

## Research Article

# Effects of Different Therapeutic Schedules on Patients with COVID-19: A Prospective Case–Control Study in China

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**Background and Aims.** At present, a targeted drug has not been found for patients infected with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). This study assessed the effects of different therapeutic schedules on patients with COVID-19. **Methods.** The clinical characteristics, the prognosis of patients with western medicine (WM) treatment, and the combination of traditional Chinese medicine and western medicine (TCM-WM) treatment were retrospectively explored from January 20, 2020 to February 20, 2021. **Results.** 19 patients (15.20%) and 7 patients (5.60%) in the WM treatment group developed into severe type and critically ill, which were higher than 5 patients (9.43%) and 0 patients (0.00%) in the TCM-WM treatment group ( $p = 0.306$  and  $p = 0.08$ ). The time from admission to severe in the WM treatment group was significantly shorter than that of the TCM-WM treatment group (7.5 vs. 11.2,  $p < 0.001$ ). Compared with patients in the TCM-WM treatment group, the average stay time and the negative nucleic acid time of patients in the WM treatment group were both significantly longer (both  $p < 0.05$ ). Besides, there existed no statistical difference for the safety of the two treatment options and nucleic acid test positive 14 days after discharge between the two groups. In line with the performance for severe patients, the average stay, the nucleic acid negative time, and the days of hormone therapy in the WM treatment group were all significantly longer than that of the TCM-WM treatment group (32.5 vs. 18.8,  $p < 0.001$ ; 24.5 vs. 14.5,  $p < 0.001$ ; 6.5 vs. 3.0,  $p < 0.001$ ). **Conclusions.** TCM-WM has better performance in both the disease progression and treatment of severe patients. We recommended that timely TCM-WM should be treated with patients with COVID-19.

## 1. Introduction

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection has spread in Wuhan, from December 2019, leading to coronavirus disease-19 (COVID-19), and most of the cities located in China and over 60 countries and/or regions have successively developed such cases [1, 2]. SARS-CoV-2 is very infectious, pathogenic, and harmful, and the latent period is about 1-14 days [3, 4]. The manifestations of SARS-CoV-2 infection mainly include fever, fatigue, and dry cough [5]. Some patients present symptoms, including runny nose, sore throat, nasal congestion, and diarrhea [6]. Those with severe symptoms usually present dyspnea and hypoxemia one week after the disease appear. Severe cases will quickly progress to symptoms, such as acute respiratory distress syndrome, metabolic acidosis and coagulation dysfunction, and septic shock, which are difficult to correct, resulting in death [7, 8].

The understanding of COVID-19 needs to be deepened [9]. At present, targeted drug has not been found [10]. Symptomatic support still is the main measure. The major of patients are mild type, which is self-limited disease. However, patients with moderate type were treated with western medicine (WM), such as interferon A, lopinavir/ritonavir according to the WHO guidelines [11]. For patients with severe type and critically ill, we can give respiratory support, hormone treatment appropriate of dose, and traditional Chinese medicine (TCM) for auxiliary treatment.

So far, WM is still the main treatment method for COVID-19. However, the percentage of severe cases is still very high; hence, this highly contagious disease needs effective treatment [12, 13]. In our study, the clinical characteristics and prognosis of patients receiving WM and TCM-WM treatments were analyzed, and the effects of different treatments therapeutic schedule were also compared. It is believed that this study would provide new insight into the treatment for COVID-19 patients.

## 2. Patients and Methods

**2.1. Patients.** 178 eligible COVID-19 patients from Jan 20, 2020 to Feb 20, 2021, who were enrolled from the Second People's Hospital of Yancheng City, the First People's Hospital of Yancheng City, the Second People's Hospital of Fuyang City, the Xixi hospital of Hangzhou City, and the Fifth People's Hospital of Wuxi City, were screened as the WM treatment group ( $n = 125$ ) and the TCM-WM treatment group ( $n = 53$ ) of the study. The protocol for enrolled patients is shown (Figure 1). All enrolled patients met the criteria from WHO [11]. This study was performed according to the Helsinki Declaration. The Fifth People's Hospital of Wuxi City Ethics Committee approved this study, and the approval number is No. 2020-002-1. We obtained the informed consents from all participants and their families.

**2.2. Definition of Cases.** COVID-19 patients were defined based on the epidemiological history and consistent with any two clinical manifestations and the pathogenic evidence, as previously described [14]. We used the real time-PCR to

detect the coronavirus RNA [14]. We described in detail the clinical classification definition, which was shown in Table S1.

In this study, we defined the WM treatment group and TCM-WM treatment group as follows: WM treatment group: patients admitted to hospital for diagnosis should be timely treated with atomized 5 million U of reconstituted human interferon alfa-2b injection for twice a day, lopinavir and ritonavir tablets orally for twice a day, or intravenous injection of ribavirin (500 mg for adults, twice a day) and the patients without early antiviral treatment and combined with other therapy, such as antibiotic and hormone therapy; TCM-WM treatment group: in addition to the above WM treatment, combination of TCM treatment, which was described in detail in Table S2.

