

Analysis on the medication rule of traditional Chinese medicine in the treatment of COVID-19 patients

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Abstract

Objective: To describe patterns of utilization of traditional Chinese medicine (TCM) in the treatment of patients with coronavirus disease 2019 (COVID-19).

Methods: Adult patients with COVID-19 who received TCM treatment were divided into a non-serious group (mild and moderate types) and a serious group (severe and critical types) according to their admission conditions. The medical records and prescriptions of these patients were investigated to determine their TCM utilization patterns.

Results: In all, 3,872 COVID-19 patients were included. Oral Chinese traditional patent medicine (CPM) was the most commonly used type of TCM (83.2%), followed by decoction (64.4%). As for medication pattern, the proportion of multi-drug combinations was higher than single drug use (55.0% vs. 45.0%). Decoction combined with oral CPM was the most common combination (39.1%, 1,514/3,872). Orally administered, injected, and externally applied CPM were significantly more common in the serious group than in the non-serious, while decoction and non-drug TCM treatments were more common in the non-serious than in the serious group. Multi-drug combinations were used for the majority of patients in both groups, mainly in the form of decoction combined with oral CPM. Serious patients were analysed by three groups of different prognoses and outcomes, including discharged after improvement, discharged after relapse and improvement, died finally. The two most common medication patterns were decoction combined with oral CPM and oral CPM alone in the two finally discharged groups. Oral CPM alone or used in combination with injected CPM were seen most commonly in the death group. Significant differences were established in medication patterns among patients in these three groups.

Conclusions: Oral CPM was the mainly used TCM for COVID-19 patients, followed by decoction. More common medication pattern was multi-drug combination, especially decoction combined with oral CPM. The treatment measures and medication patterns of TCM commonly used in COVID-19 patients with the range of conditions found in this study should be further explored in the future to provide a more complete reference for COVID-19 treatment.

Keywords: COVID-19, Descriptive analysis, Drug utilization, Medication pattern, Traditional Chinese medicine (TCM)

Introduction

Coronavirus disease 2019 (COVID-19) is a novel acute respiratory infectious disease caused by the novel

coronavirus (2019-nCoV or SARS-CoV-2). Clinically, COVID-19 is classified into four types: mild, moderate, severe, and critically ill^[1]. The World Health Organization (WHO) declared the COVID-19 outbreak a “pandemic” on March 11, 2020^[2]. By mid-November 2021, there had been more than 253 million confirmed cases and more than 5 million deaths reported to WHO^[3]. The pandemic is still underway as of this writing. Several variants of the virus such as the delta variant have emerged, and pose important challenges to disease treatment, prevention, and control. In November 2021, Merck and Pfizer announced that they had developed the new oral antiviral drugs Molnupiravir and Paxlovid, respectively, which have been proven to have specific effects on COVID-19^[4–5]. There was no specific treatment for COVID-19 patients before this. The guidelines of the United States and WHO recommended general treatment, antiviral treatment, immunotherapy, glucocorticoid therapy, and respiratory support as the main measures to save patients’ lives^[6–7].

The use of traditional Chinese medicine (TCM) is recommended in China’s COVID-19 diagnosis and treatment guidelines^[1]. *The Diagnosis and treatment plan for COVID-19 (trial version3)* firstly defines TCM treatment protocol. Subsequent versions of the diagnosis and treatment plans adjusted the details of this approach and recommended new TCM treatments^[8–9]. Doctors

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prescribe various TCM treatment measures based on the disease stage and symptom differentiation. A white paper on China's actions to combat COVID-19 published by the State Council of China noted that the utilization rate of TCM and the total effective rate of confirmed cases in Hubei Province exceeded 90%^[10]. Several large-scale studies in China have shown that Chinese traditional patent medicine (CPM) such as *Lianhua Qingwen* capsule, *Xuebijing* injection, and prescription decoction such as *Qingfei Paidu* decoction, are effective in alleviating clinical symptoms, improving the prognosis of severe patients and reducing the mortality rate^[11-13]. Studies have also preliminarily explored the potential effect of TCM on the SARS-CoV-2 delta variant^[14].

