Efficacy of Integrative Chinese-Western Medicine Treatments for COVID-19 Patients in ICU in Yichang, Hubei, China

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Abstract

Background

The prognosis of severe COVID-19 patients is poor. Traditional Chinese Medicine had an advantage in keeping microenvironmental balance in treating SARS and COVID-19.

Methods

This prospective cohort study compared the efficacy and safety of integrative Chinese-Western medicine (ICWM) treatments with Western medicine (WM) treatments in severe or critically ill patients. The outcomes included: mortality, hospital stay in ICU, days with ventilator-assisted ventilation, etc.

Results

A total of 72 confirmed COVID-19 patients in ICU were included. The median age of patients was 66 years (IQR: 53-77.5), and there were 32 female patients (44.4%). There were no significant differences in laboratory tests and complications after treatments between groups. A total of 36 (50%) patients died during hospitalization, and the mortality in the ICWM group (28.6%) was significantly lower than that of the WM group (63.6%, adjusted $P=0.011$). And the time of assisted ventilation was shorter in the ICWM group (adjusted $P=0.341$). However, the median hospital stay was significantly longer in the ICWM group (18 vs. 14 days, adjusted $P=0.05$).

Conclusions

ICWM treatments could significantly reduce mortality for severe or critically ill patients with COVID-19, and it was safe and cost-effective to add Chinese medicine.

Background

COVID-19 has been rapidly spreading around the world [1]. As of April 16, 2020, there were a total of 83,799 cases of confirmed COVID-19 and 3,352 deaths across China, and the number reached 2006,042 and 136,119 in countries and regions outside of China respectively, which seriously endangered the health of people around the world and affected the social life and economy [2]. Most of the infected patients have mild clinical manifestations and a good prognosis [3]. And multiple organ failure and acute respiratory distress syndrome (ARDS) often occur in severe patients, who are often accompanied by chronic diseases, and the prognosis is poor [4].

At present, Covid-19 vaccines and antiviral drugs are still in the stage of development and clinical trials [5, 6]. The disease also belongs to the category of Traditional Chinese Medicine (TCM) epidemic, the cause is the body felt by the epidemic, and the location is in the lung according to TCM theory. Based on the previous experience of TCM in the treatment of SARS and COVID-19, the sixth version of the program on the diagnosis and treatment of COVID-19 in China (February 18, 2020) introduced the TCM

recommendations for COVID-19 [7]. So we employed integrative Chinese-Western Medicine (ICWM) treatments for some patients admitted to the intensive care unit (ICU) with confirmed infection with 2019-nCoV since February 20, 2020. The study intends to analyze the clinical characteristics of severe and critically ill patients and to explore the efficacy of ICWM treatments compared with Western medicine treatments alone.

Methods

This study was a prospective cohort study that observed patients admitted to ICU with confirmed COVID-19 in the Third People's Hospital of Yichang, Hubei, China (a designated infectious diseases hospital). We defined patients who received only Western medicine treatments as the Western medicine (WM) group, and those who have added TCM decoction to Western medicine treatment were classified as the ICWM group. The differences will be observed in mortality, days with assisted ventilation, hospital stay, and complications during hospitalization between the two groups of patients. The study has been reviewed by the Ethics Review Committee of the Third People's Hospital Affiliated to Fujian University of Chinese Medicine, and all patients have signed informed consent.

Populations

All enrolled patients were severe or critically ill with COVID-19. The diagnostic and classification criteria were referred to as the interim guideline on COVID-19 of the World Health Organization (WHO) and China [7,8]. Detailed inclusion criteria are as follows: 1. Age ≥ 18 years; 2. Positive 2019-nCoV PCR test of respiratory specimens before admission; 3. Severe pneumonia with/without the following situations: ARDS, multiple organ failure, sepsis, or shock. Exclusion criteria: 1. Those who took chloroquine phosphate; 2. Those who have been enrolled in trials of other TCM drugs.

