Chinese Journal of Natural Medicines

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Citation: Yongjiu XIAO, Binbin LI, Chang LIU, Xiuyu HUANG, Ling MA, Zhirong QIAN, Xiaopeng ZHANG, Qian ZHANG, Dunqing LI, Xiaoqing CAI, Xiangyong YAN, Shuping LUO, Dawei XIANG, Kun XIAO, Effects of traditional Chinese medicine on treatment outcomes in severe COVID-19 patients: a single-centre study, Chinese Journal of Natural Medicines, 2024, 22(1), 89-96. doi: 10.1016/S1875-5364(24)60565-0.

View online: https://doi.org/10.1016/S1875-5364(24)60565-0

Available online at www.sciencedirect.com

ScienceDirect

Chinese Journal of Natural Medicines 2024, **22**(1): 89-96
doi: 10.1016/S1875-5364(24)60565-0

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•Original article•

Effects of traditional Chinese medicine on treatment outcomes in severe COVID-19 patients: a single-centre study

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Available online 20 Jan., 2024

[ABSTRACT] As the search for effective treatments for COVID-19 continues, the high mortality rate among critically ill patients in Intensive Care Units (ICU) presents a profound challenge. This study explores the potential benefits of traditional Chinese medicine (TCM) as a supplementary treatment for severe COVID-19. A total of 110 critically ill COVID-19 patients at the Intensive Care Unit (ICU) of Vulcan Hill Hospital between Feb., 2020, and April, 2020 (Wuhan, China) participated in this observational study. All patients received standard supportive care protocols, with a subset of 81 also receiving TCM as an adjunct treatment. Clinical characteristics during the treatment period and the clinical outcome of each patient were closely monitored and analysed. Our findings indicated that the TCM group exhibited a significantly lower mortality rate compared with the non-TCM group (16 of 81 *vs* 24 of 29; 0.3 *vs* 2.3 person/month). In the adjusted Cox proportional hazards models, TCM treatment was associated with improved survival odds (P < 0.001). Furthermore, the analysis also revealed that TCM treatment could partially mitigate inflammatory responses, as evidenced by the reduced levels of proinflammatory cytokines, and contribute to the recovery of multiple organic functions, thereby potentially increasing the survival rate of critically ill COVID-19 patients.

[KEY WORDS] COVID-19; Pneumonia; Novel coronavirus; Critically ill; Traditional Chinese medicine; Clinical outcome

[CLC Number] R285.6 **[Document code]** A **[Article ID]** 2095-6975(2024)01-0089-08

Introduction

The advent of a novel viral pneumonia, caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), was officially designated as coronavirus disease 2019 (COVID-19) and escalated to the status of a Public Health Emergency of International Concern by the World Health Organization (WHO) on Jan. 30, 2020. The initial outbreak precipitated a substantial infection event in China, with a marked concentration of cases in Wuhan [1]. Subsequent to the emergence of COVID-19, the evolution of the virus gave rise to

[Received on] 02-Aug.-2023

[Research funding] This work was supported by the National Science Foundation for Young Scientists of China (No. 82100096), the National Science Foundation for Young Scientists of Beijing (No. 7214254), the National Natural Science Foundation of China (Nos. 81902426 and 81872441) and the Emergency Scientific Research Project for COVID-19 (No. 20yjky007).

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These authors have no conflict of interest to declare.

several variants of concern. The most prominent of these include the Alpha variant, first identified in the U.K., Beta in South Africa, Gamma in Brazil, and Delta in India, with the latter's sub-lineage B.1.617.2 (Delta) being recognized as a recent variant [2]. In Nov. 2021, another variant surfaced in South Africa, named Omicron (B.1.1.529), which displayed an augmented potential for transmission and infectivity over prior variants, becoming the predominant strain driving the global pandemic [3, 4]. According to research data, the infection and transmission capabilities of Omicron surpass those of previously known variants, solidifying its status as the leading contributor to the pandemic spread [5].