However, studies of TCM treatment for COVID-19 have mainly focused on the effect of single CPM use or prescription decoction alone. There has been no large sample size report on TCM utilization or medication patterns in the clinical practice of treating COVID-19 patients by CPM, prescription decoction, or non-drug TCM treatment measures as recommended in the national guidelines. This study therefore conducted a descriptive analysis of the use of TCM during hospitalization of COVID-19 patients to clarify the utilization and medication patterns of TCM in COVID-19 patients, provide a scientific basis for the application of TCM in the treatment of COVID-19, and provide other countries with a reference for this information.

Methods

Participants

The participants were patients over 18 years of age diagnosed based on *The Diagnosis and treatment plan for COVID-19* who received TCM treatment in two hospitals in Wuhan from January 18, 2020 to April 26, 2020. They were divided into a non-serious (including mild and moderate cases categorized based on the *diagnosis and treatment plan for COVID-19*) and a serious (including severe and critically ill categorized based on the same criteria) group according to their admission conditions at admission. Age, gender, comorbidities, symptoms and signs at admission, clinical outcome, and drug prescriptions were all extracted from electronic medical records.

Inclusion criteria

The inclusion criteria were the following:

- (1) Confirmed cases diagnosed based on the *Diagnosis and treatment plan for COVID-19 (trial version7)* published by the National Health Commission and State Administration of Traditional Chinese Medicine of China^[15]. The clinical classifications include mild, moderate, severe, and critically ill types.
- (2) Treated with TCM during hospitalization.
- (3) Patients aged over 18 years.

Exclusion criteria

Patients whose medical records and prescriptions were unavailable or incomplete are excluded.

Definition of TCM treatment measures

TCM in this study included decoction, orally administered CPM, injected CPM, externally administered CPM,

and non-drug TCM treatment such as acupuncture and moxibustion. TCM utilization was defined as the use of at least one of the aforementioned TCM treatment measures at some point during the course of the disease. Medication patterns included single drug use and multi-drug combinations. Single drug use was defined as the use of one kind of the various mentioned TCM treatment measures (the utilization of Western medicines was not observed in this study, so the use of a TCM alone would also include the use of various drugs in a single category or the combination of a TCM with other Western medication). The use of multi-drug combinations are defined as the combined use of two or more categories of TCM listed above.

Statistical analyses

R 4.0.2 software was used for statistical analyses. The measurement data are expressed as means ± standard deviations, and count data are expressed as numerals (percentages). Independent-sample *t*-tests and chi-square tests were performed on the measurement and count data of different groups. $P < 0.05$ was considered statistically significant.

Results

Clinical features of enrolled patients

As shown in Table 1, a total of 3,872 COVID-19 patients were included, 1,571 in the non-serious group and 2,301 in the serious group. People over 60 years old accounted for the majority of the patients and were more likely to be in the serious group. Patients with comorbidities such as hypertension, diabetes, cerebrovascular disease, lower respiratory disease, and chronic liver disease had a significantly increased probability to be in serious conditions ($P < 0.05$). Serious patients were more likely to have the symptoms of dyspnea and abnormal lung CT results than fever and cough ($P < 0.05$). Most patients in both groups were eventually cured and discharged, but the death rate and length of hospital stay in the serious group were significantly higher and longer ($P < 0.05$).

TCM utilization and medication patterns of all patients together and by group

All patients

Oral CPM accounted for the highest proportion of instances of TCM utilization (3,220, 83.2%), followed by decocted CPM (2,493, 64.4%), injected CPM (373, 9.6%), externally applied CPM (138, 3.6%), and non-drug TCM treatment (182, 4.7%). Single drugs were used for 1,742 patients (45.0%), including a single use of decoction and four kinds of CPM. The use of oral CPM alone accounted for the highest proportion of single CPM use (1,225, 31.6%). A total of 2,130 patients (55.0%) used multi-drug combinations, of which decoction combined with oral CPM was the most common (1,514, 39.1%), followed by a combination of decoction, oral CPM, and injected CPM (187, 4.8%). All other drug combinations were used in less than 4% of participants. Details are available in Table 2.