**2.3. Data Collection.** The data was collected, including clinical characteristics, demographic data, epidemiological history, chest CT, laboratory parameters, hospitalization length, and prognosis. At admission, all the cases received laboratory test, mainly including blood biochemistry, blood routine, and coagulation function. The epidemiological history was defined as follows: I generation: people had an exposure history in Huanan seafood market in South China; II generation: people had a travel history to Wuhan; III generation: people were infected by imported cases; and IV generation, people were infected by the III generation population.

**2.4. Statistical Analysis.** In this study, we performed the statistical analysis with SPSS 18.0. We expressed the continuous data as means  $\pm$  standard deviations and used student's  $t$ -test to analyze.  $p < 0.05$  was considered statistically significant. Besides, we expressed the categorical data as numbers (percentages) and used the chi-squared test to compare. Finally, we analyzed the categorical data using the Spearman rank correlation.

## 3. Results

**3.1. Clinical Characteristics and Features of COVID-19 Patients.** In our study, we retrospectively studied 178 cases in five hospitals from Jiangsu, Anhui, and Zhejiang provinces. The demographics, baseline, and clinical characteristics of all 178 cases were shown (Table 1). Among the enrolled patients, 109 (61.24%) were female, with the overall mean age of 44.09 years (SD 15.01). There existed no significant difference in sex and age between the WM treatment group and TCM-WM treatment group (both  $p > 0.05$ ). In addition, 35 patients (19.66%) were I generation, 73 patients (41.01%) were II generation, 42 patients (23.60%) were III generation, and 28 patients (15.73%) were IV generation.

In the result of nucleic acid detection in respiratory samples, about 7.30% patients had more than three tests before they got positive results. About a fifth of the patients had one kind of underlying diseases at least, of which cardiovascular diseases and diabetes mellitus were the main ones. Fever and dry cough were the main manifestations of SARS-CoV-2-infected patients, which

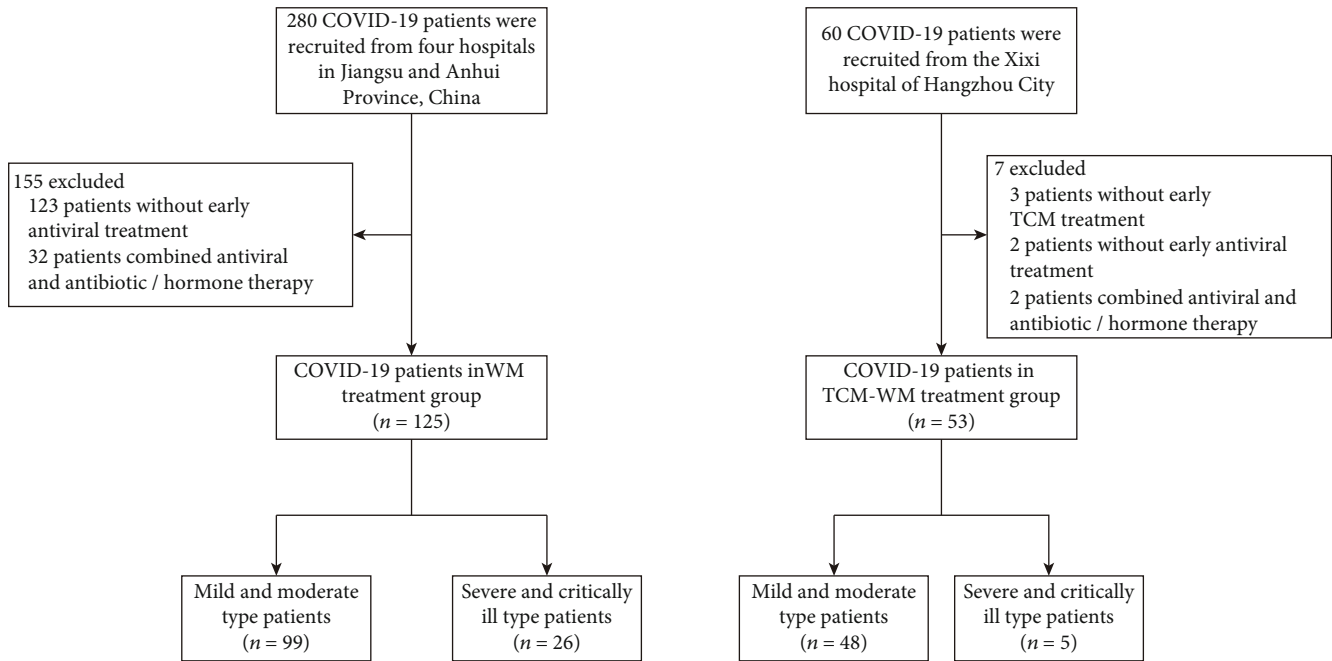


FIGURE 1: The protocol for enrolled patient with COVID-19.

accounted for 76.40% and 50.56%, respectively. The patients had shortness of breath (33.15%) and muscle ache (10.11%), respectively.

