

# Clinical features and the traditional Chinese medicine therapeutic characteristics of 293 COVID-19 inpatient cases

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**Abstract** Coronavirus disease 2019 (COVID-19) is now pandemic worldwide and has heavily overloaded hospitals in Wuhan City, China during the time between late January and February. We reported the clinical features and therapeutic characteristics of moderate COVID-19 cases in Wuhan that were treated via the integration of traditional Chinese medicine (TCM) and Western medicine. We collected electronic medical record (EMR) data, which included the full clinical profiles of patients, from a designated TCM hospital in Wuhan. The structured data of symptoms and drugs from admission notes were obtained through an information extraction process. Other key clinical entities were also confirmed and normalized to obtain information on the diagnosis, clinical treatments, laboratory tests, and outcomes of the patients. A total of 293 COVID-19 inpatient cases, including 207 moderate and 86 (29.3%) severe cases, were included in our research. Among these cases, 238 were discharged, 31 were transferred, and 24 (all severe cases) died in the hospital. Our COVID-19 cases involved elderly patients with advanced ages (57 years on average) and high comorbidity rates (61%). Our results reconfirmed several well-recognized risk factors, such as age, gender (male), and comorbidities, as well as provided novel laboratory indications (e.g., cholesterol) and TCM-specific phenotype markers (e.g., dull tongue) that were relevant to COVID-19 infections and prognosis. In addition to antiviral/antibiotics and standard supportive therapies, TCM herbal prescriptions incorporating 290 distinct herbs were used in 273 (93%) cases. The cases that received TCM treatment had lower death rates than those that did not receive TCM treatment (17/273 = 6.2% vs. 7/20 = 35%,  $P = 0.0004$  for all cases; 17/77 = 22% vs. 7/9 = 77.7%,  $P = 0.002$  for severe cases). The TCM herbal prescriptions used for the treatment of COVID-19 infections mainly consisted of Pericarpium Citri Reticulatae, Radix Scutellariae, Rhizoma Pinellia, and their combinations, which reflected the practical TCM principles (e.g., clearing heat and dampening phlegm). Lastly, 59% of the patients received treatment, including antiviral, antibiotics, and Chinese patent medicine, before admission. This situation might have some effects on symptoms, such as fever and dry cough. By using EMR data, we described the clinical features and therapeutic characteristics of 293 COVID-19 cases treated via the integration of TCM herbal prescriptions and Western medicine. Clinical manifestations and treatments before admission and in the hospital were investigated. Our results preliminarily showed the potential effectiveness of TCM herbal prescriptions and their regularities in COVID-19 treatment.

**Keywords** COVID-19; traditional Chinese medicine; clinical features

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## Introduction

Coronavirus disease 2019 (COVID-19), which is caused by SARS-CoV-2 infection, has now become pandemic worldwide with more than ten millions confirmed cases.

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Similar to those of the common cold and flu, the symptoms of COVID-19 are fever and cough. Most (over 80%) COVID-19 cases are moderate with good outcomes [1]. However, patients with critical cases of COVID-19 experience difficulty breathing. Cases with acute respiratory distress syndrome (ARDS) and multiple organ failure tend to have high mortality rates [2–4] because of the lack of effective therapies with antiviral drugs that are exclusive for COVID-19. In China, in addition to supportive treatment with Western medicine (e.g., antivirals), patients with COVID-19 receive personalized herbal prescriptions that are derived from traditional Chinese medicine (TCM). This combined treatment approach has been applied in 80% of COVID-19 cases and contributed to the low mortality rate in most cities outside of Hubei Province in China [5].

Prior studies on the treatment of COVID-19 with a combination of TCM herbal prescriptions and Western medicine have mainly involved less than 100 confirmed cases [6,7]. Conducting similar research with a moderate scale of observed clinical data to obtain results with increased reliability is necessary. We collected 293 retrospective COVID-19 cases in the form of electronic medical records (EMRs) from the largest TCM hospital in Wuhan, Hubei Provincial Hospital of Traditional Chinese Medicine. The values in structured data fields (e.g., demographic information, diagnoses, clinical orders, and laboratory tests) in the EMRs were normalized. TCM clinical named entities, such as symptoms and patent medicines, were extracted from admission records and discharge records by using text mining methods. We developed an information extraction system for extracting the various expressions of phenotype terms in clinical text by using a framework of human–machine collaboration strategies. This approach assured the data quality of the final extracted named entities.