COVID-19 patients frequently present with symptoms typical of upper respiratory infections, including fever, dry cough, and shortness of breath. Additionally, non-specific clinical signs, such as lymphopenia and elevated lactate dehydrogenase levels, have been documented [1]. The current therapeutic strategies for COVID-19 primarily focus on anti-infective treatments, supportive care, and antiviral interventions. However, specific therapies for severe COVID-19 cases remain unverified in terms of effectiveness. The mainstays of treatment for these patients are supplemental oxygen therapy and supportive management for conditions like acute hypoxic respiratory failure and acute respiratory distress syndrome (ARDS) [6-8]. Developing more effective treatments to combat severe manifestations of COVID-19 is a critical area of medical research. In this context, traditional Chinese medicine (TCM) has emerged as a supportive intervention [9, 10]. The Huashi Baidu Formula, for instance, has been effective in alleviating severe symptoms of COVID-19, such as inhibited defecation and red tongue, and has demonstrated a capacity to decrease IL-6 and TNF-α cytokine expression in cell models [11]. Similarly, Shenhuang Granule, developed by the team at Longhua Hospital affiliated with the Shanghai University of Traditional Chinese Medicine, has been shown to prevent the progression of severe COVID-19 and significantly reduce the mortality rate of these patients [12]. Moreover, findings from the Dongzhimen Hospital of Beijing University of Chinese Medicine suggest that severe patients who utilized TCM exhibited a higher transition rate to mild and moderate symptomology with no reported deaths, which underscores the potential role of TCM in managing COVID-19 severity [13]. Community protection against respiratory diseases has also been augmented through the use of Huoxiang Zhengqi Oral Liquid and Jinhao Jiere Granules [14]. When used in conjunction with Western medicine, Huoxiang Zhengqi Dropping Pills and Lianhua Qingwen Granules have shown promise in improving patient outcomes [15]. The integration of Jiawei Maxing Shigan Tang with standard treatment regimens has similarly been conducive to positive patient responses [16]. Additionally, in some cases, the short-term application of neuromuscular blockade with agents like cisatracurium has proven beneficial in enhancing patient oxygenation [17].

Previous studies have indicated that the plasma of patients with severe COVID-19 is characterized by high concentrations of cytokines, including GCSF, IP10, MCP1, MIP1A, and TNFα, indicating that there is an association between cytokine storm and disease severity [18, 19]. Many efforts have been invested in the development of antiviral vaccines and examining the efficacy of pre-existing antiviral agents. Current evidence suggests that dexamethasone, when used as a treatment option, offers benefits similar to those of supplemental oxygen therapy, notably improving the survival rate of affected patients [20]. Among several small molecule antiviral drugs studied (remdesivir, favipiravir, lopinavir, etc.), remdesivir has demonstrated particular promise, reducing the average recovery time from 15 to 11 days according to data from U.S. clinical trials [21, 22]. As a result, remdesivir was approved by the U.S. Food and Drug Administration (FDA) for COVID-19 treatment on Oct. 22, 2020. Nonetheless, contrasting findings from a WHO-sponsored global study revealed that remdesivir might have minimal impact on patient survival and treatment duration. Additionally, small molecule antiviral agents may cause serious adverse events, including vomiting, low blood pressure and abnormal liver and kidney function. Although other antiviral therapies, immunomodulators, and anticoagulants are under clinical research, there is an urgent need to develop safer and more potent drugs.

Lianhua Qingwen (LHQW), a traditional Chinese medicinal formulation, synergistically blends two classic TCM prescriptions: Yinqiao San and Maxing Shigan Tang. It has been historically prescribed to alleviate symptoms of influenza-like illnesses [23]. Emerging evidence indicates that LHQW is effective in enhancing viral clearance and providing symptomatic relief [24]. Notably, research by LI *et al.* has provided evidence that LHQW exerts beneficial effects on antiviral activities and the inflammatory response, potentially offering preventive measures against COVID-19 [25]. A study involving individuals who were in close contact with confirmed COVID-19 cases showed that the administration of LHQW capsules for 14 days during quarantine and medical observation significantly decreased the incidence of positive viral nucleic acid tests from nasal and pharyngeal swabs, thereby effectively averting SARS-CoV-2 infection [26]. Furthermore, HU *et al.* discovered that a 14-day treatment regimen with LHQW capsules substantially enhanced the recovery of clinical symptoms such as fever, fatigue, and cough in COVID-19 patients, reduced the duration of these symptoms, improved pulmonary imaging findings, and increased the clinical recovery rate compared to conventional treatment [27].