**3.2. Laboratory Abnormalities and Imaging Features of COVID-19 Patients.** The laboratory findings were summarized in Table 2. Through the blood routine test, it was showed that both the count of WBC and the lymphocyte count were lower than the normal range. However, the levels of platelet, neutrophil, monocyte, and hemoglobin were still in normal range. Blood biochemistry tests showed that only 4 patients (2.25%) showed liver dysfunction, 2 patients (1.12%) showed renal dysfunction, and 15 patients (8.42%) showed hyperglycemia. LDH, CK, and creatine kinase-MB levels were increased in 35 patients (19.66%), 37 patients (20.79%), and 36 patients (20.22%), respectively, while there were 19 patients (10.67%) with lower PaO<sub>2</sub> and 18 cases (10.11%) with lower PaO<sub>2</sub>/FiO<sub>2</sub>. However, the mean values of them were all still in normal range.

As for coagulation function and infection-related biomarkers, the levels of PT, APTT, and D-dimer were within the normal range. The levels of CRP and ESR were increased in 67 patients (37.64%), and 45 patients (25.28%), respectively. Only 1 case (0.56%) had elevated PCT level. Coinfection test, including 9 types of respiratory pathogens, bacteria, and fungi, showed that only 1 case (0.56%) had positive blood culture.

Among the 178 patients, 162 (91.01%) had abnormal chest CT, 122 (68.54%) had bilateral pneumonia, and 40 (22.47%) presented unilateral pneumonia, respectively. However, there were still 16 patients (8.99%) with no abnormal density shadow in bilateral lung parenchyma (Table 1).

**3.3. Performance of Different Therapeutic Schedules in the Progression of COVID-19 Patients.** To compare the performance of different therapeutic schedule in the progression of patients with COVID-19, 178 patients were divided into the WM treatment group ( $n = 125$ ) and TCM-WM treatment group ( $n = 53$ ). All cases were mild type or moderate type at the time of admission. On admission, among 125 patients in the WM treatment group, 17 patients (13.60%) were mild type, and 108 patients (86.40%) were moderate type. All the 53 cases in the TCM-WM treatment group were moderate type. After admission, 19 patients (15.20%) and 7 patients (5.60%) in the WM treatment group developed into severe type and critically ill, which were higher than 5 patients (9.43%) and no patient (0.00%) in the TCM-WM treatment group ( $p = 0.306$  and  $p = 0.08$ ) (Figures 2(a) and 2(b)). The time from admission to severe in the WM treatment group was significantly shorter than that of the TCM-WM treatment group (7.5 vs. 11.2,  $p < 0.001$ ) (Figure 2(c)).

The average stay of the WM treatment group was 20 days, which was also significantly longer than that of the TCM-WM treatment group (20.5 vs. 14.9,  $p < 0.001$ ) (Figure 2(d)). In addition, the nucleic acid negative time in the WM treatment group was significantly longer than that of the TCM-WM treatment group (18.5 vs. 10.7,  $p < 0.001$ ) (Figure 2(e)). After 14 days of discharge, we performed nucleic acid detection of respiratory samples. The results showed that 1 case (0.80%) was positive in the WM treatment group and 2 cases (3.80%) in the TCM-WM treatment group. No statistical difference was found between these two groups ( $p = 0.161$ ) (Figure 2(f)).

In order to evaluate the safety of the two treatment options, we compared the injury ratio of liver and kidney caused by drugs. There existed no significant statistical

TABLE 1: Baseline characteristics of SARS-CoV-2-infected patients.

Variables	Total patients (n = 178)	WM treatment group (n = 125)	TCM-WM treatment group (n = 53)	p
Age (y)				0.769
Mean (SD)	44.09 ± 15.01	44.01 ± 15.42	44.28 ± 14.15	
Range				
<18	3 (1.69%)	2 (1.60%)	1 (1.89%)	
18-24	11 (6.18%)	8 (6.40%)	3 (5.66%)	
25-49	95 (53.37%)	66 (52.80%)	29 (54.72%)	
50-64	59 (33.15%)	42 (33.60%)	17 (32.08%)	
>=65	10 (5.61%)	7 (5.60%)	3 (5.66%)	
Sex				0.855
Female	109 (61.24%)	76 (60.80%)	33 (62.26%)	
Male	69 (38.76%)	49 (39.20%)	20 (37.74%)	
Agglomerative epidemic				0.001
Generation I	35 (19.66%)	14 (11.20%)	21 (39.62%)	
Generation II	73 (41.01%)	62 (49.60%)	11 (20.75%)	
Generation III	42 (23.60%)	33 (26.40%)	9 (16.98%)	
Generation IV	28 (15.73%)	16 (12.80%)	12 (22.64%)	
Number of nucleic acid tests				0.005
The first time	133 (74.72%)	84 (67.20%)	49 (92.45%)	
The second time	32 (17.98%)	29 (23.20%)	3 (5.66%)	
The third time	11 (6.18%)	10 (8.00%)	1 (1.89%)	
The fourth time	2 (1.12%)	2 (1.60%)	0 (0.00%)	
Comorbidities				0.976
Cardiovascular and cerebrovascular diseases, cerebrovascular diseases	20 (11.24%)	15 (12.00%)	5 (9.43%)	
Endocrine system diseases	12 (6.74%)	9 (7.20%)	3 (5.66%)	
Digestive system disease	8 (4.49%)	5 (4.00%)	3 (5.66%)	
Respiratory system diseases	4 (2.25%)	3 (2.40%)	1 (1.89%)	
Other disease	4 (2.25%)	2 (1.60%)	2 (3.77%)	
Signs and symptoms at admission				0.661
Fever	136 (76.40%)	97 (77.60%)	39 (73.58%)	
Cough	90 (50.56%)	68 (54.40%)	22 (41.51%)	
Shortness of breath	29 (33.15%)	25 (20.00%)	4 (7.55%)	
Muscle ache	18 (10.11%)	14 (11.20%)	4 (7.55%)	
Chest X-ray and CT findings				0.024
Bilateral pneumonia	122 (68.54%)	82 (65.60%)	40 (75.47%)	
Unilateral pneumonia	40 (22.47%)	27 (21.60%)	13 (24.53%)	
No abnormal density shadow	16 (8.99%)	16 (12.80%)	0 (0.00%)	
Clinical outcome				1.000
Remained in hospital	0 (0.00%)	0 (0.00%)	0 (0.00%)	
Discharged	178 (100.00%)	125 (100.00%)	53 (100.00%)	
Died	0 (0.00%)	0 (0.00%)	0 (0.00%)	