Western medicine treatments

The following antiviral drugs were used according to the patient conditions: α -interferon, ribavirin, abidol or lopinavir, and ritonavir tablets.[7] In principle, no more than three antiviral drugs were used at the same time. Antibiotics were given to patients with fever and significantly elevated peripheral blood leukocytes or positive blood bacterial culture. All patients were given oxygen inhalation and monitored for vital signs. Ventilator-assisted ventilation was considered for patients with respiratory distress and/or hypoxemia when oxygen inhalation cannot relieve them. Corresponding supportive treatments would be given if the patient has complications or adverse events associated with the disease itself or treatments.

TCM treatments

TCM syndrome differentiation and formulation referred to the diagnosis and treatment program on the new coronavirus infectious pneumonia (trial sixth edition) in China [7]. The program divided severe or critically ill patients with COVID-19 into three manifestations: severe (1. *syndrome of pestilent toxin blocking lung*; 2. *syndrome of dual blaze of Qi and blood*), and critically (3. *syndrome of internal block*

and external collapse) [7,9]. Recommended formulations for the three manifestations have been published [7,10].

Outcome measurement

All resident doctors were responsible for recording the patient's epidemiology, clinical manifestations, laboratory tests, chest CT, treatment plan, and clinical outcomes 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.

The primary outcome was mortality; other outcomes included: mortality, hospital stay in ICU, days with ventilator-assisted ventilation, and complications during hospitalization. Ventilator-assisted ventilation used only for rescue before death is not recorded. Laboratory tests were assessed at admission and 10±2 days after admission. Neutrophil-lymphocyte-ratio (NLR) was calculated by blood neutrophil count /lymphocyte count. Complications recorded included acute cardiac injury (ACI), acute kidney injury (AKI), acute liver injury (ALI), acute respiratory distress syndrome (ARDS) and arrhythmia.

Statistical analysis

Measurement data were expressed by median (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 TCM treatments 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. Then we took subgroup analysis by patients of different ages (</ ≥60 years), gender, and severity. 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.

Results

Patients and Baseline Characteristics

A total of 72 confirmed COVID-19 patients in ICU were included. And all patients had a 2019nCoV-related epidemiological history. The WM group finally involved 44 patients and 28 patients for the ICWM group. The median age of patients was 66 years (IQR: 53-77.5), and there were 32 female patients (44.4%). Among the patients, the most common comorbidities were hypertension (51.4%) and diabetes (31.9%). There were 56 (77.8%) patients with fever and cough, while the median oxygen saturation (SaO₂) under oxygen inhalation was 94% (IQR: 91%-96.2%). The median time from onset to admission in the ICWM group was 8 days (IQR: 3-20), and 5 days (IQR: 3-7) in the WM group ($P=0.041$). There was no significant difference in other baseline characteristics between the ICWM group and the WM group except for the history of malignancy and mean arterial pressure (Table 1).

Laboratory tests and complications

There was no statistical difference in laboratory tests between the two groups at admission except prothrombin time (PT) and aspartate aminotransferase (AST) (Table 2). However, the clinical difference between groups was not significant for PT and AST. The lymphocyte, neutrophil count, and NLR of the ICWM group were similar to the WM group at admission. At about 10 days after admission, the lymphocyte count of two groups decreased, while the neutrophil count and NLR were higher than before. The mean C-reactive protein (CRP) was similar at admission ($P=0.359$); while it was lower in the ICWM group (IQR: 10-42.5 mg/L) than that of WM group (IQR: 7.6-116.7 mg/L, $P=0.016$) at about 10 days after admission. Besides, the liver function, kidney function in the ICWM group seemed better than that of the WM group after treatments.

ARDS occurred in 58 (80.6%) patients (WM: 81.8%, ICWM: 78.6%), and 26 (36.1%) patients were given non-invasive ventilator-assisted ventilation (WM: 45.5%, ICWM: 21.4%), and 28 (38.9%) patients received invasive ventilator-assisted ventilation (WM: 31.8%, ICWM: 50.0%) within 72 hours of admission. Other more common complications during hospitalization were shock (total 48.6%, WM 54.5%, ICWM 39.3%) and ALI (total 33.3%, WM 27.3%, ICWM 42.9%), etc. However, there was no significant difference between the two groups (Table 3).