The aim of this study, which was based on the medical records of 110 critically ill COVID-19 patients hospitalized in the Intensive Care Unit (ICU) of Vulcan Hill Hospital between Feb. 2, 2020, and April 15, 2020 (Wuhan, China), was to conduct an in-depth analysis of cytokine changes during the inflammatory response and to evaluate the effect of TCM treatment on the patient's survival rate.

Methods

Study design

This retrospective cohort study was conducted in the ICU of Vulcan Hill Hospital between Feb. 2, 2020, and April 15, 2020 (Wuhan, China). The research protocol received approval from the Ethics Committee of Vulcan Hill Hospital, and informed consent was secured from all patients. Patients were eligible for inclusion if they tested positive for SARS-CoV-2 using the real-time reverse-transcriptase polymerase chain reaction (RT-PCR) assay from both nasal and pharyngeal swabs and demonstrated pneumonia on computed tomography (CT) scans, according to the Guidelines of Diagnosis and Treatment Protocol for COVID-19 (5th edition). Critically ill COVID-19 patients were identified by one or more of the following criteria: a, respiratory distress with a respiratory rate ≥ 30 times·min^{-1}; b, blood oxygen saturation ≤ 93%; c, arterial oxygen partial pressure/inspired oxygen partial pressure ≤ 300 mmHg. Patients with one of the following conditions were excluded from the study: a, patients who were transferred to the hospital with critical underlying diseases; b, patients with severe underlying disease who died within 72 h after admission; c, patients who lacked essential clinical data. Following these stipulations, a total of 110 patients fulfilled the inclusion criteria and were consequently enrolled in the analysis. The follow-up duration extended to the finalization of this report, providing a comprehensive view of the study population's outcomes.

TCM treatment

The study utilized two proprietary TCM prescription types as described in Table 1. Type 1 prescription was a derivative of the Huoxiang Zhenqi Prescription, and Type 2 prescription was based on Jiawei Maxing Shigan Decoction. Both prescriptions are established in the prevention and treatment of infectious diseases. Consistent with TCM practices, we tailored these prescriptions to the patients' unique clinical symptoms and the differential diagnosis principles inherent to TCM. Adjustments included modifying original components to target immune modulation, symptomatic relief, and anti-inflammatory effects. To prepare the medicinal concoctions, herbs were decocted in 1000 mL of pure water for approximately 30 min until the volume reduced to approximately 600 mL. The resulting tincture was then divided into three 200 mL doses and administered orally three times daily for 7−14 days.

Data collection and procedures

We conducted a comprehensive review of the medical records for COVID-19 patients, from which we extracted detailed demographic, clinical laboratory, treatment, and outcome data from the hospital's electronic medical records. All data were meticulously checked for accuracy and completeness by two attending physicians, Dr. XIAO Yongjiu (the 940th Hospital of Jiont Logistics Support Force of Chinese People's Liberation Army, Lanzhou, China) and Dr. XIAO Kun (Chinese People's Liberation Army (PLA) General Hospital, Beijing, China). Based on the therapeutic drugs administered, the patients were divided into the TCM group and the non-TCM group. Each group comprised only critically ill COVID-19 patients. The application of TCM treatment was

Table 1 Two types of prescriptions for 81 critically ill COVID-19 patients.

Type 1 prescription component	Weight	Type 2 prescription component	Weight
Atractylodis Rhizoma	12 g	Roasted Ephedra	6 g
Citri Reticulatae Pericarpium	10 g	Armeniacae Semen Amarum	10 g
Magnoliae officinalis Cortex	10 g	Gypsum Fibrosum	20 g
Poria	15 g	Agastaches Herba	10 g
Agastaches Herba	10 g	Atractylodis Rhizoma	10 g
Tsaoko Fructus	6 g	Fried Atractylodis Macrocephalae Rhizoma	12 g
Belamcandae Rhizoma	6 g	Fructus Tsaoko	6 g
Forsythiae Fructus	6 g	Poria	20 g
Roasted Ephedra	6 g	Rhei Radix et Rhizoma	5 g
Notopterygii Rhizoma et Radix	10 g	Lepidii Semen	15 g
Zingiberis Rhizoma Recens	6 g	Paeoniae Radix Rubra	10 g
Arecae Semen	10 g	Salviae Miltiorrhizae Radix et Rhizoma	10 g
Chuanxiong Rhizoma	10 g	Pheretima	10 g
Trichosanthis Fructus	10 g	Persicae Semen	10 g
		Trichosanthis Fructus	10 g
		Scutellariae Radix	10 g
		Glycyrrhizae Radix	6 g