Abbreviation: SARS-CoV-2: severe acute respiratory syndrome coronavirus 2; BMI: body mass index; ECMO: extracorporeal membrane oxygenation.

difference between these two groups (0.80% vs.0.00%,  $p = 0.516$ ) (Figure 2(g)).

*3.4. Performance of Different Therapeutic Schedules in the Treatment of Severe Patients with COVID-19.* Next, we studied the performance of different therapeutic schedules on the treatment of severe cases. Due to the few critical ill cases, we

combined critical ill cases with severe type cases, which was called severe patients. After treatment of severe patients with different regimens, we found that the average stay of the WM treatment group was 32.5 days, significantly longer than that of the TCM-WM treatment group (32.5 vs. 18.8,  $p < 0.001$ ) (Figure 3(a)). The nucleic acid negative time in the WM treatment group was also significantly longer than

TABLE 2: Laboratory test results of SARS-CoV-2 patients.

Variables	Total patients (n = 178)	WM treatment group (n = 125)	TCM-WM treatment group (n = 53)	p
<b>Blood routine</b>				
White blood cell count ( $\times 10^9/L$ )	4.9 (4.0-6.7)	5.0 (4.1-6.4)	4.9 (4.0-6.3)	0.412
Neutrophil count ( $\times 10^9/L$ )	3.0 (2.3-3.8)	3.1 (2.5-3.9)	3.0 (2.3-4.1)	0.512
Lymphocyte count ( $\times 10^9/L$ )	1.2 (0.8-1.7)	1.3 (0.9-1.9)	1.2 (0.8-1.8)	0.406
Monocyte count ( $\times 10^9/L$ )	0.5 (0.3-0.7)	0.5 (0.3-0.8)	0.4 (0.3-0.5)	0.296
Platelet count ( $\times 10^9/L$ )	202 $\pm$ 63	198 $\pm$ 60	206 $\pm$ 62	0.421
Hemoglobin (g/L)	133.2 $\pm$ 15.1	131.9 $\pm$ 13.8	134.3 $\pm$ 19.9	0.362
<b>Blood biochemistry</b>				
Alanine aminotransferase (U/L)	21 (14-36)	21 (15-39)	20 (11-34)	0.698
Albumin (g/L)	41.5 (38.3-44.7)	42.1 (39.1-45.2)	40.2 (38.1-42.8)	0.137
Blood urea nitrogen (mmol/L)	4.2 (3.0-5.2)	4.2 (3.2-5.2)	4.3 (2.8-5.0)	0.286
Serum creatinine ( $\mu\text{mol/L}$ )	59.7 (49.5-74.2)	58.6 (48.8-72.0)	61.0 (51.0-72.0)	0.136
Lactate dehydrogenase (U/L)	191 (155-278)	182 (149-265)	199 (154-310)	0.105
Glucose (mmol/L)	5.9 (4.8-7.0)	5.7 (4.7-6.8)	6.3 (5.2-8.1)	0.085
Creatine kinase (U/L)	67 (49-125)	69 (54-111)	63 (47-90)	0.347
Creatine kinase-MB (U/L)	11 (8-17)	12 (7-18)	10 (8-13)	0.255
PaO <sub>2</sub>	99 (84-136)	94 (82-113)	108 (94-147)	0.117
PaO <sub>2</sub> /FiO <sub>2</sub>	473 (365-607)	466 (344-592)	495 (393-616)	0.108
<b>Coagulation function</b>				
Activated partial thromboplastin time (s)	30.7 $\pm$ 3.7	31.0 $\pm$ 4.2	29.9 $\pm$ 3.0	0.093
Prothrombin time (s)	12.1 (11.6-13.2)	12.2 (11.7-13.4)	11.8 (11.5-12.5)	0.104
D-dimer( $\mu\text{g/L}$ )	0.3 (0.2-0.8)	0.3 (0.2-0.6)	0.2 (0.1-0.4)	0.136
<b>Infection-related biomarkers</b>				
C-reactive protein	7.8 (3.2-19.9)	7.7 (3.6-19.8)	8.0 (4.0-23.5)	0.079
Procalcitonin	0.6 (0.3-1.0)	0.9 (0.3-1.2)	0.3 (0.2-0.5)	0.017
Erythrocyte sedimentation rate	14.5 (8.3-26.9)	13.9 (8.4-22.0)	15.5 (8.0-37.8)	0.062
<b>Coinfection</b>				
Other viruses	1 (0.56%)	1 (0.80%)	0 (0.00%)	0.106
Bacteria	1 (0.56%)	1 (0.80%)	0 (0.00%)	0.106
Fungi	0 (0.00%)	0 (0.00%)	0 (0.00%)	1.000

