.1016/S0140-6736(20)31180-6.
24. National Health Commission of the People's Republic of China: Notice on printing and distributing the diagnosis and treatment plan of pneumonia with new coronavirus infection (trial version 7). 20200304.
25. Cao B, Wang Y, Wen D, et al. A Trial of Lopinavir-Ritonavir in Adults Hospitalized with Severe Covid-19. N Engl J Med 2020;382:1787-99.
26. Chen RC, Tang XP, Tan SY, et al. Treatment of severe acute respiratory syndrome with glucosteroids: the Guangzhou experience. Chest 2006;129:1441-52.
27. Twomey JD, Luo S, Dean AQ, et al. COVID-19 update: The race to therapeutic development. Drug Resist Updat2020;53:100733.
28. Wu C, Hu X, Song J, et al. Mental health status and related influencing factors of COVID-19 survivors in Wuhan, China. Clin Transl Med 2020;10:e52.

Cite this article as: Cheng K, Xiong W, Zhou X, Li H, Zheng J, Xu J. Diagnosis and treatment of 471 patients with 2019 novel coronavirus disease (COVID-19). Ann Transl Med 2021;9(2):163. doi: 10.21037/atm-21-236