Patients with different admission conditions

First, the utilization of TCM and the proportions of oral CPM (86.7%), injected CPM (12.0%), and external CPM

Table 1**Clinical characteristics of all patients and patient groups according to admission condition.**

Clinical features	Overall (N=3,872)	Non-serious group (N=1,571)	Serious group (N=2,301)	P
Age [y, M±S]	59.33±14.52	56.28±14.24	61.41±14.34	<0.001
18–35 [n (%)]	364 (9.4)	186 (11.8)	178 (7.7)	<0.001
36–59 [n (%)]	1,467 (37.9)	715 (45.5)	752 (32.7)	
≥60 [n (%)]	2,041 (52.7)	670 (42.6)	1,371 (59.6)	
Sex [n (%)]				
Male	1,860 (48.0)	728 (46.3)	1,132 (49.2)	0.087
Female	2,012 (52.0)	843 (53.7)	1,169 (50.8)	
Comorbidities [n (%)]				
Hypertension	1,136 (29.3)	420 (26.7)	716 (31.1)	0.004
Diabetes	713 (18.4)	185 (11.8)	528 (22.9)	<0.001
Hyperlipidemia	49 (1.3)	27 (1.7)	22 (1.0)	0.053
Cardiovascular disease	244 (6.3)	91 (5.8)	153 (6.6)	0.312
Cerebrovascular disease	100 (2.6)	27 (1.7)	73 (3.2)	0.007
Lower respiratory disease	80 (2.1)	20 (1.3)	60 (2.6)	0.006
Chronic kidney disease	57 (1.5)	30 (1.9)	27 (1.2)	0.083
Chronic liver disease	60 (1.5)	40 (2.5)	20 (0.9)	<0.001
Tumor	39 (1.0)	14 (0.9)	25 (1.1)	0.664
Admission symptoms and signs [n (%)]				
Fever	2,397 (61.9)	1,025 (65.2)	1,372 (59.6)	<0.001
Cough	2,287 (59.1)	963 (61.3)	1,324 (57.5)	0.021
Dyspnea	1,171 (30.2)	407 (25.9)	764 (33.2)	<0.001
Abnormal lung CT	3,164 (81.7)	1,226 (78.0)	1,938 (84.2)	<0.001
Clinical outcome [n (%)]				
Discharge	3,763 (97.2)	1,565 (99.6)	2,198 (95.5)	<0.001
Death	109 (2.8)	6 (0.4)	103 (4.5)	
Length of hospital stay [d, M±S]	24.46±11.82	20.58±9.48	27.11±12.51	<0.001

(4.4%) were significantly higher in the serious group than in the non-serious group (78.0%, 6.2%, and 2.4%, respectively). Decoction and non-drug TCM treatments were more commonly used in the non-serious group (non-serious group: 70.0%, 9.4% vs. serious group: 60.5%, 1.5%). All of these differences between the two groups were statistically significant ($P < 0.05$). In the medication patterns, the proportions of single drug use were 44.0% (691/1,571) and 45.7% (1,051/2,301) in the non-serious and serious groups respectively; the proportions of the use of multi-drug combinations were 56.0% (880/1,571) and 54.3% (1,250/2,301). The most common drug combination was decoction with oral CPM (39.7% in the non-serious group vs. 38.7% in the serious group). Commonly used combinations in the non-serious group included the following: decoction combined with non-drug TCM treatment; a combination of decoction, oral CPM, and injected CPM; and a combination of decoction, oral CPM, and non-drug TCM treatment. Commonly used combinations in the serious group included (1) a combination of decoction, oral CPM, and injected CPM and (2) oral CPM combined with injected CPM. The proportions of other combinations were all less than 3% in both groups. The details are available in Table 2.