This retrospective observation study described the epidemiologic features, clinical manifestations, treatments, and outcomes of 293 COVID-19 cases treated with combined TCM and Western medicine therapies.

## Materials and methods

### Data collection

This single-center retrospective study was performed at Hubei Provincial Hospital of Traditional Chinese Medicine. The EMRs (e.g., epidemiological, symptoms, and diagnoses), laboratory test results, and radiology reports of all inpatients in the pulmonary disease department from January 15, 2020 to March 2, 2020 were collected. In accordance with the diagnostic criteria of the fifth edition of the COVID-19 diagnosis and treatment plan [8], 26

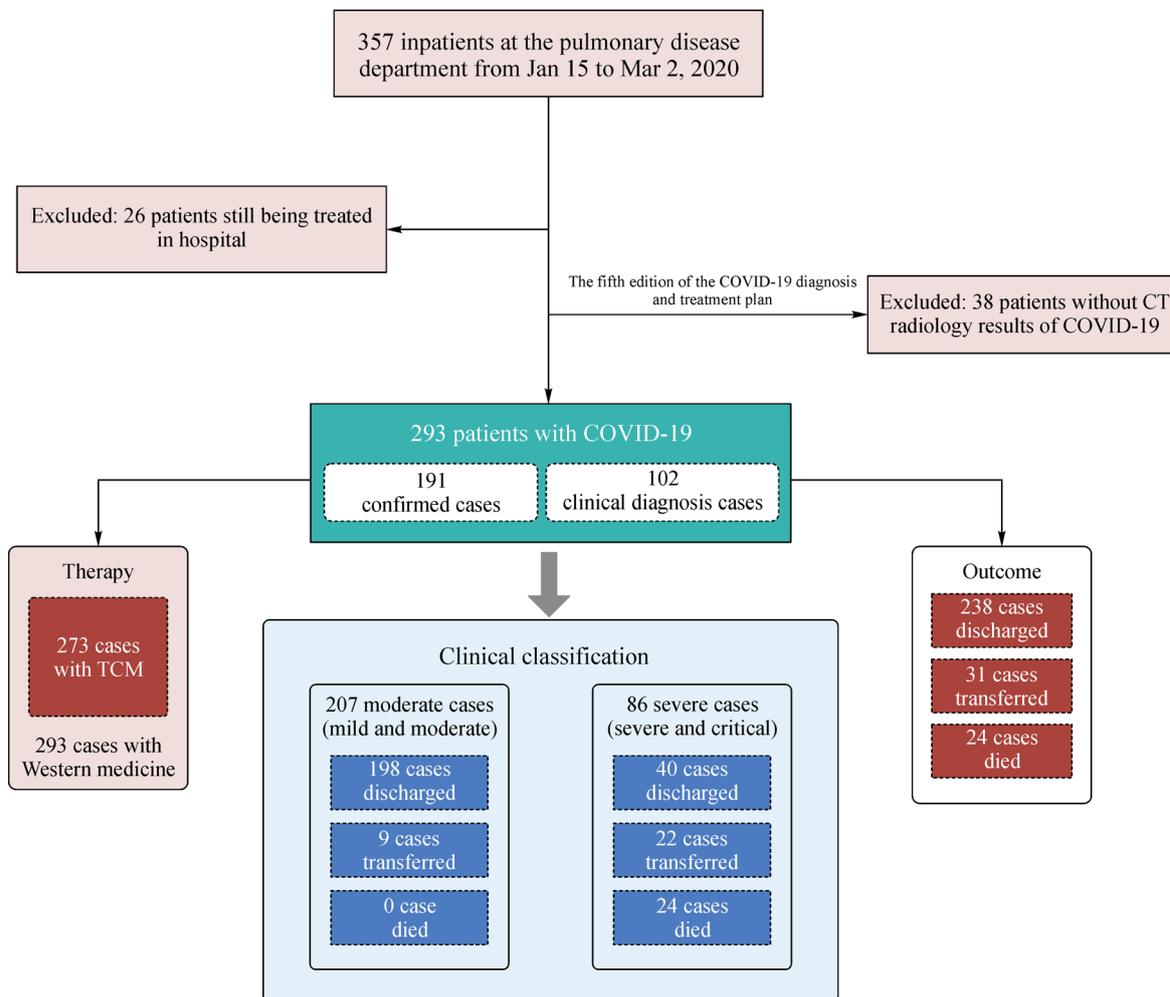
patients who were still hospitalized and 38 inpatients without CT radiology results for COVID-19 were excluded, leaving 293 inpatients in the final analysis (Fig. 1). Among the 293 cases, only 191 were positive for SARS-CoV-2 nucleic acid, and 102 cases lacked this information. However, suspected cases with the characteristic manifestations of COVID-19 (e.g., patchy ground-glass opacities, nodules, and patchy exudation) on CT scans were also treated as clinically confirmed cases even though their nucleic acid test results were negative (i.e., clinically diagnosed cases). As a result, 102 patients were also considered as positive cases. Under the guidance of clinical classification, these 293 patients were then divided into the moderate (including mild and moderate cases) and severe groups (including severe and critical cases) [9].