initiated during the early stages of each patient's ICU hospitalization.

Statistical analysis

We described baseline demographic and clinical characteristics using means and standard deviations for normally distributed variables, medians with interquartile ranges for skewed data, and frequencies with percentages for categorical data. Intergroup differences were evaluated using the Wilcoxon rank-sum test for continuous non-normally distributed data and Pearson's chi-squared test for categorical data. We analyzed clinical and laboratory data using a mixed-effects model for repeated measures, which accounted for individual variability through random effects. The model treated changes from baseline as the dependent variable and included baseline values, the duration of hospitalization, and treatment types as covariates. The primary outcome measure was the difference in the least-squares (LS) mean between groups. The potential influence of TCM on COVID-19 mortality rates was examined using multivariate Cox proportional hazards regression, yielding hazard ratios (HRs) and 95% confidence intervals (CIs) for the risk of death. A *P*-value of less than 0.05 was indicative of statistical significance. All statistical analyses were conducted using Stata version 16.0 (Stata Corp., College Station, TX, USA).

Results

Comparison of outcomes between TCM treatment and non-TCM treatment in all 110 critically ill COVID-19 patients

In this comparative study, 110 critically ill COVID-19 patients admitted to the ICU of Vulcan Hill Hospital were assessed following RT–PCR confirmation of infection (GeneoDX Co., Ltd., Shanghai, China). Demographic details, clinical features, and medication histories ar collated in Table 2. All the patients were critically ill and given supportive treatment. Specifically, 110 patients were divided into two groups: the TCM group (n = 81, including 13 patients also receiving convalescent plasma therapy) and the non-TCM group (n = 29). The patients' ages ranged from 59 to 82 years. Hypertension prevalence was slightly lower in the TCM group (50.6%) than in the non-TCM group (55.2%). Furthermore, the incidence of coronary heart disease was lower in the TCM group (3.7%) than that in the non-TCM group (10.3%). Diabetes was reported in 16% of TCM-treated patients against 27.6% in their counterparts, and a history of pulmonary diseases was noted in 13.6% of the TCM group compared with 6.9% in the non-TCM group. No significant differences in the presence of these comorbidities were observed between the two groups (P > 0.05). Notably, patients with immunosuppression, fatty liver, and liver cirrhosis were also enrolled in the TCM group.

Baseline laboratory data of all enrolled patients, summarized in Table 3, revealed significant differences between the TCM and non-TCM groups. The non-TCM group exhibited higher levels of creatinine, prothrombin time (PT), thrombin time (TT), and serum phosphorus than the TCM group (P < 0.05). Conversely, the TCM group had higher measurements of total protein, serum calcium, and total carbon dioxide than the non-TCM group (P < 0.05). Although platelet (PLT) counts appeared slightly elevated in the TCM group, this difference was not statistically significant (P > 0.05). Comparable parameters between the two groups included white blood cell count (WBC), lymphocyte percentage (LYM%), the percentage of neutrophilic granulocytes (NEUT%), C-reactive protein (CRP), globulin, aspartate aminotransferase (AST), alanine aminotransferase (ALT), lactate dehydrogenase (LDH), creatine kinase (CK), D-dimer, blood glucose, serum

Table 2 Baseline demographic and clinical characteristics of 110 critically ill COVID-19 patients in the TCM (n = 81) and non-TCM groups (n = 29).