Patients in the serious group with different prognoses and outcomes

Of the 2,301 patients in the serious group, 2,028 were discharged after improvement, 170 were discharged after relapse and improvement, and 103 died finally after continuous progression. The use of decoction, oral CPM, and non-drug TCM treatments all appeared more often in

the relapse group (68.8%, 92.9%, 4.1%) than in the improvement group (62.0%, 86.4%, 1.3%) or in the progression to death group (18.4%, 80.6%, 1.0%). Injected CPM appeared more often in the progression to death group (35.0%) than in the relapse group (16.5%) or the improvement group (10.4%). There were significant differences among the three groups in the proportion of the use of all types of TCM except externally applied CPM. In the TCM medication pattern, the two medication patterns that appeared most often in the two discharged groups were decoction combined with oral CPM and single oral CPM use, while in the progression to death group, the use of oral CPM and combination of oral CPM and injected CPM were most common. There were significant differences in the patterns of medication used among the three groups ($P < 0.05$). See Table 3 for details. The changing trend in weekly medication patterns in serious patients is shown in Figure 1.

Discussion

Evidence regarding the use of TCM application for COVID-19 treatment

Theoretical basis of TCM

COVID-19 is considered a *yi* condition in TCM. In the *Ming* dynasty, Wu Youke, a Chinese medical scientist, described the etiology of *yi* diseases as *yi qi* in his work *Treatise on Warm-Heat Pestilence (Wen Yi Lùn)*. The recommended treatment is to eliminate *yi qi* as a first priority and to strengthen *Vital qi* to eliminate the pathogenic factor^[16]. TCM has established a complete theory to regard *yi* as a disease, and this theory has

Table 2
TCM utilization and medication patterns of all patients and patient groups with different admission conditions.

TCM category	All (N=3,872)	Non-serious group (N=1,571)	Serious group (N=2,301)	P
TCM utilization [n (%)]				
Decoction	2,493 (64.4)	1,100 (70.0)	1,393 (60.5)	<0.001
CPM				
Oral CPM	3,220 (83.2)	1,226 (78.0)	1,994 (86.7)	<0.001
Injected CPM	373 (9.6)	98 (6.2)	275 (12.0)	<0.001
External CPM	138 (3.6)	37 (2.4)	101 (4.4)	0.001
Non-drug TCM treatment	182 (4.7)	148 (9.4)	34 (1.5)	<0.001
TCM medication pattern [n (%)] ^a				
Single drug use ^b				<0.001
-1	489 (12.6)	249 (15.8)	240 (10.4)	
-2	1,225 (31.6)	439 (27.9)	786 (34.2)	
-3	24 (0.6)	3 (0.2)	21 (0.9)	
-4	4 (0.1)	0 (0)	4 (0.2)	
Multi-drug combination ^b				<0.001
-1-2	1,514 (39.1)	623 (39.7)	891 (38.7)	
-1-3	21 (0.5)	4 (0.3)	17 (0.7)	
-1-4	12 (0.3)	3 (0.2)	9 (0.4)	
-1-5	90 (2.3)	79 (5.0)	11 (0.5)	
-2-3	100 (2.6)	20 (1.3)	80 (3.5)	
-2-4	23 (0.6)	7 (0.4)	16 (0.7)	
-2-5	1 (<0.1)	1 (0.1)	0 (0)	
-1-2-3	187 (4.8)	56 (3.6)	131 (5.7)	
-1-2-4	76 (2.0)	19 (1.2)	57 (2.5)	
-1-2-5	60 (1.5)	48 (3.1)	12 (0.5)	
-1-3-4	3 (0.1)	0 (0)	3 (0.1)	
-1-3-5	6 (0.2)	4 (0.3)	2 (0.1)	
-1-4-5	3 (0.1)	3 (0.2)	0 (0)	
-2-3-4	1 (<0.1)	0 (0)	1 (<0.1)	
-2-3-5	1 (<0.1)	1 (0.1)	0 (0)	
-1-2-3-4	11 (0.3)	0 (0)	11 (0.5)	
-1-2-3-5	16 (0.4)	7 (0.4)	9 (0.4)	
-1-2-4-5	2 (0.1)	2 (0.1)	0 (0)	
-1-2-3-4-5	3 (0.1)	3 (0.2)	0 (0)	

CPM: Chinese traditional patent medicine.

