

Clinical Characteristics of 254 COVID-19 Inpatients in Yichang, Hubei, China, and Efficacy of Integrated Chinese and Western Medicine Treatment

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Introduction: There is no effective treatment plan for coronavirus disease 2019 (COVID-19). We employed a combination of Chinese and Western medicine treatment for some COVID-19 inpatients.

Methods: This study was a prospective cohort study that observed non-critical COVID-19 inpatients. The differences will be observed in the time from admission to two consecutive 2019-nCoV nucleic acid test negatives and the Visual Analog Scale (VAS) score between the two groups.

Results: A total of 254 confirmed COVID-19 patients were included in this study. The median time from the admission to two consecutive negative nucleic acid tests was 14 days for the integrated Chinese and Western Medicine (ICWM) group, while the Western Medicine (WM) group was 16 days. Besides, the median VAS score of the ICWM group was 0, which was an average decrease of 2 points compared to the time of admission.

Conclusion: For non-critical COVID-19 patients, it was safe and have more benefits to add traditional Chinese medicine decoction based on WM treatment.

Keywords: clinical characteristics, COVID-19 inpatients, efficacy, integrated Chinese and Western medicine treatment

Introduction

COVID-19 has been rapidly erupting in China since the first case was diagnosed in December 2019. Many countries around the world have also shown a spreading trend since March 2020.¹ From 3 January 2020 to 3:25pm Central European Summer Time (CEST), 27 October 2022, there were a total of 8,804,745 confirmed patients and 28,061 deaths across China, and 626,090,018 confirmed cases of COVID-19, including 6,564,556 deaths, reported to World Health Organization (WHO) (<https://covid19.who.int/>), which seriously endangered the health of people around the world while greatly affecting the social life and economy.² Coronaviruses can cause multiple systemic infections in many animals, and the most common for humans are respiratory infections,³ such as Severe Acute Respiratory Syndrome (SARS),⁴ and Middle East respiratory syndrome (MERS).⁵ COVID-19 has a large span regardless of age or severity.³ Most of the infected patients have mild clinical manifestations and good prognosis, while severe patients are often accompanied by chronic diseases, such as chronic obstructive pulmonary disease, diabetes, chronic nephritis, uremia, post-organ transplantation and chronic infections (such as Human Immunodeficiency Virus (HIV)).⁶ And multiple organ failure and adverse drug reactions often occur in the later stage of disease in severe patients.⁷ Many studies have shown that herbal medicine offers multi-organ protection against SARS-CoV-2.⁷ The post-acute sequelae of SARS-CoV-2 infection (PASC)

is an important public health issue that can have a long-term impact on pulmonary and multiple extrapulmonary tissues and organs.⁷

Since the current understanding of COVID-19 is not comprehensive, there have been many attempts to find effective antiviral treatment plan.⁸ To date, the pharmaceutical community has made significant progress in mitigating the SARS-CoV-2 threat through the development of small molecule drugs.^{9–11} However, promising bullets still do not exist.¹² As an indispensable resource for promising compounds, traditional medicine,⁸ and natural products,^{13,14} have attracted significant attention in countering SARS-CoV-2 infection.

With the experience of other hospitals and literature reports,^{15–17} our hospital employed a combination of traditional Chinese and Western medicine treatment for some COVID-19 inpatients in the Third People's Hospital of Yichang, Hubei (City Infectious Disease Hospital) after taking over this hospital in February 20, 2020. The study intends to analyze the clinical and laboratory characteristics of non-critical COVID-19 patients in the region and to compare the clinical efficacy of integrated Chinese and Western medicine treatment with Western medicine treatment alone to provide some evidence for the treatment of non-critical COVID-19 patients.

Methods

This study was a prospective cohort study that observed patients diagnosed with COVID-19 in the Third People's Hospital of Yichang City, Hubei Province. We defined patients who received only Western medicine treatments as the WM group, and those who added traditional Chinese medicine decoction to Western medicine treatment were classified as the ICWM group. The differences will be observed in the time from admission to two consecutive 2019-nCoV nucleic acid test negatives and improvement in clinical symptoms between the two groups of patients. The present study complies with the ethical guidelines for medical and health research involving human subjects reviewed and approved by the Third People's Hospital Affiliated with the Fujian University of Traditional Chinese Medicine and the Declaration of Helsinki. The legal representative is JianHong Chen. The participants provided their written informed consent to participate in this study.