Clinical outcome

A total of 36 (50%) patients died during hospitalization, and the mortality in the ICWM group (28.6%) was significantly lower than that of the WM group (63.6%). After using a multivariate regression analysis to adjust the related risk factors, there was still a significant difference between the two groups ($P=0.011$) (Table 4). Besides, the time of assisted ventilation was shorter in the ICWM group comparing with the WM group, but not significant (adjusted $P=0.341$). However, the median hospital stay was significantly longer in the ICWM group (18 vs. 14 days, adjusted $P=0.001$); and we found the same result after excluding dead patients (20 vs. 15.5 days, $P=0.406$). In the subgroup analysis, we found a similar trend in the above outcomes for the male /female patients (suppl. Table1) and young /aged (suppl. Table2). ICWM treatments could reduce the mortality both of severe and critically ill patients (suppl. Table3). And hospital stay of the ICWM group was shorter than that of the WM group for severe patients; while it was longer for critically ill patients.

Discussion

2019-nCoV is a new coronavirus that is not completely equivalent to MERS and SARS [11], and humans are universally susceptible to it [12], but elderly patients are in more serious condition [13, 14]. The median age of patients in our ICU was 66 years old, which was similar to other reports [3, 15, 16]. And our patients were severe or critically ill; in the first 72 hours of admission, 75% of patients were given mechanical ventilation because of refractory respiratory distress or hypoxemia. Recently, Mahase [17] indicated that most patients require mechanical ventilation within 24 hours of critical care. Studies have also found that severe cases tend to have lower lymphocytes counts, higher leukocytes count, NLR, and

inflammatory parameters, such as CRP [18, 19]. Among the above indicators reflecting the severity of COVID-19, there was no significant difference at admission between the two groups in our study.

The utilization of TCM for COVID-19 is substantial in China, over 85% of confirmed cases included TCM treatments nationally (Wuhan over 67%) [10]. Back in the SARS epidemic, a report released by WHO and a meta-analysis indicated that ICWM treatment had the potential benefits to alleviate symptoms, reduce complications and cost, and was safe [20, 21]. Recently, Luo et. al [9] found that TCM had an advantage in keeping microenvironmental balance in treating COVID-19. Another study investigating the efficacy of ICWM treatment on COVID-19 found that ICWM treatments could improve clinical symptoms better and faster [22]. But TCM treatments in the study included TCM decoction, Chinese patent medicine, and TCM injection simultaneously [22].

This prospective cohort study analyzed the clinical characteristics of 72 severe or critically ill patients, and the efficacy and safety of ICWM treatments. The total mortality was 50% which was similar to the current report, and the mortality in the ICWM group was lower than previously reported [15]. We found that adding TCM decoction to WM treatments could significantly reduce the mortality of COVID-19. After adjusting the risk factors associated with severity at admission, including NLR and CRP, there was still a significant difference between the two groups. However, we found that the hospital stay of patients in the ICWM group was longer. It seemed to be contradictory to another study of ICWM [22]. One explanation was that our patients were all severe or critically ill. On the other hand, we suppose that the same severity will bring the same mortality; and our results presented a similar severity at admission between groups but a lower level of inflammation during hospitalization in the ICWM group. For example, leukocytes count, NLR, and CRP were lower in the ICWM group than the WM group after treatments (Table 2). Then we suspected that TCM smoothed the rising slope of the inflammatory storm of these patients who should have died, but also bring longer inflammatory response time. As discovered by a network pharmacology study, *Qing-fei-pai-du* decoction can regulate excessive immune response by Th17 cell differentiation, T cell and B cell signaling, and TNF signaling pathway in COVID-19 [23]. We may call it “time for life”.