### Information extraction of text records from EMR data

For investigating the trajectories of clinical manifestations and any prior treatments before admissions, we developed a clinical information extraction [10] tool to extract the various expressions of symptoms, mentions of drugs and therapies, and chronic diseases that were recorded in the medical histories of patients with COVID-19 from EMRs. Our information-extraction–annotation system used a framework based on the collaboration of dictionary-based annotation with manual verification strategies. This framework helped us fully extract the various expressions of phenotype terms in the clinical text and assure the data quality of the final extracted named entities. We typically extracted TCM clinical named entities, such as symptoms, drugs, and TCM patent medicines, within longitudinal events from admission records. Extraction would help us detect the longitudinal patterns of TCM symptoms and treatments for COVID-19.

### Data normalization

Data standardization and normalization are required given that in EMRs, most data values are expressed in fine granularities to maintain an accurate profile of clinical entities. We normalized disease descriptions with the help of the International Classification of Disease Codes, Ninth Revision [11] and constrained symptom manifestations on the basis of the taxonomy of Symptom Ontology [12]. We finally identified 132 comorbid diseases with 13 systems and 99 symptoms in 8 symptom categories in this dataset. By using similar manual processing steps, we obtained 29 distinct terms of manifestations of the pulse and tongue, 12 terms of properties and flavors (e.g., bitter), 12 terms of channel tropism (e.g., stomach channel), and 254 terms of efficacy (e.g., antiviral) for TCM herbs and 35 drug categories of conventional therapies. All the admission data of the patients were verified and standardized by



**Fig. 1** Data filtering and grouping flow chart. COVID-19, coronavirus disease 2019; TCM, traditional Chinese medicine.

trained medical researchers to ensure highly accurate terminological mappings.

### Statistical and data analysis

Descriptive and continuous variables were expressed as mean  $\pm$  SD or median (IQR) and subjected to Mann–Whitney U test. Categorical variables were expressed numerically as percentages and compared via  $\chi^2$  test or Fisher’s exact test between different groups. A two-sided  $\alpha$  of less than 0.05 was considered statistically significant. All calculations and regression analysis were carried out by using SciPy and Statsmodels, which are a Python-based ecosystem of open-source software for mathematics, science, and engineering. Given that multiple herbs are typically found in a TCM prescription, we used the association rule mining algorithm (i.e., Apriori) [13] to obtain high-frequency herb combinations from prescriptions. Furthermore, we applied complex network analysis [14,15] to investigate the core herb combinations that had high coverage in clinical prescriptions.

## Results

### Clinical features of 293 relevant inpatients with COVID-19

Among 293 cases, 191 were confirmed cases (65%) that were positive for SARS-CoV-2 nucleic acid and 102 were clinically diagnosed cases (35%) with confirmed positive chest CT reports. A total of 273 (93%) patients received integrated TCM and Western medicine therapies. In this study, 24 cases died during hospitalization, 238 cases were discharged, and 31 cases were transferred to other hospitals (e.g., Jinyintan Hospital). The average age of these patients was 57 years. Among the patients, 54% were female and 46% were male. Severe cases had longer average hospital stays (15.5 days vs. 14 days) and shorter symptom onset time (9 days vs. 11.5 days) than moderate cases. A total of 178 (61%) patients had disease comorbidities, particularly diseases of the metabolic and circulatory system. Hypertension was the most common comorbidity (24%), followed by diabetes (16%) and coronary heart disease