Populations

All enrolled patients were diagnosed with COVID-19. The diagnostic criteria were referred to that the WHO interim guidance on COVID-19.⁶ Patient inclusion criteria: 1. Age \geq 18 years; 2. Positive 2019-nCoV PCR test of respiratory specimens before admission; 3. Clinical symptoms were mild or accompanied by fever, cough, and other symptoms, with or without imaging manifestations of pneumonia. Exclusion criteria: 1. The respiratory failure occurred and required mechanical ventilation; 2. The shock occurred; 3. Intensive Care Unit (ICU) monitoring and treatment were required for combined organ failure; 4. Those who took chloroquine phosphate and/ or those who were enrolled in chloroquine trials.

Western Medicine Treatment

All patients were given oxygen and monitored for vital signs and antiviral therapy after admission according to the patient's condition and laboratory test results: α -interferon (5 million U + normal saline 2mL, nebulized inhaled Bis in Die (BID)), ribavirin (500mg/ time, intravenous drip, BID for 5–10 days), abidol (200mg for oral, Ter in Die (TID) for 5–10 days), lopinavir and ritonavir tablets (600mg for oral, TID for 5–10 days). In principle, no more than 2 antiviral drugs were used at the same time. Antibiotics were given to patients with fever and elevated peripheral blood leukocytes or positive blood bacterial cultures. Those with basic diseases were treated accordingly based on their condition and previous medication.

Chinese Medicine Treatment

Chinese medicine syndrome differentiation referred to the diagnosis and treatment program for the new coronavirus infectious pneumonia (trial edition 7) in China,¹⁵ and we formulated the following therapeutic principles based on syndrome differentiation (See details in [Table S1](#)). 1. Acute stage ([Figure S1](#)) (1) Dampness-heat accumulation in the lung: to clear heat and resolve dampness, and to remove virus in the lung; (2) Cold-dampness distressing lung: to resolve dampness and detoxicate, and to remove virus in the lung; 2. Subacute stage ([Figure S2](#)).

(1) Lung and spleen “Qi” deficiency: to invigorate the spleen for benefiting the lung, and to strengthen the spleen and nourish “Qi”; (2) “Qi” and “Yin” deficiency: to tonify “Qi” and “Yin”, and to nourish “Yin” and moisturize the lung; (3) Dampness distressing and heat retention: to clear heat and promote diuresis, and to dredge the respiratory tract.

Data Collection

All resident doctors were responsible for recording the patient’s epidemiology, clinical manifestations, laboratory tests, chest CT, treatment plan and clinical outcome information in the electronic medical records, and the trained personnel recorded the above information in a special data collection form. The data collection form was reviewed daily, and errors and omissions found were queried and corrected timely. We used a VAS¹⁸ to evaluate the presence or absence of dyspnea and its severity. A score of 0 indicates no dyspnea, and a score of 10 indicates unbearable dyspnea. The degree of dyspnea was marked on a scale of about 10cm by the patient according to the clinical symptoms and was assessed at admission and 10 days after admission. We collected throat swabs for detecting 2019-nCoV with real-time fluorescent RT-PCR using the 2019 new coronavirus nucleic acid detection kit (Guangzhou Da’an Gene Engineering Technology Co., Ltd.). All samples were sent to the laboratory within 8 hours after collection, and nucleic acid detection would be completed within 24 hours. It was usually tested once every 3 days, and the nucleic acid was re-examined the next day after it becomes negative, and the date of two consecutive negative nucleic acid tests was recorded. Complications and their dates during the hospital stay were recorded, including acute cardiac injury (ACI), acute kidney injury (AKI), acute liver damage (ALD), acute respiratory distress syndrome (ARDS), arrhythmia, anemia, and allergy.

Statistical Analysis

Measurement data were expressed by Interquartile Range (IQR), and count data were expressed by rate or composition ratio. The mean comparison between the two groups was performed by *t*-test or *Kruskal Wallis* rank-sum test; rate comparison was performed by chi-square test or Fisher exact test. Risk factors at admission related to Chinese medicine treatment and disease outcomes were screened based on univariate analysis results and previous literature. Multivariate regression analysis was used to compare the effects of the two treatments after adjusting for age, gender, and above risk factors. *Spearman* correlation analysis was used to compare the correlation between blood oxygen saturation and VAS scores for dyspnea. Then we took subgroup analysis by patients of different ages (</ ≥50 years), gender, and mild/ severe. Take $\alpha=0.05$ (two sides). Empower (R) (www.empowerstats.com; X&Y solutions, Inc., Boston MA) and R software, version 3.1.2 (<http://www.r-project.org>) were used for all statistical analyses.