In terms of safety, the added TCM treatment did not significantly affect the coagulation, kidney, 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 TCM was safe for severe or critically ill COVID-19 patients. Until now, there are no definite antiviral drugs specifically targeting 2019-nCoV [24]. Remdesivir has been indicated promising anti-viral effects in both intracellular and extracellular [25, 26], but its clinical efficacy and safety have not yet been proven [12]. Besides, the currently used antiviral drugs have different degrees of damage to the kidney, liver, bone marrow, and peripheral nerves [24]. And with the advantages of efficacy and safety and low cost (about 3–5 dollars per day), TCM treatments may be recommended currently, especially when intensive care resources are scarce.

The main limit of this study was that it was observational, the sample size was small, and there was an imbalance between the two groups at admission. However, we adjusted the risk factors in multivariate regression analysis to minimize the effect of these baseline biases on the research results. Besides, the SaO_2 was measured under oxygen inhalation due to the urgency of the epidemic situation and the research conditions. This study revealed that the addition of TCM decoction significantly reduced mortality and improved the clinical symptoms. But it is unknown how TCM plays a role in this disease, its pharmacological mechanism should be further explored.

Conclusions

For severe or critically ill patients with COVID-19, ICWM treatments could significantly reduce mortality. The potential mechanism may be that TCM smoothed the rising slope of the inflammatory storm. And it was safe and cost-effective to add TCM decoction to Western medicine treatments.

Abbreviations

WM: Western medicine, ICWM: integrative Chinese-Western medicine, ICU: intensive care unit, TCM: Traditional Chinese Medicine, ACI: acute cardiac injury, AKI: acute kidney injury, ALI: acute liver injury, ARDS: acute respiratory distress syndrome, COPD: chronic obstructive pulmonary disease, CKD: chronic kidney disease, MAP: Mean arterial pressure, SaO_2 : oxygen saturation, WBC: white blood cell, NLR: neutrophil-lymphocyte-ratio, PT: prothrombin time, APTT: activated partial thromboplastin time, BUN: blood urea nitrogen, SCr: serum creatinine, CK: creatine kinase, LDH: lactate dehydrogenase, ALT: alanine aminotransferase, AST: aspartate aminotransferase, CRP: C-reactive protein.

Declarations

Ethics approval and consent to participate

The study has been reviewed by the Ethics Review Committee of the Third People's Hospital Affiliated to Fujian University of Chinese Medicine, and all patients have signed informed consent.

Consent for publication

Not applicable.

Availability of data and materials

Extra data is available by email to Dr. Min Zhang (Minzhang-2018@163.com) on a reasonable request.

Competing interests

None declared.

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None.

Authors' contributions

Ziwen Yuan and Min Zhang drafted the main manuscript and made statistical analysis. Ting Peng, Chen Liang, Zhengfeng Lin, Qiuping Peng, Hongbo Liu, Xiaojie Wei, Wusong Huang, Run Fang, Yanfeng Shao, and Shengnan Xiong collected and sorted data. Bing Luo and Weijun Zhao drafted the text about traditional Chinese medicine treatment. Jingcheng Li and Quan Ming revised the manuscript for important intellectual contributions. All authors read the final manuscript and approved submissions.