(6%). Severe cases tended to have a higher degree of comorbidities than moderate cases. Approximately 83% of patients had manifestations of the respiratory tract. Coughing was the most prevalent symptom (51%), and nearly half of the cases suffered from digestive and neurological system discomfort, such as loss of appetite and insomnia. In addition, chest tightness, wheezing, and breathing difficulty might indicate severe conditions. Although their overall mean values were within the normal range, severe cases tended to have higher frequencies and values of breath and blood pressure than moderate cases. This observation was similar between the survivors and nonsurvivors (Tables 1 and 2). For TCM-specific manifestations, a high number of cases manifested yellow fur (57%) and reddish tongue (53%), and a higher number of patients with severe cases exhibited dull tongue and rapid pulse, which usually indicates the heat properties of the coronavirus from the pathological perspective of TCM. Similar results were also reflected in TCM syndromes, such as the syndrome of phlegm-heat lung obstruction.

Although most patients with COVID-19 had normal white blood cell and neutrophil counts at the beginning of the disease, they tended to have abnormal lymphocyte counts and elevated C-reactive protein and IL-6 levels, indicating the possibility of secondary infection. These parameters slightly returned to normal after treatment. In addition, myoglobin, bilirubin, and  $\gamma$ -GT levels were clearly higher in severe cases than in moderate cases. Notably, triglyceride and total cholesterol levels were higher in moderate cases than in severe cases (1.6 mmol/L vs. 1.4 mmol/L and 4.4 mmol/L vs. 3.8 mmol/L). The ratio of partial of oxygen saturation was significantly lower in severe cases than in moderate cases, implying an increased likelihood of developing ARDS and receiving mechanical ventilation (Table 3).

Next, we fitted clinical outcomes through multivariate logistic regression (discharged = 0, transferred = 2, and died = 4) by using demographic features; clinical classification; and the clinical manifestations of symptoms, comorbidities, and TCM syndromes with >10 frequency.

**Table 1** Characteristics of moderate and severe COVID-19 cases

Demographics and clinical characteristics	Total ( <i>n</i> = 293)	Moderate ( <i>n</i> = 207)	Severe ( <i>n</i> = 86)	<i>P</i> values
Age (year)	57.1±15.6	54.0±15.0	64.6±14.5	1.25E−07**
Sex				2.50E−05**
Female	158 (54%)	128 (62%)	30 (35%)	
Male	135 (46%)	79 (38%)	56 (65%)	
Hospital stay duration (day)	14.5±6.1	14.0±5.1	15.5±7.9	5.14E−02
Onset time (day)	10.8±7.2	11.5±7.5	9.1±6.3	1.58E−02*
Any comorbidity	178 (61%)	108 (52%)	70 (81%)	3.09E−06**
Endocrine and metabolic diseases	101 (34%)	58 (28%)	43 (50%)	3.12E−04**
Diabetes mellitus	47 (16%)	25 (12%)	22 (26%)	4.13E−03**
Circulatory system diseases	91 (31%)	47 (23%)	44 (51%)	1.64E−06**
Hypertension	69 (24%)	40 (19%)	29 (34%)	8.17E−03**
Coronary heart disease	19 (6%)	8 (4%)	11 (13%)	4.72E−03**
Cerebral infarction	11 (4%)	2 (1%)	9 (10%)	3.73E−04**
Digestive system diseases	39 (13%)	13 (6%)	26 (30%)	3.88E−08**
Chronic gastritis	5 (2%)	1 (0.5%)	4 (5%)	4.41E−02*
Genital system diseases	22 (8%)	11 (5%)	11 (13%)	2.70E−02*
Chronic kidney disease	4 (1%)	0 (0%)	4 (5%)	1.01E−02*
Signs and symptoms				
Respiratory system symptoms	243 (83%)	171 (83%)	72 (84%)	8.18E−01
Coughing	148 (51%)	101 (49%)	47 (55%)	3.61E−01
Chest tightness	104 (35%)	61 (29%)	43 (50%)	8.24E−04**
Wheezing	104 (35%)	59 (29%)	45 (52%)	1.04E−04**
Respiratory difficulty	34 (12%)	14 (7%)	20 (23%)	5.97E−05**
General symptoms	181 (62%)	121 (58%)	60 (70%)	8.18E−01
Fever	102 (35%)	57 (28%)	45 (52%)	4.99E−05**
Digestive system symptoms	138 (47%)	86 (42%)	52 (60%)	3.13E−03**
Reduced appetite	87 (30%)	52 (25%)	35 (41%)	7.87E−03**
Nervous system symptoms	120 (41%)	75 (36%)	45 (52%)	1.07E−02*
Insomnia	96 (33%)	56 (27%)	40 (47%)	7.87E−03**
Circulatory system symptoms	24 (8%)	12 (6%)	12 (14%)	2.04E−02*