Result

Patients and Baseline Characteristics

A total of 254 confirmed COVID-19 patients were included in this study. And all patients had a 2019-nCoV-related epidemiological history. After one week of adding traditional Chinese medicine treatment, the clinical symptoms of the ICWM group improved more significantly, and the subjective feeling of the patients was better than those of the WM group. Patients admitted at a later stage all required a combination of traditional Chinese and western medicine treatment. The WM group finally involved 42 patients and 212 patients for the ICWM group.

The median age of patients was 51 years (IQR: 40.0–65.0, range: 21–88), and there were 134 female patients (52.8%). There was no significant difference in gender and age between the ICWM group and the WM group. Among the patients, the most common comorbidities were hypertension (19.7%) and diabetes (21.7%). The median time from onset to admission in the ICWM group was 1 day (IQR: 1–2, range: 1–6), and the WM group was 2 days (IQR: 1–3, range: 1–7); There was a significant difference between two groups ($P<0.05$). The most common clinical manifestations at admission were cough (162/ 63.8%) and fatigue (172/ 67.7%). There were relatively more patients with cough, fatigue, and pharyngalgia in the WM group, but there was no significant difference between the two groups in terms of the disease severity, VAS score, and SaO₂ at admission. It can be seen from the smooth fitting curve that older patients have more severe dyspnea (Figure S2). In addition, blood type O (87/ 34.3%) and A (82/ 32.3%) accounted for more patients, but there was no significant difference between the two groups (Table 1).

Table 1 Baseline Characteristics of COVID-19 Patients

N	Median (Q1-Q3)/N (%)			P-value
	Total	WM	ICWM	
	254	42	212	
Age	51.0 (40.0–65.0)	52.0 (41.0–61.8)	51.0 (39.8–65.0)	0.807
Time from onset to admission (d)	1.0 (1.0–2.0)	2.0 (1.0–3.0)	1.0 (1.0–2.0)	< 0.001*
Female	134 (52.8%)	19 (45.2%)	115 (54.2%)	0.285
Hypertension	50 (19.7%)	9 (21.4%)	41 (19.3%)	0.832
CVD	12 (4.7%)	4 (9.5%)	8 (3.8%)	0.117
DM	55 (21.7%)	14 (33.3%)	41 (19.3%)	0.063
MT	3 (1.2%)	1 (2.4%)	2 (0.9%)	0.420
ICVD	10 (3.9%)	2 (4.8%)	8 (3.8%)	0.673
COPD	7 (2.8%)	2 (4.8%)	5 (2.4%)	0.326
CKD	2 (0.8%)	1 (2.4%)	1 (0.5%)	0.304
CLD	2 (0.8%)	1 (2.4%)	1 (0.5%)	0.304
Epilepsy	5 (2.0%)	1 (2.4%)	4 (1.9%)	0.833
Fever	122 (48.0%)	20 (47.6%)	102 (48.1%)	0.953
Cough	162 (63.8%)	35 (83.3%)	127 (59.9%)	0.004*
Expectoration	80 (31.5%)	12 (28.6%)	68 (32.1%)	0.655
Fatigue	172 (67.7%)	38 (90.5%)	134 (63.2%)	< 0.001*
Pharyngalgia	154 (60.6%)	32 (76.2%)	122 (57.5%)	0.024*
Diarrhea	11 (4.3%)	2 (4.8%)	9 (4.2%)	0.881
Nausea	51 (20.1%)	9 (21.4%)	42 (19.8%)	0.834
Vomiting	34 (13.4%)	5 (11.9%)	29 (13.7%)	0.758
Hyperspasmia	5 (2.0%)	1 (2.4%)	4 (1.9%)	0.833
Anxiety	47 (18.5%)	6 (14.3%)	41 (19.3%)	0.520
Insomnia	61 (24.0%)	11 (26.2%)	50 (23.6%)	0.718
VAS at admission	2.0 (1.0–3.0)	2.0 (1.0–3.0)	2.0 (1.0–3.0)	0.301
SaO ₂ (%)	96.0 (93.0–97.0)	97.0 (95.0–97.0)	96.0 (93.0–97.0)	0.084
Blood type				0.678
A	82 (32.3%)	13 (31.0%)	69 (32.5%)	
B	41 (16.1%)	6 (14.3%)	35 (16.5%)	
AB	44 (17.3%)	10 (23.8%)	34 (16.0%)	
O	87 (34.3%)	13 (31.0%)	74 (34.9%)	