^a-1: decoction; -2: oral CPM; -3: injected CPM; -4: external CPM; -5: non-drug TCM treatment.

^bThe theoretical frequency of more than 20% cells was less than 5; Fisher's exact test was performed on the R*C contingency table.

Table 3
TCM utilization and medication patterns of patients in serious group with different prognoses and outcomes.

TCM category	Discharged from hospital finally after continuous improvement (N=2,028)	Discharged from hospital finally after continuous relapse (N=170)	Died finally after continuous progression (N=103)	P
TCM utilization [n (%)]				
Decoction	1,257 (62.0)	117 (68.8)	19 (18.4)	<0.001
CPM				
Oral CPM	1,753 (86.4)	158 (92.9)	83 (80.6)	0.010
Injected CPM	211 (10.4)	28 (16.5)	36 (35.0)	<0.001
External CPM	85 (4.2)	11 (6.5)	5 (4.9)	0.368
Non-drug TCM treatment	26 (1.3)	7 (4.1)	1 (1.0)	0.012
TCM medication pattern [n (%)] ^a				<0.001
-1	229 (11.3)	7 (4.1)	4 (3.9)	
-2	686 (33.8)	45 (26.5)	55 (53.4)	
-1-2	808 (39.8)	80 (47.1)	3 (2.9)	
-2-3	62 (3.1)	5 (2.9)	13 (12.6)	
-1-2-3	111 (5.5)	12 (7.1)	8 (7.8)	
-1-2-4	52 (2.6)	4 (2.4)	1 (1.0)	
Other ^b	80 (3.9)	17 (10.0)	19 (18.4)	

CPM: Chinese traditional patent medicine

^a-1: decoction; -2: oral CPM; -3: injected CPM; -4: external CPM.

^b17 kinds of other medication patterns listed in table 2 but not in table 3, such as -3, -4, -1-3,-1-4 and so on were combined into Other because no more than 30 patients received any one of these combinations.