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References

1. Zhu N, Zhang D, Wang W, Li X, Yang B, Song J, et al. A Novel Coronavirus from Patients with Pneumonia in China, 2019. *N Engl J Med*. 2020;382:727–33. doi:10.1056/NEJMoa2001017.
2. Bogoch II, Watts A, Thomas-Bachli A, Huber C, Kraemer M, Khan K. Potential for global spread of a novel coronavirus from China. *JOURNAL OF TRAVEL MEDICINE*. 2020;27. doi:10.1093/jtm/taaa011.
3. Wang D, Hu B, Hu C, Zhu F, Liu X, Zhang J, et al. Clinical Characteristics of 138 Hospitalized Patients With 2019 Novel Coronavirus-Infected Pneumonia in Wuhan, China. *JAMA*. 2020. doi:10.1001/jama.2020.1585.
4. Chen N, Zhou M, Dong X, Qu J, Gong F, Han Y, 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. doi:10.1016/S0140-6736(20)30211-7.
5. Shanmugaraj B, Siri wattananon K, Wangkanont K, Phoolcharoen W. Perspectives on monoclonal antibody therapy as potential therapeutic intervention for Coronavirus disease-19 (COVID-19). *Asian Pac J Allergy Immunol*. 2020;38:10–8. doi:10.12932/AP-200220-0773.
6. Zhu FC, Li YH, Guan XH, Hou LH, Wang WJ, Li JX, et al. Safety, tolerability, and immunogenicity of a recombinant adenovirus type-5 vectored COVID-19 vaccine: a dose-escalation, open-label, non-randomised, first-in-human trial. *LANCET*. 2020;395:1845–54. doi:10.1016/S0140-6736(20)31208-3.
7. National Health Commission and National Administration of Traditional Chinese Medicine. The diagnosis and treatment program on the new coronavirus infectious pneumonia (trial version 6). National Health Commission and National Administration of Traditional Chinese Medicine. 2020.

8. World Health Organization. Clinical management of severe acute respiratory infection (SARI) when COVID-19 disease is suspected: Interim guidance. World Health Organization. 2020.
9. Luo E, Zhang D, Luo H, Liu B, Zhao K, Zhao Y, et al. Treatment efficacy analysis of traditional Chinese medicine for novel coronavirus pneumonia (COVID-19): an empirical study from Wuhan, Hubei Province, China. *Chin Med*. 2020;15:34. doi:10.1186/s13020-020-00317-x.
10. Chan KW, Wong VT, Tang S. COVID-19: An Update on the Epidemiological, Clinical, Preventive and Therapeutic Evidence and Guidelines of Integrative Chinese-Western Medicine for the Management of 2019 Novel Coronavirus Disease. *Am J Chin Med*. 2020:1–26. doi:10.1142/S0192415X20500378.
11. Prompetchara E, Ketloy C, Palaga T. Immune responses in COVID-19 and potential vaccines: Lessons learned from SARS and MERS epidemic. *Asian Pac J Allergy Immunol*. 2020;38:1–9. doi:10.12932/AP-200220-0772.
12. Adhikari SP, Meng S, Wu YJ, Mao YP, Ye RX, Wang QZ, et al. Epidemiology, causes, clinical manifestation and diagnosis, prevention and control of coronavirus disease (COVID-19) during the early outbreak period: a scoping review. *Infectious Diseases of Poverty*. 2020;9:29. doi:10.1186/s40249-020-00646-x.
13. Lian J, Jin X, Hao S, Cai H, Zhang S, Zheng L, et al. Analysis of Epidemiological and Clinical features in older patients with Corona Virus Disease 2019 (COVID-19) out of Wuhan. *CLINICAL INFECTIOUS DISEASES*. 2020. doi:10.1093/cid/ciaa242.
14. Mo P, Xing Y, Xiao Y, Deng L, Zhao Q, Wang H, et al. Clinical characteristics of refractory COVID-19 pneumonia in Wuhan, China. *CLINICAL INFECTIOUS DISEASES*. 2020. doi: 10.1093/cid/ciaa270.
15. Bhatraju PK, Ghassemieh BJ, Nichols M, Kim R, Jerome KR, Nalla AK, et al. Covid-19 in Critically Ill Patients in the Seattle Region - Case Series. *N Engl J Med*. 2020. doi:10.1056/NEJMoa2004500.
16. Liu K, Chen Y, Lin R, Han K. Clinical features of COVID-19 in elderly patients: A comparison with young and middle-aged patients. *J Infect*. 2020. doi:10.1016/j.jinf.2020.03.005.
17. Mahase E. Covid-19: most patients require mechanical ventilation in first 24 hours of critical care. *BMJ*. 2020;368:m1201. doi:10.1136/bmj.m1201.
18. Qin C, Zhou L, Hu Z, Zhang S, Yang S, Tao Y, et al. Dysregulation of immune response in patients with COVID-19 in Wuhan, China. *CLINICAL INFECTIOUS DISEASES*. 2020. doi:10.1093/cid/ciaa248.
19. Zhang W, Zhao Y, Zhang F, Wang Q, Li T, Liu Z, et al. The use of anti-inflammatory drugs in the treatment of people with severe coronavirus disease 2019 (COVID-19): The Perspectives of clinical immunologists from China. *CLINICAL IMMUNOLOGY*. 2020;214:108393. doi:10.1016/j.clim.2020.108393.
20. World Health Organization. Clinical trials on treatment using a combination of Traditional Chinese medicine and Western medicine. World Health Organization. 2004;pp:1–194.
21. Liu X, Zhang M, He L, Li Y. Chinese herbs combined with Western medicine for severe acute respiratory syndrome (SARS). *Cochrane Database Syst Rev*. 2012;10:D4882. doi:10.1002/14651858.CD004882.pub3.