Abbreviations: WM, Western medicine; ICWM, integrated Chinese and Western medicine; CVD, cardiovascular disease; DM, diabetes mellitus; MT, malignancy tumor; ICVD, ischemic cerebrovascular disease; COPD, chronic obstructive pulmonary disease; CKD, chronic kidney disease; CLD, chronic liver disease; *P< 0.05.

Laboratory Tests and Complications

The level of HGB of the ICWM group was significantly lower than that of the WM group at admission, and there was no significant difference between the two groups after 10 days of treatment and before discharge. There was no significant difference in blood urea nitrogen between the two groups at admission. After treatment, BUN in the ICWM group was significantly lower than that in the WM group. Other indicators like blood routine, liver function, kidney function, blood coagulation, and blood gas analysis, were not significantly different between the two groups before and after treatment (Table 2).

The most common complications during hospitalization were anemia (WM: 11.9%, ICWM: 8.0%), ACI (WM 7.1%, ICWM 2.4%) and ALD (WM 9.5%, ICWM 7.1%), etc.; only a few patients had allergic reactions or ARDS, and no patients suffered AKI (Table 3). However, there was no significant difference between the two groups (Table S2), indicating that Chinese medicine treatment did not increase the incidence of complications.

Table 2 Changing of Laboratory Findings of COVID-19 Patients

N	At Admission		P-value	10 Days After Admission		P-value	At Discharging		P-value
	WM	ICWM		WM	ICWM		WM	ICWM	
	42	212		42	212		42	212	
WBC (×10 ⁹ /L)	5.8 (4.7–7.4)	5.4 (4.6–6.4)	0.485	5.4 (4.5–6.8)	5.9 (5.1–6.8)	0.342	5.4 (5.1–6.1)	5.9 (5.1–6.8)	0.210
NEUT (×10 ⁹ /L)	2.6 (2.0–3.5)	3.2 (2.4–3.7)	0.076	2.8 (2.3–3.2)	2.9 (2.3–3.1)	0.543	2.7 (2.3–3.1)	2.9 (2.3–3.1)	0.679
LY (×10 ⁹ /L)	1.0 (0.9–1.1)	1.0 (0.9–1.1)	0.307	1.5 (1.1–1.9)	1.8 (1.5–2.1)	0.003*	1.9 (1.2–2.2)	2.1 (1.9–2.3)	0.033*
HGB (g/L)	130.0 (123.2–139.2)	125.0 (121.0–134.0)	0.025*	127.5 (115.5–135.0)	124.0 (120.0–132.0)	0.876	129.0 (115.2–134.8)	126.0 (121.0–132.0)	0.449
PT (s)	11.5 (11.0–12.3)	11.6 (11.2–12.3)	0.684	11.3 (10.9–12.3)	11.4 (11.0–11.9)	0.78	11.6 (11.0–12.3)	11.3 (10.9–11.9)	0.01*
APTT (s)	32.5 (30.2–34.7)	32.4 (30.2–34.1)	0.902	31.1 (29.8–32.1)	31.2 (30.2–32.2)	0.347	31.1 (29.8–32.1)	31.2 (30.2–32.2)	0.347
D-dimer (mg/L)	0.5 (0.4–0.8)	0.5 (0.4–0.7)	0.891	0.6 (0.4–0.8)	0.6 (0.5–0.7)	0.921	0.5 (0.5–0.7)	0.5 (0.5–0.6)	0.617
BUN (mmol/L)	3.6 (2.7–4.5)	3.4 (2.8–3.9)	0.164	2.9 (2.1–3.4)	2.1 (1.5–2.8)	< 0.001*	3.2 (2.5–3.8)	2.1 (1.5–2.6)	< 0.001*
SCr (μmol/L)	55.0 (42.2–72.8)	54.0 (42.0–66.2)	0.384	56.0 (48.2–74.5)	61.0 (52.0–73.0)	0.53	65.0 (51.2–78.8)	61.0 (52.0–76.0)	0.244
CK (U/L)	66.0 (59.0–78.8)	67.0 (56.0–82.0)	0.838	68.0 (61.0–77.8)	77.0 (68.0–87.2)	0.004*	81.0 (77.0–95.8)	79.5 (76.8–91.0)	0.866
LDH (U/L)	185.5 (154.5–216.8)	177.0 (156.0–210.0)	0.221	177.5 (159.5–198.0)	176.0 (154.0–198.0)	0.266	154.0 (136.8–170.8)	164.0 (132.0–187.0)	0.247
ALT (U/L)	25.0 (19.5–31.0)	24.0 (21.0–31.0)	0.94	25.5 (19.5–29.8)	24.0 (19.8–31.0)	0.872	22.5 (17.2–24.8)	24.0 (21.0–32.0)	0.006*
AST (U/L)	24.0 (21.0–30.0)	25.0 (20.8–31.2)	0.76	25.0 (21.0–31.8)	25.0 (20.8–31.0)	0.629	25.5 (22.2–32.8)	24.5 (20.0–31.0)	0.06
PH	7.4 (7.4–7.4)	7.4 (7.4–7.4)	0.912	7.4 (7.4–7.4)	7.4 (7.4–7.4)	0.84	7.4 (7.4–7.4)	7.4 (7.4–7.4)	0.029*
Lactate (mmol/L)	0.8 (0.6–1.0)	0.8 (0.7–1.0)	0.809	0.8 (0.7–1.0)	0.9 (0.7–1.0)	0.692	0.8 (0.7–1.0)	0.9 (0.7–1.0)	0.239