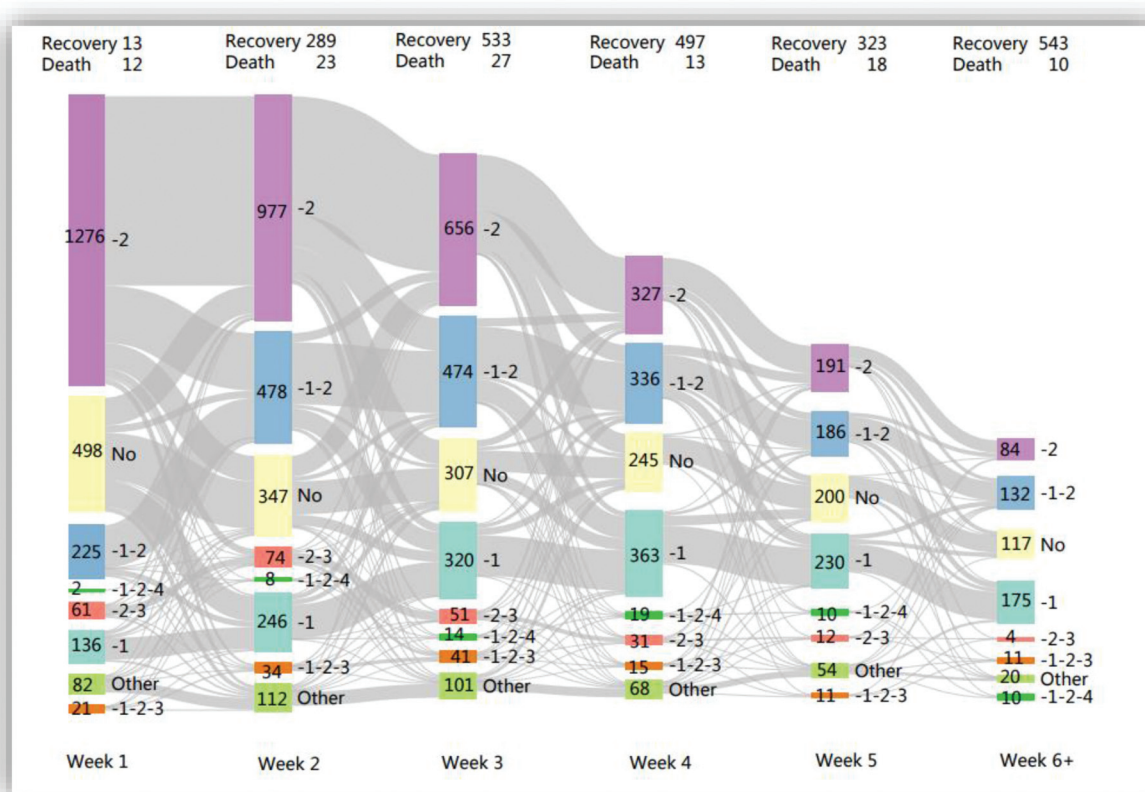


Figure 1. Trends in weekly medication patterns in serious patients. Note: -1: decoction alone; -2: oral CPM alone; -1-2: decoction combined with oral CPM; -2-3: oral CPM combined with injected CPM; -1-2-3: combination of decoction, oral CPM, and injected CPM; -1-2-4: combination of decoction, oral CPM, and external CPM; other: as described in Table 2; no: did not use TCM. The number marked on the bar is the number of people using the given medication pattern. The gray line shows the trends in medication administration.

important guiding implications for understanding and treating COVID-19^[17]. After TCM treatment measure have been adopted in the *Diagnosis and treatment plan for COVID-19*, TCM diagnoses and recommendations for treatments have been updated and expanded based on more clinical experience to identify the right direction for the TCM treatment of COVID-19.

Evidence of modern basic medical science and pharmacology

Modern basic medical science and pharmacology studies have provided evidence regarding the application of TCM in the treatment of COVID-19. Many Chinese herbs, such as scutellaria, radix isatidis, and flos lonicerae and decoction such as *Qingfei Paidu* decoction, have definite antiviral effects, which can inhibit the replication of different viruses including influenza virus and coronavirus^[18-19]. Oral CPM *Lianhua Qingwen* capsules have been found to significantly inhibit the replication of SARS-CoV-2 *in vitro*^[20]. At the same time, TCM has positive effects on immunomodulation by restraining excessive immune activation and the cytokine storm caused by COVID-19 and resisting acute lung injury^[21]. Moreover, the study of network pharmacology has identified integrative network mechanisms of TCM in COVID-19 treatment, which regulates the organism integrally and works against COVID-19 through multiple ingredients, targets, and means^[22-23].

Clinical practice of TCM application in the treatment of COVID-19

Clinical characteristics of patients

COVID-19 patients in this study who were older (over 60 years old) and had other underlying diseases (such as hypertension, diabetes, cerebrovascular diseases, lower respiratory tract diseases, or chronic liver diseases) were more likely to be serious cases upon admission to the hospital. The death rate of serious patients was higher, and the length of hospital stay was longer. These observations are consistent with the results of previous research^[24].

Discussion of results for all patients and patients with different admission conditions

Oral CPM was administered on a large-scale during the treatment of all patients, including in both the non-serious and serious groups. In all, non-serious and serious patients, the proportion of oral CPM utilization was the highest (83.2%, 3,220/3,872; 78.0%, 1,226/1,571; 86.7%, 1,994/2,301). The two medication patterns that were most commonly used were decoction combined with oral CPM (39.1%, 1,514/3,872; 39.7%, 623/1,571; 38.7%, 891/2,301) and a single use of oral CPM (31.6%, 1,225/3,872; 27.9%, 439/1,571; 34.2%, 786/2,301). The large-scale application of CPM may be related to easy preservation. It is most convenient to use in