(Continued)

Demographics and clinical characteristics	Total ( <i>n</i> = 293)	Moderate ( <i>n</i> = 207)	Severe ( <i>n</i> = 86)	<i>P</i> values
Palpitations	24 (8%)	12 (6%)	12 (14%)	2.04E−02*
Temperature (°C)	36.9±0.7	36.8±0.7	37.0±0.8	1.03E−01
Breathing	20.9±4.1	20.3±2.7	22.2±5.9	9.25E−04**
Blood pressure				
Systolic pressure (mmHG)	126.3±16.4	123.0±13.7	132.9±19.2	1.99E−06**
Diastolic pressure (mmHG)	75.9±10.3	75.0±9.3	77.7±11.9	2.05E−02*
Tongue fur and pulse manifestations				
Reddish tongue	155 (53%)	112 (54%)	43 (50%)	5.21E−01
Dull tongue	12 (4%)	5 (2%)	7 (8%)	2.44E−02*
Yellow fur	167 (57%)	125 (60%)	42 (49%)	6.90E−02
Greasy fur	73 (25%)	52 (25%)	21 (24%)	8.99E−01
Rapid pulse	42 (14%)	22 (11%)	20 (23%)	4.97E−03**
TCM syndromes				
Syndrome of pathogenic qi lung invasion	91 (31%)	56 (27%)	35 (41%)	2.15E−02*
Syndrome of phlegm-heat lung obstruction	84 (29%)	62 (30%)	22 (26%)	4.51E−01
Syndrome of stagnant and jamming wind-heat	33 (11%)	26 (13%)	7 (8%)	2.76E−01
Syndrome of wind-heat weifen invasion	18 (6%)	13 (6%)	5 (6%)	8.80E−01
Syndrome of phlegm-dampness lung obstruction	14 (5%)	10 (5%)	4 (5%)	8.14E−01
Laboratory findings				
WBC ((3.5–9.5) × 10 <sup>9</sup> /L)	5.0 (3.9–7.0)	4.9 (3.9–6.2)	5.8 (3.9–8.0)	7.14E−02
Neutrophil count ((1.8–6.3) × 10 <sup>9</sup> /L)	3.5 (2.6–5.3)	3.4 (2.5–4.2)	4.6 (3.1–6.6)	1.55E−03**
Lymphocyte count ((1.1–3.2) × 10 <sup>9</sup> /L)	1.0 (0.7–1.4)	1.2 (0.9–1.6)	0.7 (0.5–1.0)	6.76E−09**
C-reactive protein (<3 mg/L)	18.2 (4.2–63.5)	8.1 (2.3–25.4)	58.3 (22–117.5)	1.89E−12**
Triglycerides (<1.7 mmol/L)	1.6 (1.1–2.0)	1.6 (1.2–2.1)	1.4 (1.1–1.79)	3.71E−02*
Myoglobin (<100 ng/mL)	54.0 (35.3–91.5)	43.6 (35.3–58.4)	76 (45.7–147.1)	4.88E−03**
Total bilirubin (<21 μmol/L)	8.0 (6.2–11.6)	7.2 (5.8–9.7)	10.3 (7.2–13.6)	6.97E−05**
Total cholesterol (<5.17 mmol/L)	4.2 (3.5–4.9)	4.4 (3.9–5.0)	3.8 (3.4–4.4)	2.17E−03**
LDL (<3.4 mmol/L)	2.2 (1.8–2.6)	2.3 (1.9–2.8)	2.0 (1.7–2.5)	1.47E−02*
HDL (1.29–1.55 mmol/L)	1.1 (0.9–1.2)	1.1 (0.9–1.2)	1.0 (0.9–1.2)	5.38E−02
ALT (13–40 U/L)	22.0 (18.0–34.0)	20.0 (17.0–27.0)	33.0 (22.0–49.0)	8.18E−07*
γ-GT (7–45 U/L)	23.0 (15.0–40.0)	22.0 (14.3–35.8)	26.5 (17.0–47.5)	5.54E−02
Uric acid (155–357 μmol/L)	300 (234.5–369)	315 (241–364.5)	285 (231.5–396)	7.66E−01
Platelet count ((125–350) × 10 <sup>9</sup> /L)	210 (163.3–253)	228 (171–267)	190 (140–240)	8.96E−03**
Prothrombin time (9.9–12.9 s)	12.1 (11.5–12.6)	11.9 (11.4–12.4)	12.5 (11.9–13.6)	1.33E−04**
Oxygen saturation (96%–98%)	97.1 (94.9–98.7)	97.8 (97.0–99.0)	96.1 (93.3–98.7)	4.39E−03**
Interleukin-6 (<7 pg/mL)	14.6 (4.4–39.5)	9.8 (2.5–18.7)	34.2 (13.7–87.9)	9.95E−05**