that of the TCM-WM treatment group (24.5 vs. 14.5,  $p < 0.001$ ) (Figure 3(b)). In addition, the days of hormone therapy in the WM treatment group were also significantly longer than that of the TCM-WM treatment group (6.5 vs. 3.0,  $p < 0.001$ ) (Figure 3(c)). The proportion of patients treated with mechanical ventilation and/or ECMO in the WM treatment group was significantly higher than that of the TCM-WM treatment group (100.00% vs. 40.00%,  $p < 0.001$ ) (Figure 3(d)).

**3.5. Case Presentations.** An 88-year-old female was admitted. She had fever for 2 days. The temperature was 38.8°C, respiration 18 times/min, heart rate 89 times/min, and blood pressure 136/64 mmHg. The patient herself denied the epidemic area sojourn history but had the contact history with her son-in-law who was from Wuhan to Hangzhou. The routine blood test results showed the WBC count of  $4.88 \times 10^9/L$ , lymphocytes ratio of 14.8%, and CRP level of 28 mg/L. And the blood gas test showed that pH value of 7.39, PaCO<sub>2</sub> of 28.5 mmHg, and oxygen partial pressure of 85.8 mmHg. Blood

biochemistry showed ALT level of 26 U/L, UREA level of 9.2 mmol/L, creatinine level of 105  $\mu\text{mol/L}$ , lower sodium (128 mmol/L), and lower chlorine (96 mmol/L). The nucleic acid test for COVID-19 with respiratory samples showed positive. Imaging examination showed that the two lungs were scattered in ground glass, patchy high-density shadows with blurred edges, mainly under the pleura, and no definite pleural effusion was observed (Figures 4(a) and 4(b)). The diagnosis for her was COVID-19 (severe case).

After taken to hospital, the patient was given atomized 5 million U of reconstituted human interferon alfa-2b injection for twice a day, lopinavir and ritonavir tablets orally for twice a day, and 0.2 g of abidol hydrochloride granules for 3 times a day, combined with short-term hormone shock anti-inflammatory and other medications, supplementing with albumin/electrolyte, diuretic, and other symptomatic supportive treatments.

Until February 2nd, the patient's symptoms and peak temperature did not improve. The chest CT showed no