	Non-TCM group (n, %)	TCM group (n, %)	P-value
Demographic Characteristics			
Age	69 ± 10	70 ± 12	0.73
Sex (male percentage)	19 (65.5%)	49 (60.5%)	0.63
Preclinical Conditions			
Hypertension	16 (55.2%)	41 (50.6%)	0.67
Coronary heart disease	3 (10.3%)	3 (3.7%)	0.18
Diabetes	8 (27.6%)	13 (16.0%)	0.17
Malignant tumor	0 (0.0%)	2 (2.5%)	0.39
Structural lung disease	2 (6.9%)	11 (13.6%)	0.34
Immunosuppression	0 (0.0%)	1 (1.2%)	0.55
Fatty liver	0 (0.0%)	1 (1.2%)	0.55
Liver cirrhosis	0 (0.0%)	1 (1.2%)	0.55

Table 3 Clinical laboratory baseline data of 110 critically ill COVID-19 patients in the TCM (*n* = 81) and non-TCM groups (*n* = 29).

	Non-TCM group (*n*, %)	TCM group(*n*, %)	*P*-value
WBC (10^9/L)			0.61
< 4	0 (0.0%)	2 (3.2 %)	
4–10	16 (58.3%)	34 (54.0%)	
> 10	11 (40.7%)	27 (42.9%)	
LYM% < 20	24 (82.8%)	54 (66.7%)	0.10
NEUT% ≥ 60	26 (89.7%)	62 (76.5%)	0.13
PLT (10^9/L) ≥ 100	16 (55.2%)	49 (60.5%)	0.62
Total Protein/($g·L^{-1}$)	57.3 ± 7.5	61.6 ± 6.4	0.021
Globulin/($g·L^{-1}$)			0.78
< 20	1 (5.6%)	3 (5.7%)	
20–35	16 (88.9%)	44 (83.0%)	
> 35	1 (5.6%)	6 (11.3%)	
CRP/($mg·L^{-1}$)	90.7 ± 81.3	61.0 ± 65.9	0.10
Creatinine/($μmol·L^{-1}$) > 133	7 (24.1%)	2 (2.5%)	0.001
AST/($U·L^{-1}$) > 40	8 (27.6%)	11 (13.6%)	0.09
ALT/($U·L^{-1}$) > 50	5 (17.2%)	13 (16.0%)	0.88
DBIL/($μmol·L^{-1}$)	7.8 (4.7, 11.8)	4.8 (3.2, 9.6)	0.23
IBIL/($μmol·L^{-1}$)	6.6 (4.3, 10.1)	5.7 (4.5, 8.4)	0.53
LDH/($U·L^{-1}$) > 245	13 (44.8%)	26 (32.1%)	0.22
CK/($U·L^{-1}$) > 185	3 (10.3%)	2 (2.5 %)	0.08
D-Dimer	18 (62.1%)	49 (60.5%)	0.88
Blood glucose/($mmol·L^{-1}$)	9.3 ± 4.2	8.2 ± 3.7	0.32
PT/(s)	16.8 ± 4.6	14.8 ± 2.8	0.025
TT/(s)	24.6 ± 15.3	17.3 ± 11.7	0.037
Serum potassium/($mmol·L^{-1}$)	4.2 ± 0.7	4.2 ± 0.7	0.89
Serum sodium/($mmol·L^{-1}$)	142.1 ± 6.6	141.2 ± 7.3	0.65
Serum chlorine/($mmol·L^{-1}$)	106.0 ± 5.7	103.2 ± 7.3	0.14
Serum calcium/($mmol·L^{-1}$)	1.9 ± 0.1	2.1 ± 0.2	< 0.001
Serum phosphorus/($mmol·L^{-1}$)	1.3 ± 0.8	0.9 ± 0.4	0.006
Serum magnesium/($mmol·L^{-1}$)	0.9 ± 0.2	0.9 ± 0.1	0.48
Total carbon dioxide/($mmol·L^{-1}$)	22.1 ± 5.9	25.3 ± 5.2	0.049

sodium, serum chlorine, the levels of direct bilirubin (DBIL) and indirect bilirubin (IBIL), and oxygen saturation measurements. However, these differences were not independent factors associated with mortality in critically ill COVID-19 patients (data not shown).