22. Xia W, An C, Zheng C, Zhang J, Huang M, Wang Y, et al. Clinical study on 34 cases of new coronavirus pneumonia treated with integrated traditional Chinese and Western medicine. *Journal of Traditional Chinese Medicine*. 2020.

23. Zhao J, Tian S, Yang J, Liu J, Zhang W. Investigating the mechanism of Qing-Fei-Pai-Du-Tang for the treatment of novel coronavirus pneumonia by network pharmacology. *Chinese Traditional Herbal Drugs*. 2020:829–35.

24. Lodise TP, Rybak MJ. COVID-19: Important Therapy Considerations and Approaches in this Hour of Need. *PHARMACOTHERAPY*. 2020. doi:10.1002/phar.2396.

25. Sheahan TP, Sims AC, Zhou S, Graham RL, Pruijssers AJ, Agostini ML, et al. An orally bioavailable broad-spectrum antiviral inhibits SARS-CoV-2 in human airway epithelial cell cultures and multiple coronaviruses in mice. *Sci Transl Med*. 2020. doi:10.1126/scitranslmed.abb5883.

26. Yang Y, Islam MS, Wang J, Li Y, Chen X. Traditional Chinese Medicine in the Treatment of Patients Infected with 2019-New Coronavirus (SARS-CoV-2): A Review and Perspective. *International Journal of Biological Sciences*. 2020;16:1708–17. doi:10.7150/ijbs.45538.

Tables

Table 1. Baseline Characteristics of COVID-19 Patients in ICU.

	Median (Q1-Q3) /N (%)			P-value
	Total	WM	ICWM	
N	72	44	28	
Age (years)	66 (53-77.5)	66 (52-77)	68 (54-79)	0.404
Sex				0.449
female	32 (44.4%)	18(40.9%)	14 (50.0%)	
Comorbidities				
Hypertension	37 (51.4%)	21 (47.7%)	16 (57.1%)	0.591
Cardiovascular disease	18 (25.0%)	8(18.2%)	10 (35.7%)	0.105
Diabetes	23 (31.9%)	16 (36.4%)	7 (25.0%)	0.454
Malignancy	4 (5.6%)	0 (0.0%)	4 (14.3%)	0.020
Cerebrovascular disease	14 (19.4%)	8 (18.2%)	6 (21.4%)	0.767
COPD	10 (13.9%)	4 (9.1%)	6 (21.4%)	0.172
CKD	12 (16.7%)	8 (18.2%)	4 (14.3%)	0.755
HIV infection	0(0%)	0(0%)	0 (0.0%)	-
Signs and symptoms				
Fever	56 (77.8%)	32 (72.7%)	24 (85.7%)	0.196
Cough	56 (77.8%)	32 (72.7%)	24 (85.7%)	0.196
Expectoration	41 (56.9%)	26 (59.1%)	15 (53.6%)	0.828
Fatigue	38 (52.8%)	24 (54.5%)	14 (50.0%)	0.706
Pharyngalgia	14 (19.4%)	8(18.2%)	6 (21.4%)	0.767
Diarrhea	4 (5.6%)	4 (9.1%)	0 (0.0%)	0.511
Nausea	4 (5.6%)	0 (0.0%)	2 (14.3%)	0.152
Dizziness	9 (12.5%)	3 (6.8%)	6 (21.4%)	0.144
Headache	6 (8.3%)	2(4.5%)	4 (14.3%)	0.199
Anxiety	4 (5.6%)	2 (4.5%)	2(7.1%)	0.640
Insomnia	26 (36.1%)	14 (31.8%)	12 (42.9%)	0.342
Temperature (°C)	36.8 (36.5-37.8)	36.9 (36.5-37.7)	36.7 (36.5-38.0)	0.513
SaO2(%)	94.0 (91.0-	94.0 (91.0-	94.5 (91.0-96.0)	0.852