Note: *P< 0.05.

Abbreviations: WM, Western medicine; ICWM, integrated Chinese and Western medicine; WBC, white blood cell; LY, lymphocyte; HGB, hemoglobin; NEUT, neutrophil; PT, prothrombin time; APTT, activated partial thromboplastin time; BUN, blood urea nitrogen; SCr, serum creatinine, CK, creatine kinase; ALT, alanine aminotransferase; AST, Aspartate aminotransferase; LDH, lactate dehydrogenase.

Table 3 Comparisons of Outcomes of COVID-19 Patients Between WM and ICWM Groups

	Outcomes, Median (Q1-Q3)	β (95% CI) P-value		
		Non-Adjusted	Model 1	Model 2
Time from admission to 2 × PCR (-) (d)				
WM	16.0 (12.0–25.0)			
ICWM	14.0 (11.0–20.0)	-2.7 (-5.1, -0.4) 0.024*	-2.9 (-5.2, -0.5) 0.019*	-2.8 (-5.5, -0.1) 0.044*
VAS at 10 days				
WM	2.0 (1.0–3.0)			
ICWM	0.0 (0.0–1.0)	-1.5 (-1.7, -1.2) < 0.001*	-1.5 (-1.7, -1.2) < 0.001*	-1.5 (-1.8, -1.3) < 0.001*
VAS Difference				
WM	-0.5 (-1.0–0.0)			
ICWM	-2.0 (-2.0–1.0)	-1.2 (-1.6, -0.9) < 0.001*	-1.3 (-1.6, -0.9) < 0.001*	-0.9 (-1.2, -0.6) < 0.001*

Notes: Model 1 adjust for: age and sex. Model 2 adjust for: age, sex, cardiovascular disease, COPD, chronic kidney disease, chronic liver disease, time from onset to admission (d), SaO₂ (%), temperature (°C), heart rate, mean arterial pressure, blood type, hemoglobin, and lymphocyte count at admission. *P < 0.05.
Abbreviations: WM, Western medicine; ICWM, integrated Chinese and Western medicine.

Clinical Outcome

Most non-critical COVID-19 imaging showed relatively limited exudative changes in the early stages, mainly involving the interstitial lung, and showing multiple ground-glass opacity. The lesions were mostly located under the pleura. With the further development of inflammation, the distribution area of the lesions gradually increased, and the scope expanded to two lungs. The density of the lesions increased and merged into a large area with an asymmetric distribution, and the bronchial blood vessel bundles become thicker. With the gradual improvement of the condition, most of the absorption period was 1–2 weeks after the onset of disease (Figure 1).