Efficacy of TCM treatment in critically ill COVID-19 patients

This investigation centered on the potential efficacy of TCM treatment in improving the survival rate of critically ill COVID-19 patients. Of the 110 critically ill COVID-19 cases evaluated, 40 died. TCM treatment was associated with improved survival outcomes [multivariate HR, 0.15; 95% confidence interval (CI), 0.08 to 0.30; P < 0.001; log-rank P < 0.001] (Table 4, Fig. 1). Furthermore, the TCM group had lower mortality than the non-TCM group (16 of 81 *vs* 24 of 29; 0.3 person/month *vs* 2.3 person/month) (Table 4). No other clinical or laboratory measures, nor past medical treatments, were found to independently predict the mortality risk in these severe cases (data not shown).

Further, we explored whether the combination with convalescent plasma therapy could enhance immunity against SARS-CoV-2 in the TCM group. Analysis revealed that for 13 patients receiving this combination therapy, clinical outcomes were statistically indistinguishable from those who received TCM alone (data not shown). The survival benefit remained nonsignificant when comparing the combination therapy to TCM monotherapy, as indicated by both multivariate analysis (HR, 0.13; 95% CI, 0.04 to 0.45; P < 0.001) and the log-rank test (P < 0.001) (Supplementary Table S1 and Fig. S1). These results suggest that convalescent plasma therapy does not contribute additional clinical benefit to patients with

Table 4 Survival rate of 110 critically ill COVID-19 patients in the TCM (n = 81) and non-TCM groups (n = 29). The results are adjusted by patients' age, sex, hypertension, coronary heart disease, diabetes, structural lung disease AST and ALT.

	Critically ill COVID-19 patients (n = 110)			
	Non-TCM group	TCM group	Unadjusted HR (CI), P-value	Adjusted HR (CI), P-value
Death due to COVID-19	n, % of Patients Inc rate			
	24 (82.7%) 2.3 person/month	16 (19.8%) 0.3 person/month	0.12 (0.06–0.23) < 0.001	0.15 (0.08–0.30) < 0.001

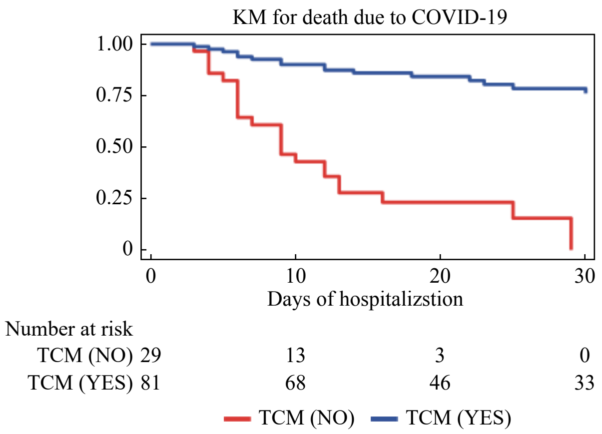

Fig. 1 Kaplan-Meier analysis of 110 COVID-19 patients in the TCM and non-TCM groups (Log-rank P < 0.001).

severe COVID-19.

Efficacy of TCM treatment associated with other features in critically ill COVID-19 patients

To reveal the molecular mechanism underlying the improved survival rate as a result of TCM, we analyzed changes in clinical biomarkers throughout the treatment (Table 5). Notably, a significant reduction in the NEUT% was observed in the TCM group compared with that in the non-TCM group (−3.23%, P = 0.02), suggesting an attenuation of peripheral inflammation (Table 5). Moreover, an increase in the globulin level by 1.48 $g \cdot L^{-1}$ (P = 0.005) in the TCM group underscored the treatment's immunomodulatory benefit. Additionally, nearly half of the patients displayed elevated levels of LDH (Table 3), indicating multiple organ dysfunction in severe COVID-19 cases before treatment. Following TCM treatment, a substantial decrease in LDH by −99.81 $U \cdot L^{-1}$ (P = 0.001) was reported when compared with the non-TCM cohort (Table 5). Further examination revealed an improvement in the total carbon dioxide levels post-TCM treatment (1.09 $mmol \cdot L^{-1}$, P = 0.033), which may signal better lung function and a more stable acid-base equilibrium. Compared with that in the non-TCM group, the remarkably reduced level of CK in the TCM group (−62.64 $U \cdot L^{-1}$, P = 0.035) additionally suggest enhanced cardiac function as a result of the treatment. Collectively, these findings support the proposition that TCM treatment improves the survival rate of patients with severe COVID-19 by facilitating the recovery of systemic functions.