	96.2)	97.0)		
Heart rate (beats/min)	88.5 (81.5-97.0)	89.0 (82.0-96.0)	87.0 (75.0-98.0)	0.335
MAP (mmHg)	93.3 (88.3-99.7)	90.3 (86.7-96.7)	99.0 (93.3-106.0)	0.002
Time from onset to admission (d)	5.5 (3.0-10.0)	5.0 (3.0-7.0)	8.0 (3.0-20.0)	0.041

Abbreviations: WM: Western medicine, ICWM: integrative Chinese-Western medicine, COPD: chronic obstructive pulmonary disease, CKD: chronic kidney disease, SaO₂: oxygen saturation, MAP: Mean arterial pressure.

Table 2. Changing of Laboratory Tests of COVID-19 Patients.

	at admission		<i>P</i> -value	10 days after admission		<i>P</i> -value
	WM	ICWM		WM	ICWM	
N	44	28		44	28	
WBC (×10 ⁹ /L)	4.8 (4.0-7.8)	5.6 (4.1-6.9)	0.959	11.9 (9.6-13.6)	9.2 (6.0-18.2)	0.263
Neutrophil (×10 ⁹ /L)	3.7 (2.1-6.7)	3.9 (3.1-6.0)	0.889	10.9 (7.6-12.4)	7.0 (4.6-14.3)	0.595
Lymphocyte (×10 ⁹ /L)	0.7 (0.6-1.0)	0.8 (0.5-1.0)	0.334	0.6 (0.4-0.9)	0.6 (0.3-0.8)	0.659
NLR	5.1 (2.6-9.3)	4.2 (3.1-11.4)	0.095	17.4 (12.1-23.7)	12.5 (6.2-50.0)	0.120
Hemoglobin (g/L)	109.0 (104.0-122.0)	114.5 (90.0-123.0)	0.905	109.0 (94.2-121.2)	100.0 (83.0-104.0)	0.058
PT (s)	11.2 (10.6-11.4)	10.5 (10.0-10.8)	0.002	11.8 (11.0-12.5)	11.3 (10.9-11.6)	0.306
APTT (s)	30.0 (24.7-34.9)	28.6 (24.0-29.3)	0.458	24.0 (22.3-30.2)	28.9 (25.2-32.9)	0.889
D-dimer (mg/L)	0.9 (0.6-2.8)	1.0 (0.6-6.6)	0.771	5.4 (2.1-16.5)	9.2 (4.0-12.9)	0.153
BUN (mmol/L)	5.1 (4.4-11.3)	6.0 (4.4-7.9)	0.235	8.6 (6.1-14.5)	5.9 (4.5-9.3)	0.147
SCr (μmol/L)	65.7 (63.3-89.7)	61.2 (49.4-69.9)	0.052	74.3 (50.5-93.8)	61.7 (45.9-83.4)	0.241
CK (U/L)	99.5 (63.2-149.8)	59.5 (35.2-81.8)	0.054	146.0 (43.0-181.0)	56.0 (24.0-156.0)	0.045
LDH (U/L)	413.0 (226.0-477.0)	308.0 (255.0-420.0)	0.095	532.5 (384.5-704.5)	382.0 (271.0-549.0)	0.737
ALT (U/L)	26.0 (18.0-35.0)	16.0 (10.0-36.0)	0.052	36.0 (20.2-73.5)	29.0 (18.0-56.0)	0.049
AST (U/L)	30.0 (21.0-48.0)	25.0 (22.0-32.0)	0.022	28.0 (22.0-43.8)	24.0 (17.0-54.0)	0.036
PH	7.4 (7.4-7.5)	7.4 (7.4-7.4)	0.759	7.4 (7.3-7.5)	7.4 (7.4-7.5)	0.767
Lactate (mmol/L)	2.0 (1.5-2.4)	2.0 (1.9-2.5)	0.634	1.9 (1.4-3.0)	1.9 (1.3-2.4)	0.968
CRP	61.0 (23.6-89.6)	27.4 (13.5-66.3)	0.359	30.7 (7.6-116.7)	28.0 (10.0-42.5)	0.016