an oral form. Injection CPM is only recommended for serious patients (severe and critically ill patients), for whom the use of oral medicine may be limited because of their worsening condition and difficulty in swallowing on their own. CPM is recommended in multiple national and local diagnosis and treatment plans for COVID-19^[25]. In all, 14 types of CPM are recommended in the most recent diagnosis and treatment plan for COVID-19 released by the National Health Commission and the Administration of traditional Chinese medicine^[1]. Six kinds of orally administered CPM, excluding *Subhexiang* and *Angong Niuhuang* pills, are recommended for non-serious patients, and eight kinds of injected CPM are used only for serious patients (severe and critically ill patients). The effectiveness of CPM against COVID-19 is an important basis for large-scale clinical application. Clinical studies have shown that a range of CPM has good effect in patients with different clinical types of COVID-19. Many drugs have been studied and shown to be effective, such as *Jinhua Qinggan* granules^[26], *Lianhua Qingwen* capsules or granules^[27], *Xuebijing* injections^[12,28–29], and so forth. Further high-quality prospective studies should be carried out to verify the exact effectiveness of these drugs.

Decoction is also widely used in COVID-19 patients. The overall utilization proportion reached 64.4% (2,493/3,872), and the combination with oral CPM constituted the most common medication pattern. Decoction is also recommended by the guidelines and is commonly used in clinical practice. In TCM, the emphasis falls on applying proper therapeutic measures in accordance with seasonal conditions, local conditions, and patients' characteristics. In COVID-19, this principle was applied by sorting patients into different syndrome types of TCM and drawing up different prescriptions. The latest diagnosis and treatment plan released by the National Health Commission includes 10 types of syndrome according to TCM and recommended corresponding decoction^[1]. Hospitals and TCM experts nationwide apply these principles and adjust them flexibly on this basis^[30]. The effectiveness of decoction used in clinical practice is another basis for its promotion. *Qingfei Paidu* decoction, for instance, has been proven to be effective against COVID-19 in a retrospective analysis with a large sample size^[13]. In the press conference held by the State Council in March 2020, based on substantial clinical evidence, the experts recommended "three medicines and three TCM prescriptions" including *Jinhua Qinggan* granules, *Lianhua Qingwen* capsules, *Xuebijing* injections, *Qingfei paidu* decoction, *Huashi Baidu* decoction, and *Xuanfei Baidu* decoction, which had been proven to have obvious effectiveness against COVID-19. These important results determined in clinical practice have been presented internationally to aid other countries' treatment regimes^[31–32].

Finally, multi-drug combinations were commonly presented during the treatment of COVID-19 patients. A total of 2,130 patients (55.0%) were treated with multi-drug combinations, including 56.0% (880/1,571) non-serious patients and 54.3% (1,250/2,301) serious patients. The diagnosis and treatment plan recommends that severe and critically ill patients are given one treatment or a combination of two treatments of CPM according to the individual condition. Injected CPM combined with decoction was also recommended^[1]. Mild and moderate patients also received multi-drug combinations on a large scale, which may be due to the

incomplete guidelines and the need for the rapid alleviation of symptoms in earlier clinical practice. Combinations of multiple CPM and decoction may increase drug-induced risks due to the overuse of congeneric drugs or drugs with the same effects^[33]. In future clinical applications, additional attention should be paid to balancing the benefits and risks of drug utilization, strengthening pharmaceutical care, and avoiding unreasonable drug combinations.

Discussion of the results of patients in the serious group with different prognoses and outcomes

Patients in the serious group with good prognoses who were ultimately discharged had a high proportion of TCM use. Among the patients in the serious group, the proportion of discharge was much higher than that of death. The utilization proportions of decoction, oral CPM, and non-drug TCM treatment in patients in the two groups that were ultimately discharged were significantly higher than those in the group of patients who died finally. In terms of medication patterns, the two most common medication patterns in the two groups finally discharged were decoction combined with oral CPM and single oral CPM and the proportions of these were much higher than in the group that died, while in the death group were single oral CPM and combined with injection CPM. This is consistent with previous research results, in which severe and critically ill patients who received TCM treatment had a significant reduction in mortality rate, and both decoction and CPM are widely used in clinical practice^[34–35].