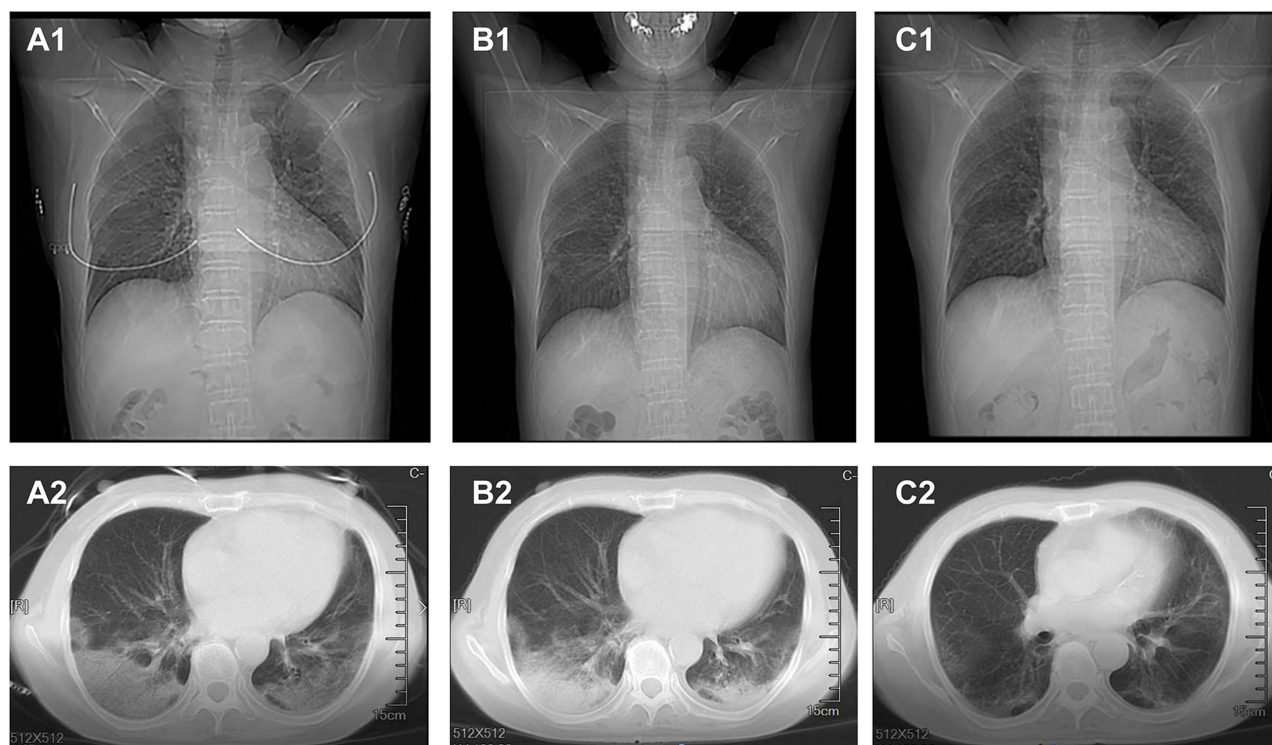


Figure 1 Chest computer topographic images of a middle-aged patient infected with 2019-nCoV. (A1 and A2) CT images on admission: the lesions were mostly located under the pleura and the pulmonary interstitium, showing multiple ground glass density shadows (GGO). (B1 and B2) CT images after treatment of traditional Chinese medicine on day 10 after hospitalization: the range expanded to double lungs and multiple lobes. The density of the lesions increased with asymmetric distribution, and the bronchial vascular bundle became thicker. (C1 and C2) CT images before discharge: inflammation is basically absorbed, with a few patchy shadows in both lower lungs.