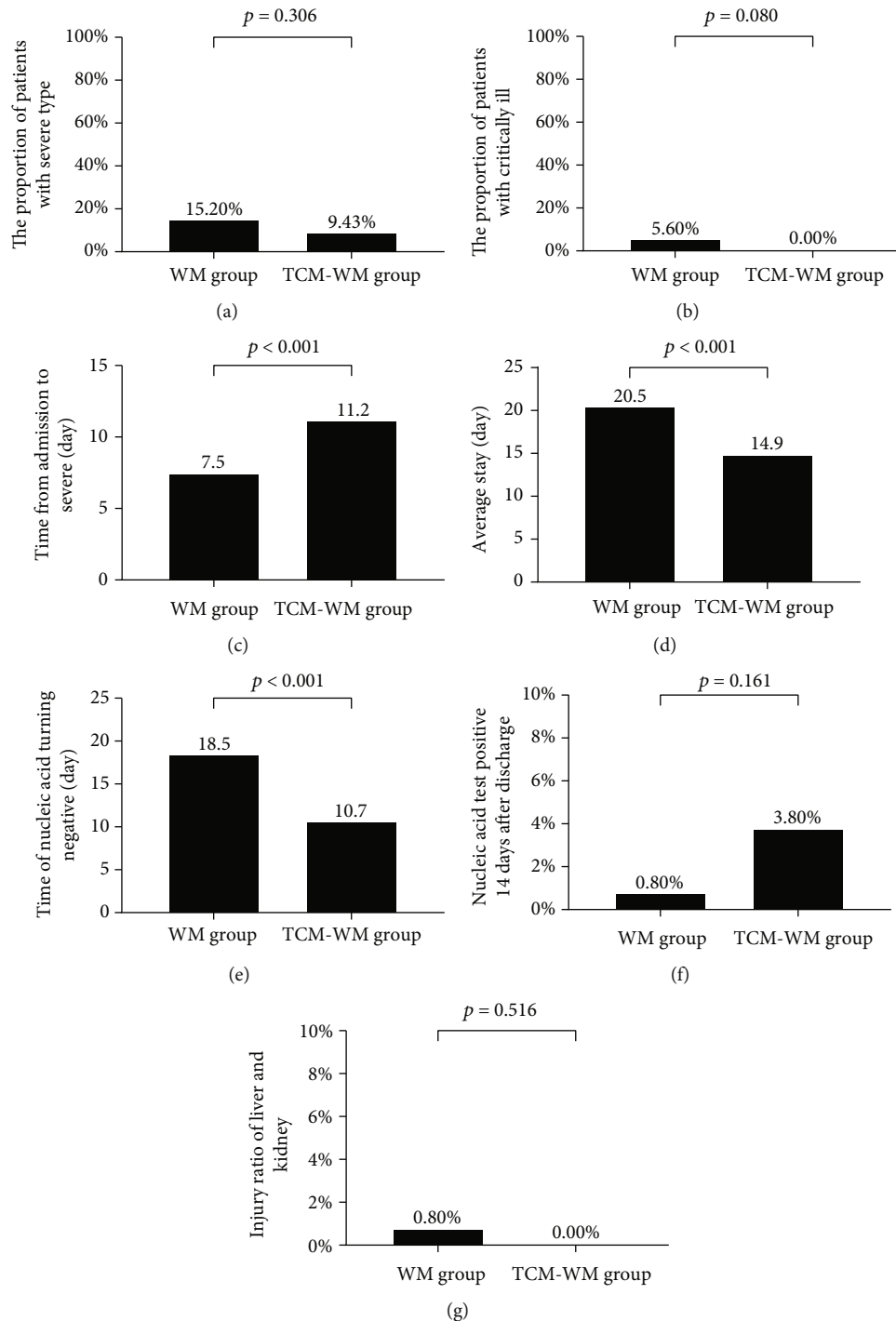


FIGURE 2: Progression of COVID-19 patients in WM treatment and TCM-WM treatment (a) The proportion of patients with severe type. (b) The proportion of patients with critically ill. (c) Time from admission to severe. (d) Average stay. (e) Time of nucleic acid turning negative. (f) Nucleic acid test positive 14 days after discharge. (g) Injury ratio of liver and kidney.

significant absorption of the two pulmonary lesions. Because of severe gastrointestinal reactions, lopinavir plus ritonavir, abidor, and hormones were discontinued. Instead, the traditional Chinese medicine treatment scheme was given immediately, including prescription No. 2 and No. 3 (Table S2).

After 3 days, the fatigue and body pain were relieved, and the heat peak was decreased. A week later, cough and chest tightness were relieved, and low fever was gone. Laboratory test was as follows: pH value of 7.39,  $\text{PaCO}_2$  of 42.1 mmHg, oxygen partial pressure of 112 mmHg, WBC count of  $3.82 \times 10^9/\text{L}$ , lymphocytes of 14.1%, urea level of