Discussion

LHQW has broad-spectrum antiviral, anti-infection, and immunomodulatory effects. Meanwhile, it can alleviate the clinical symptoms of patients and interrupt the process of virus transformation in the human body. Previous studies have implied that the early combination of LHQW arbidol may shorten the recovery time and improve the prognosis of patients with COVID-19 [24]. Furthermore, Huoxiang Zhengqi Dropping Pills and LHQW combined with western medicine therapy improved clinical symptoms and the prognosis of patients with COVID-19 [15], and Jiawei Maxing Shigan Tang combined with the recommended therapeutic regimen therapy also alleviated primary symptoms and promoted positive outcomes for patients with COVID-19 [16]. At present, the mechanism of new coronary pneumonia is not sufficiently clear.

In our present study, we observed that high levels of cytokines involved in inflammation were largely decreased after TCM treatment. Previous studies have found that different TCM prescriptions can improve COVID-19 by targeting the ACE2 and 3CLPro, targeting cytokines, targeting acute immune responses to SARS-CoV-2, and targeting pulmonary fibrosis [9]. Studies reported that Atractylodis Rhizoma is a component of Type 1 and Type 2 prescription which had anti-inflammatory effect [28], moreover, *Salvia miltiorrhiza* and Pheretima were component of Type 2 prescription that had anti-inflammatory effects as well [29, 30].

LI *et al.* reported that LHQW capsules significantly inhibited SARS-CoV-2 replication in Vero E6 cells and reduced proinflammatory cytokine production at the mRNA level [31]. The latest research has confirmed that LHQW has an inhibitory effect on the *in vitro* proliferation of a variety of different strains of influenza viruses and can block the early stage of viral infection. Mechanistically, LHQW suppresses A/PR/8/34 virus-induced p65 phosphorylation. The NF-κB signalling pathway is mainly involved in viral replication and can regulate the production of cytokines and chemokines during severe influenza infections. The phosphorylation of NF-κB inhibits the output of viral RNA and virus transmission and reduces virus-induced interleukin (IL-6 and IL-8) and tumour necrosis factor (TNF-α) levels. The gene expression of interferon-inducible protein (IP-10) and monocyte chemotactic protein (MCP-1) has a regulatory effect on the immune response to viral infection [32]. Further investigations have confirmed that LHQW can reduce the expressions of IL-8, TNF-α, IL-17, and IL-23 in serum and IL-8 and IL-17 in the sputum of AECOPD patients. Additionally, it can reduce the level of serum Th17 cytokines (IL-17 and IL-6) in patients

Table 5 Laboratory changes throughout the treatment (LSM Estimates ± SE)* of 110 critically ill COVID-19 patients in the TCM (*n* = 81) and non-TCM groups (*n* = 29).