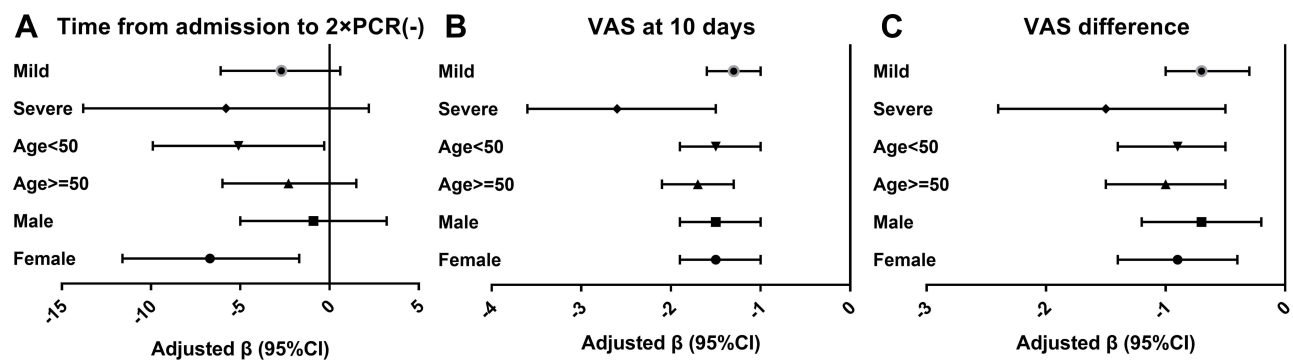


Figure 2 Efficacy of ICWM in subgroups of patients infected with 2019-nCoV. β value was calculated with multivariate regression analysis comparing ICWM group with WM group (reference group) on (A) time from admission to 2xPCR (-), (B) VAS at 10 days, and (C) VAS difference. It can be seen from the figure that the combination of traditional Chinese and Western Medicine could significantly improve the degree of dyspnea in different subgroups. It was adjusted for: age/sex; cardiovascular disease, COPD, chronic kidney disease, chronic liver disease, time from onset to admission (d), SaO₂ (%), temperature (°C), Heart rate, mean arterial pressure, blood type, hemoglobin, and lymphocyte count at admission.

Abbreviations: WM, Western medicine; ICWM, integrated Chinese and Western medicine.

No patient died or was transferred to ICU during hospitalization. The data in Table 3 suggest that the median time from admission to two consecutive negative nucleic acid tests was 14 days for the ICWM group, while the WM group was 16 days. After using multivariate regression analysis to correct the related risk factors, there were still significant differences between the two groups ($P=0.049$). Besides, after 10 days of treatment, the median VAS score of the ICWM group was 0, which was an average decrease of 2 points compared to the time of admission, and the WM decreased by an average of 0.5 points. After adjusting for related risk factors, the degree of dyspnea as 10 days after admission of the ICWM group was significantly improved compared with the WM group ($P<0.05$). In the subgroup analysis, it can be seen that for the time from admission to two consecutive negative nucleic acid tests, the ICWM group tended to reduce this time for patients of different ages, genders, and severity; There was a significant difference between the two groups for young patients under the age of 50 years and female patients ($P<0.05$). Moreover, the combination of Chinese and Western Medicine can significantly improve the degree of dyspnea in different subgroups of people (Table 3, Figure 2).

Discussion

2019-nCoV is a new coronavirus that is not completely equivalent to MERS and SARS,¹⁹ and humans are universally susceptible to it.²⁰ Since the current understanding of COVID-19 is not comprehensive,⁸ many antiviral drugs were tried to be used in the clinic to relieve clinical symptoms.²¹

Adverse Side Effects of Small Molecule Drugs Against COVID-19

Type I interferon (Type I IFN) is a type of cytokine that interferes with viral replication in target cells by releasing a large amount of protein, and interferon β (IFN- β) is the most common and effective IFN.²² Ribavirin, as another antiviral drug that inhibits intracellular virus replication, often works in synergy with IFN- β and has a certain effect in the anti-SARS virus.²³ As early as the SARS epidemic in 2004, lopinavir was used as a first-line treatment and received some curative effects.²⁴ Therefore, during the COVID-19 outbreak, lopinavir was again recommended as an antiviral drug,²⁵ but the effect is uncertain. In addition to the commonly used antiviral drugs mentioned above, remdesivir as a broad-spectrum inhibitor of RNA polymerase, especially when used in combination with IFN- β , is considered to be superior to the above-mentioned anti-viral effects in both intracellular and extracellular.^{26,27} The drug was therefore used in the treatment of the first COVID-19 patient in the United States,²⁸ but its clinical efficacy and safety have not yet been proven.²⁰ The currently used antiviral drugs have different degrees of damage to the kidney, liver, bone marrow, and peripheral nerves, so research teams around the world are committed to exploring effective treatment options for COVID-19.