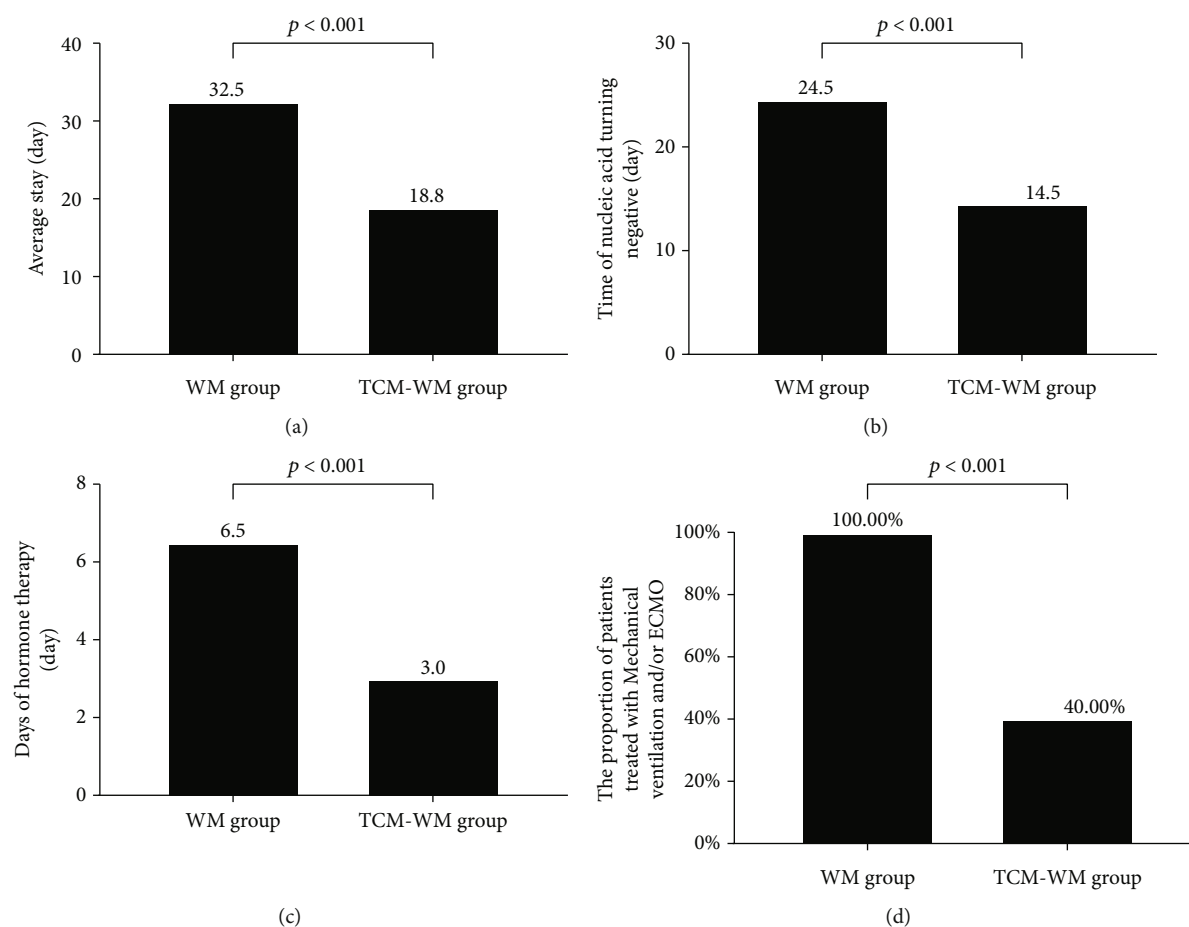


FIGURE 3: The performance in the treatment of severe COVID-19 cases between WM treatment and TCM-WM treatment (a) Average stay. (b) Nucleic acid negative time. (c) The days of hormone therapy. (d) The proportion of patients treated with mechanical ventilation and/or ECMO.

normal (8.5 mmol/L), creatinine decreased to normal (95  $\mu$ mol/L), and the level of both sodium and chlorine were normal. Imaging examination showed that the inflammation in the two lungs was significantly absorbed (Figures 4(c) and 4(d)). The patient was tested negative for nucleic acid three times on February 11th, 12th, and 13th and negative for fecal nucleic acid on February 14th. There were no obvious respiratory symptoms. She was discharged from hospital on February 15th.

#### 4. Discussion

In this study, we retrospectively investigated of 178 cases with WM treatment and the combination of TCM-WM treatment from five hospitals in Anhui, Jiangsu, and Zhejiang Provinces and assessed the effects of different therapeutic schedule on COVID-19 patients. As far as we know, there are few reports about them up to now. It is believed that this report will provide a more effective treatment for COVID-19 patients.

COVID-19 is mainly spread through the respiratory droplets and/or close contact [15, 16]. The five hospitals in this study are located in three provinces with a large number

of population input and output; so, the distribution of ecological history is relatively uniform. In this study, the age distribution was similar to the results by Zhong et al. [17]. However, major of the patients were female, which was inconsistent with the results by Yang et al. [18]. In terms of laboratory examination, both the WBC count and the lymphocyte count were lower than the normal range, which was consistent with other studies [19, 20]. Over a quarter of patients had elevated CRP and ESR, while PCT was normal. In our study, only 4 patients and 2 patients showed liver dysfunction and renal dysfunction, respectively. Consistent with our previous study [14], 7.30% patients had had more than three tests before they got positive results, and 8.99% patients presented no abnormal density shadow in in bilateral lung parenchyma. All of above have attracted enough attention in the COVID-19 screening.

Our study showed that the proportion of patients developed into severe type and critically ill in the TCM-WM treatment group was lower than in the WM treatment group; although, no statistical difference was found. The time from admission to severe in the TCM-WM treatment group was significantly longer than the WM treatment group. Our results indicated that TCM-WM treatment had