Abbreviations: WM: Western medicine, ICWM: integrative Chinese-Western medicine, WBC: white blood cell, NLR: neutrophil-lymphocyte-ratio, PT: prothrombin time, APTT: activated partial thromboplastin time, BUN: blood urea nitrogen, SCr: serum creatinine, CK: creatinekinase, LDH: lactate dehydrogenase, ALT: alanine aminotransferase, AST: aspartate aminotransferase, CRP: C-reactive protein.

Table 3. Comparisons of Complications During Hospitalization between WM and ICWM Group.

	N (%)			<i>P</i> -value
	Total	WM	ICWM	
N	72	44	28	
Acute cardiac injury	18 (25.0%)	10 (22.7%)	8 (28.6%)	0.589
Arrhythmia	6(8.3%)	2 (4.5%)	4 (14.3%)	0.199
Acute kidney injury	17 (23.6%)	7 (15.9%)	10 (35.7%)	0.100
Acute liver injury	24 (33.3%)	12 (27.3%)	12 (42.9%)	0.171
Shock	35 (48.6%)	24 (54.5%)	11 (39.3%)	0.307
ARDS	58 (80.6%)	36 (81.8%)	22 (78.6%)	0.734

Abbreviations: WM: Western medicine, ICWM: integrative Chinese-Western medicine, ARDS: acute respiratory distress syndrome.

Table 4. Comparisons of Clinical Outcomes Between WM and ICWM group.

	Outcomes	β (95%CI)/OR(95%CI) <i>P</i> -value		
	N (%) /Median (Q1-Q3)	Model 1	Model 2	Model 3
Death				
WM	28(63.6%)	1	1	1
ICWM	8 (28.6%)	0.23 (0.08, 0.64) 0.005	0.20 (0.07, 0.58) 0.003	0.00 (0.00, 0.27) 0.011
Time of assisted ventilation (d)				
WM	11(1-15)	0	0	0
ICWM	7 (0-12)	-1.03 (-4.70, 2.63) 0.582	-0.49 (-4.08, 3.10) 0.788	1.91 (-1.98, 5.80) 0.341
Hospital stay (d)				
WM	14 (6 -21)	0	0	0
ICWM	18 (12-31)	6.23 (1.64, 10.83) 0.010	6.59 (1.94, 11.24) 0.007	16.33 (12.59, 20.08) <0.001

Model 1: Non-adjusted; Model 2: adjust for: Age and Sex; Model 3: adjust for: Age; Sex; Hypertension; Diabetes; Malignancy; Cerebrovascular disease; Chronic kidney disease; Cardiovascular disease; COPD; Mean arterial pressure(mmHg); CRP at admission; NLR at admission; AST at admission; Time from onset to admission. Abbreviations: WM: Western medicine, ICWM: integrative Chinese-Western medicine.

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