Traditional Chinese Medicine May Play a Crucial Role Against COVID-19

The latest version of the program on the diagnosis and treatment of COVID-19 in China clearly stated that the disease belongs to the category of traditional Chinese Medicine epidemic, the cause is the body felt by the epidemic, and the location is in the lung.²³ In the early stage of the epidemic, the medical teams of Guang'anmen Hospital and Beijing Xiyuan Hospital of the Chinese Academy of Chinese Medical Sciences cured the first batch of 8 patients with only Chinese medicine treatment or ICWM treatment during the assistance to Wuhan Jinyintan Hospital, who was discharged on February 3, 2020.²⁷

This study was a prospective cohort study of COVID-19 inpatients diagnosed in Yichang, Hubei, China. It analyzed the clinical characteristics of 254 non-critical patients, and the effectiveness and safety of ICWM treatments. The study found that the predominant population is still mainly middle-aged with a median age of 51 years although 2019-nCoV is generally susceptible to the population, and the older patients are relatively heavier, which was consistent with previous epidemiological findings.^{20,29} And there was no significant difference in gender. In addition, patients infected with 2019-nCoV were often associated with chronic diseases, especially diabetes, cardiovascular and cerebrovascular disease, which may be related to the low immune function of this population.⁶

Our Study Indicates the Efficacy and Safety of ICWM Treatment Against COVID-19

In this study, the VAS score evaluating the degree of dyspnea of chronic obstructive pulmonary disease (COPD) patients was introduced to COVID-19 patients for the first time. In the correlation analysis, the VAS score and blood oxygen saturation at admission were significantly negatively correlated (*Spearman* correlation coefficient -0.8603 , $P < 0.05$), VAS score can also well reflect the degree of dyspnea in COVID-19 patients. From the results of this study, it can be seen there was no significant difference in the severity of the disease at admission between the ICWM and WM groups. After treatment, the condition of patients in the ICWM group improved significantly, and the median VAS score was significantly lower than that of the WM group. And this phenomenon has nothing to do with age, sex, and severity degree in non-critical patients. Not only that, the time for nucleic acid to turn negative was significantly shortened by an average of 2 days compared with the WM group, especially in young patients and female patients.

In terms of safety, the median blood urea nitrogen was not significantly different between the two groups before treatment. Then this item of the ICWM group was significantly lower than that of the WM group after treatments, indicating that Chinese medicine has no obvious nephrotoxicity in the treatment of COVID-19. It even has a certain protective effect on the kidney. Because some Chinese medicine used in these patients has certain advantages for nourishing "Qi" and nourishing blood, and strengthening the spleen and kidney, especially for patients who have kidney damage in the basic disease or impaired renal function during antiviral treatment. There was a difference in the hemoglobin between two groups of patients when they were admitted to the hospital, but there was no significant difference between the two groups after treatment, indicating that Chinese medicine may have a protective effect on the bone marrow suppression caused by antiviral drugs. Besides, the increased Chinese medicine treatment did not significantly affect the coagulation, cardiac and liver function, and other aspects of COVID-19 patients, and did not increase the incidence of COVID-19-related complications during hospitalization. We can see that the addition of traditional Chinese medicine was safe for non-critical COVID-19 patients.

Limitations of the Present Study

The main limitation of this study was that this study was observational, and there was an imbalance between the two groups at the admission. For example, the time from onset to admission of patients in the WM group was one day longer than those in the ICWM group. The WM group has a higher proportion of patients with cough and fatigue, which may affect the results of the study. However, we adjusted the above factors in Multivariate regression analysis to minimize the effect of these baseline biases on the research results. Besides, due to the urgency of the epidemic situation and the research conditions, the patient's dyspnea was evaluated using the patient's self-assessed VAS score,¹⁸ which may lack objectivity, but can reflect the changes in the subjective feelings of patients to a certain extent. This study revealed that the addition of traditional Chinese medicine decoction significantly improved the

clinical symptoms and shortened the course of COVID-19. But it is unknown how traditional Chinese medicine plays a role in this disease, its pharmacological mechanism should be further explored. In addition, China's novel coronavirus has been successfully isolated from China's CDC on January 24th of this year. With the help of the three-phase clinical trial, we hope the novel coronavirus vaccine to be listed. It is expected that the application and popularization of the new vaccine can effectively prevent and control the spread of the epidemic.

For non-critical COVID-19 patients, it was safe to add traditional Chinese medicine decoction based on western medicine treatment, and ICWM treatments may shorten the time of 2019-nCoV nucleic acid test to turn negative and improve the clinical symptoms of patients. It is necessary to further verify the effect in clinical trials.

Disclosure

The authors declare no conflicts of interest in this work.

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