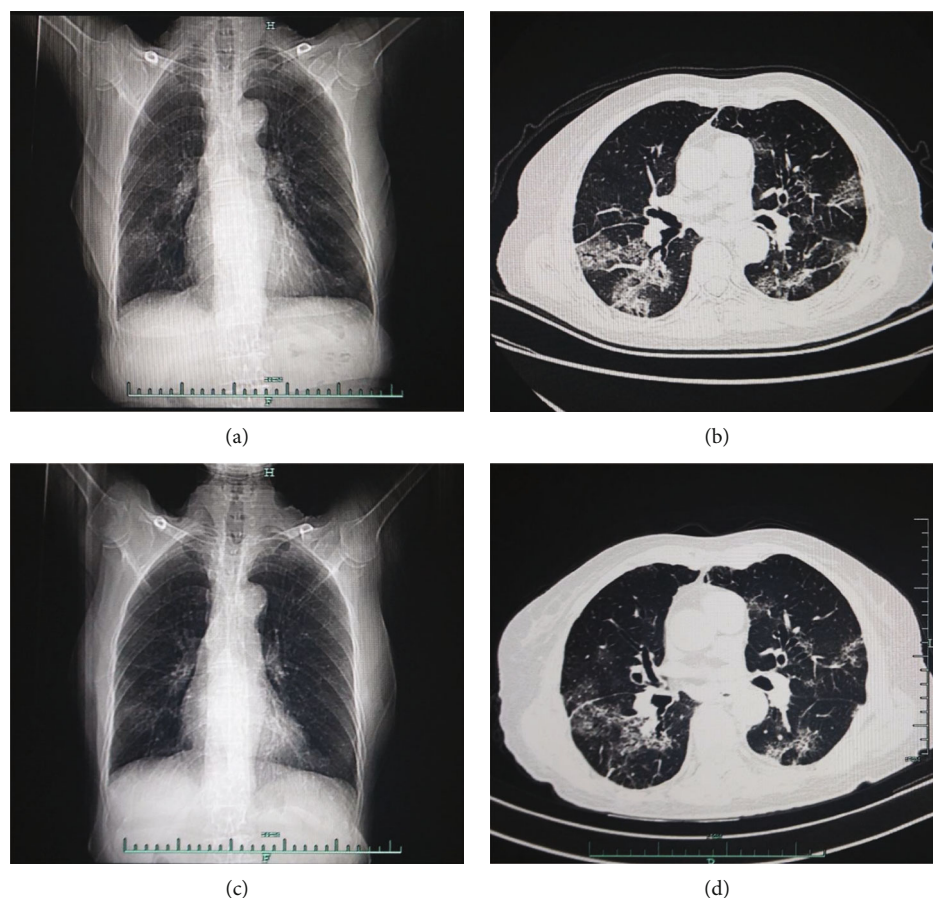


FIGURE 4: Chest X-ray and CT images of the reported case. (a, b) Chest X-ray and CT images showed that the two lungs were scattered in ground glass, patchy high-density shadows with blurred edges, mainly under the pleura, and no definite pleural effusion was observed. (c, d) Chest X-ray and CT images showed that the inflammation in the two lungs was significantly absorbed after TCM-WM treatment.

a better performance in the COVID-19 progression. Moreover, the average stay time and the negative nucleic acid time in the TCM-WM treatment group were both significantly shorter than in the WM treatment group, which illustrated that the effect of TCM-WM was significantly better than the WM group. In terms of drug safety and disease recurrence, no significant difference existed between these two groups.

In line with the performance for severe patients between WM treatment and TCM-WM treatment, limited case study results show that the average stay and the nucleic acid negative time in the WM treatment group were all significantly longer than the TCM-WM treatment group. The dosage of hormone in the WM treatment group was significantly higher than the TCM-WM treatment group, and the percentage of patients treated with mechanical ventilation and/or ECMO in the WM treatment group was all significantly higher than the TCM-WM treatment group. All of those partly testified that the TCM-WM treatment had better performance for severe patients.

Several studies have showed that for thousands of years, TCM has been taken for the treatment of the infectious diseases [21, 22]. TCM can greatly improve clinical symptoms, reduce complications, and therefore improve the quality of

life. Early whole process intervention functions in disease control and early recovery. In 2003, SARS was an infectious disease, which was caused by coronavirus. It was also classified as “febrile disease” [23, 24]. TCM played an active role in disease prevention and treatment [25, 26]. COVID-19 belongs to the category of “epidemic diseases” from the perspective of TCM [27]. The etiology of COVID-19 is to feel the Qi of pestilence, and the disease is in the lung, with the basic characteristics of “dampness, heat, toxin and stasis” [28]. TCM believes that it should be based on the characteristics of the stage of disease onset, the combination of disease differentiation, and syndrome differentiation [29].

In this study, we also report an 88-year-old female who was admitted diagnosed as COVID-19 (severe type). She was first treated with WM treatment. Her symptoms not only did not improve but even worsened. Due to gastrointestinal reactions, we have increased the treatment of traditional Chinese medicine instead of antiviral drugs. Ten days later, the nucleic acid test turned negative. Chest CT reexamination showed that the inflammation in the two lungs was somewhat absorbed, and there were no obvious respiratory symptoms. She was discharged from hospital. This case further suggested that traditional Chinese medicine treatment has a good performance.



This study also has several limitations. Firstly, this study is a retrospective study involving multicenters; therefore, the bias of study may affect the results. Secondly, the number of severe cases is too small. The performance of the two groups in the treatment of the severe group needs further large samples to verify. Third, the basic diseases of patients may affect the therapeutic effect of patients, while our study did not discuss it in detail.

## 5. Conclusion

Compared with WM treatment, TCM-WM has better performance in both the disease progression and treatment of severe patients. We recommended that timely TCM-WM should be timely treated with patients with COVID-19.

## Abbreviations

WM:	Western medicine
TCM:	Traditional Chinese medicine
TCM-WM:	Traditional Chinese medicine and western medicine
SAR-CoV-2:	Severe acute respiratory syndrome coronavirus 2
COVID-19:	Coronavirus disease-19
WBC:	White blood cell
LDH:	Lactate dehydrogenase
CK:	Creatine kinase
PT:	Prothrombin time
APTT:	Activated partial thromboplastin time
CRP:	C-reactive protein
ESR:	Erythrocyte sedimentation rate
PCT:	Procalcitonin
ALT:	Alanine aminotransferase.

## Data Availability

All data relevant to the study are included in the article.

## Ethical Approval

This study was performed according to the Helsinki Declaration. The Fifth People's Hospital of Wuxi City Ethics Committee approved this study, and the approval number is No. 2020-002-1.

## Consent

The authors have obtained the informed consents from all participants and their families.

## Conflicts of Interest

The authors have no competing interest to declare.

## Authors' Contributions

J.W., Y.W., Z.C., and Z.L. contributed to the study concept and design, data acquisition, and manuscript drafting. J.Y., G.Z., X.Z., and B.J. contributed to the data interpretation and statisti-

cal analysis. Z.L., H.H., and D.W. contributed to the collection of samples. S.L., L.L., and H.C. contributed to the study concept and design, supervision, and manuscript critical revision. The manuscript has been checked and approved by all the authors. Jian Wu, Yuan Wang, Zhaobin Cai, and Zechen Lin contributed equally to this work.

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## Supplementary Materials

Table S1: clinical classifications. Table S2: traditional Chinese medicine prescription for COVID-19. (*Supplementary Materials*)

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