	Non-TCM group	TCM group	Treatment	*P*-value
WBC	−3.48 ± 0.54	−3.29 ± 0.26	0.19 (−1.00, 1.37)	0.76
LYM%	−6.16 ± 0.98	−6.73 ± 0.45	−0.56 (−2.76, 1.63)	0.61
NEUT%	−5.88 ± 1.24	−9.11 ± 0.57	−3.23 (−5.98, −0.47)	0.02
PLT	−76.99 ± 8.8	−59.53 ± 4.10	17.45 (−2.06, 36.97)	0.08
Globulin	−4.47 ± 0.46	−2.99 ± 0.23	1.48 (0.46, 2.51)	0.005
Creatinine	−36.84 ± 7.64	−23.86 ± 3.65	12.98 (−4.40, 30.36)	0.14
AST	−65.39 ± 15.95	−69.59 ± 7.87	−4.20 (−40.17, 31.77)	0.82
ALT	−72.53 ± 14.35	−56.57 ± 6.94	15.96 (−16.25, 48.17)	0.63
DBIL	−6.34 ± 2.95	−10.03 ± 1.62	−3.69 (−10.72, 3.35)	0.30
IBIL	−4.71± 1.65	−5.79 ± 0.83	−1.08 (−4.71, 2.56)	0.56
LDH	−28.23 ± 22.03	−128.04 ± 9.85	−99.81 (−150.94, −48.68)	0.001
CK	−53.78 ± 25.52	−116.43 ± 12.15	−62.64 (−120.86, −4.43)	0.035
D-Dimer	−2.25 ± 0.52	−3.25 ± 0.27	−1.00 (−2.17, 0.17)	0.09
Blood glucose	−1.96 ± 0.37	−1.91 ± 0.18	−0.05 (−0.78, 0.80)	0.91
PT	−2.52 ± 0.47	−2.40 ± 0.23	0.11 (−0.93, 1.16)	0.83
TT	−2.04 ± 0.55	−3.16 ± 0.29	−1.12 (−2.34, −0.11)	0.07
Serum Potassium	−0.45 ± 0.08	−0.58 ± 0.04	−0.13 (−0.31, 0.05)	0.16
Serum Sodium	−4.06 ± 0.72	−4.38 ± 0.36	−0.32 (−2192, 1.27)	0.70
Serum Chlorine	−2.89 ± 0.55	−3.61 ± 0.28	−0.72 (−1.94, 0.49)	0.25
Serum Calcium	−0.08 ± 0.02	−0.12 ± 0.01	−0.04 (−0.08, −0.005)	0.08
Serum Phosphorus	−0.29 ± 0.5	−0.32 ± 0.02	−0.03(−0.14, 0.08)	0.13
Serum magnesium	−0.08 ± 0.02	−0.09 ± 0.01	−0.01 (−0.05, 0.03)	0.51
Total carbon dioxide	−3.42 ± 0.45	−2.32 ± 0.23	1.09 (0.09, 2.10)	0.033

* Adjusted for baseline values

with COPD, increase the level of Treg cytokines (IL-10 and TGF-β), and improve the lungs of patients by regulating the balance of Th17/Treg cytokines in the body features. When used in children with mycoplasma pneumoniae pneumonia (MPP) with atelectasis, it can upregulate $CD3^+$ and $CD4^+$, downregulate the expression of $CD8^+$ in T lymphocyte subsets, reduce serum CRP, IL-6, and PCT levels, and regulate the imbalance of T lymphocyte subsets to inhibit inflammation [33].

Our study has several limitations. Firstly, the total sample size is not big enough and non-TCM group is relatively small. Thus, interpretation of our findings might be limited by the sample size. Secondly, the absence of quantifiable viral load metrics precludes a definitive assessment of the TCM's antiviral efficacy. Third, the study does not provide insight into the long-term prognostic implications of TCM interventions. The exigencies of the clinical situation also precluded the formulation of a placebo-controlled group, a standard requirement for rigorous clinical trial designs. Consequently, our conclusions necessitate corroboration through prospective, adequately powered, placebo-controlled clinical trials to substantiate the utility of TCM in the treatment regimen of the conditions studied.

In conclusion, this observational, retrospective study demonstrated that TCM treatment has largely improved the survival rate of critically ill COVID-19 patients. Therefore, we recommend using TCM treatment to accelerate recovery and improve the prognosis of critically ill COVID-19 patients. Multiple-center studies with larger sample sizes are imperative to substantiate these observations.

Ethics Approval and Consent

The study was approved by the 940th Hospital of Jion Logistics Support Force of Chinese People's Liberation Army. Written informed consent for participation was not required for this study in accordance with the national legislation and the institutional requirements. The registration No. of the study/trial: No. 2022KYLL157.

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Cite this article as: XIAO Yongjiu, LI Binbin, LIU Chang, HUANG Xiuyu, MA Ling, QIAN Zhirong, ZHANG Xiaopeng, ZHANG Qian, LI Dunqing, CAI Xiaoqing, YAN Xiangyong, LUO Shuping, XIANG Dawei, XIAO Kun. Effects of traditional Chinese medicine on treatment outcomes in severe COVID-19 patients: a single-centre study [J]. *Chin J Nat Med*, 2024, **22**(1): 89-96.