This study found that the categories of TCM use were different in the three groups of serious patients. The proportion of utilization of injected CPM in patients who died finally after continuous progression was significantly higher than those in the two groups who were ultimately discharged. This result may be due to the continuously worsening condition of patients. They may have developed symptoms of somnolence and convulsion, for instance, or required invasive mechanical ventilation for respiratory support. In such a case, patients cannot swallow autonomously, and the use of decoction and orally administered CPM is limited^[1,36]. The latest diagnosis and treatment plan recommends eight kinds of injected CPM for the treatment of severe and critically ill patients^[1], among which, many drugs, such as *Xuebijing* injection^[12,28–29], *Xiyanping* injection^[37–38], *Tanreqing* injection^[39], and *Reduning* injection^[40], have been shown to have good effect in clinical studies.

Strengths and limitations

This study is the first one to describe TCM use in clinical practice qualitatively in a large sample size population. The study comprehensively reported the utilization of medication patterns of various TCM in detail, including common combination patterns and monotherapy patterns. It provides a reference for clinical medication. However, this study only reports the category of TCM for clarity rather than listing all the names of drugs for there are too many medicines used in clinical practice to list them all. Besides, when serious patients' conditions were grouped by the clinical outcome, only in-hospital deaths reported by medical records were recorded. Deaths after hospital discharge were not included. Additionally,

further research is needed to explore the influencing factors of the differences in the utilization proportion and patterns of TCM and their impact on the progression and outcome of the disease.

Prospects of TCM treatment of COVID-19

During the COVID-19 outbreak, TCM, as a treatment unique to China, has been proven to be effective in many respects. It plays an important role in China's fight against the virus, and may also be valuable for other countries in their response to the pandemic. It has been used in South Korea, Italy, and Hungary^[32,41]. Treatment of coronavirus diseases with TCM did not start with COVID-19 but with SARS in 2003. A meta-analysis showed that TCM can reduce the mortality of SARS patients, shorten the time of fever reduction, and shorten the length of hospital stay^[42].

In addition, TCM is effective in the prevention of SARS^[43]. The philosophy of TCM includes to cure a disease before its onset, and it stresses that prevention is the best treatment. Due to the continued emergence of COVID-19 at present, using TCM to prevent will be of great value for epidemic prevention and control. The previous use of TCM to prevent SARS and the H1N1 flu provides experience and evidence that can be used in the present case^[44]. There have also been theoretical discussions on preventing disease with TCM for high-risk populations such as children and the elderly^[45]. Summaries of specific preventive drugs in different regions have also appeared^[46]. However, systematic real-world studies to confirm the preventive effects of TCM are still lacking. More studies in large samples are needed to identify effective prescriptions for prevention.

Finally, TCM shows unique effect for severe and critically ill patients in the fight against COVID-19, and the application of TCM in emergency and critical care medicine is an important direction that deserves further study^[47]. The important role of TCM in China during the treatment of COVID-19 can also inspire the application of traditional and natural medicine in other countries and promote more research into ethnic medicine^[48].

Conclusion

This study described the drug utilization and medication patterns of TCM in 3,872 COVID-19 patients. In all, oral CPM was the most common used for COVID-19 patients, followed by decoction. Multi-drug combination was more common, especially decoction combined with oral CPM. Drug utilization and mainly used medication patterns were different in patients with different conditions and outcomes. The treatment measures and medication patterns found in this study should be further explored in the future, hoping to provide a more complete reference for COVID-19 treatment.

Conflicts of interest statement

None.

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Author contributions

Feng Sun, Haibo Song, Hong Cheng, Lixia He, and Siyan Zhan participated in the research design; Hong Cheng and Suyu Gao participated in the data collection and assembly; Qingqing Yang, Xiaoyu Tan, Xianming Cai, and Yinming Tao participated in data analyses; Yiming Tao and Qingqing Yang participated in the writing of the manuscript; and all authors participated in the revision and final approval of the manuscript.

Ethical approval of studies and informed consent

This study was approved by the Medical Ethics Committee, Zhongnan Hospital of Wuhan University (Wuhan, China) (Approved No. 2021015K).

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