Data are presented as mean±SD or median (IQR), *n* (%), or *n/N* (%), where *N* is the total number of patients in a group. *P* values were calculated via Mann-Whitney U test,  $\chi^2$  test, or Fisher's exact test as appropriate. *P* values were used to compare moderate and severe groups. Onset time means the earliest record of symptoms before admission. WBC, white blood cell count; ALT, aspartate aminotransferase;  $\gamma$ -GT,  $\gamma$ -glutamyltransferase; LDL, low-density lipoprotein; HDL, high-density lipoprotein. \* *P*<0.05, \*\* *P*<0.01.

We found that the fitted model could explain 51.7% of variance of the clinical outcomes. Several significant associations were detected (Table 4). The risk factors for death included advanced age (coefficient = 0.753, *P* = 0.002); gender (female = 1, male = 2; coefficient = 0.173, *P* = 0.042); severe disease condition (coefficient = 0.856, *P* < 0.0001); and clinical manifestations, including coughing up of phlegm (coefficient = 0.329, *P* = 0.006) and cerebral infarction (coefficient = 0.758, *P* = 0.001). We also found that patients with fatigue (coefficient = −0.23, *P* = 0.01) and yellow fur (coefficient = −0.31, *P* = 0.042) were more likely to be discharged than to be deceased.

### Therapeutic characteristics of Western medicine and TCM patent prescriptions

Western medicine with antibacterial and antiviral agents remained the first choices for the treatment of the 293 inpatient cases (Tables 5 and 6). Specifically, 258 (88%) patients received antibacterial agents, 247 (84%) patients received antiviral agents, and 135 (46%) patients received glucocorticoids. Arbidol was given to 199 (68%) patients, ribavirin to 56 (19%) patients, and interferon to 52 (18%) patients. Large amounts of hormones (e.g., methylprednisolone), digestive system drugs (e.g., omeprazole), and

**Table 2** Characteristics based on the prognosis of severe cases

Demographics and clinical characteristics	Discharged (n = 40)	Transferred (n = 22)	Died (n = 24)	P values
Age (year)	58.3±13.5	66.3±13.8	73.6±11.8	1.02E−04**
Sex				1.25E−02*
Female	21 (53%)	4 (18%)	5 (21%)	
Male	19 (48%)	18 (82%)	19 (79%)	
Hospital stay duration (day)	17.7±5.3	15.5±9.8	11.9±8.6	2.03E−03**
Onset time (day)	10.9±6.3	7.6±5.8	7.7±6.5	8.91E−02
Any comorbidity	33 (83%)	16 (73%)	21 (88%)	8.59E−01
Hypertension	13 (33%)	8 (37%)	8 (33%)	9.45E−01
Diabetes mellitus	11 (28%)	4 (18%)	7 (29%)	8.86E−01
Coronary heart disease	4 (10%)	3 (14%)	4 (17%)	6.96E−01
Acute coronary syndrome	0 (0%)	0 (0%)	3 (13%)	9.30E−02
Cerebral infarction	3 (8%)	1 (5%)	5 (21%)	2.42E−01
Complications				
Respiratory failure	6 (15%)	3 (14%)	11 (46%)	6.86E−03**
Signs and symptoms				
Coughing	22 (55%)	12 (55%)	13 (54%)	9.48E−01
Wheezing	27 (68%)	6 (27%)	12 (50%)	1.65E−01
Fever	24 (60%)	11 (50%)	10 (42%)	1.55E−01
Chest tightness	21 (53%)	10 (45%)	12 (50%)	8.46E−01
Insomnia	19 (48%)	10 (45%)	11 (46%)	8.97E−01
Reduced appetite	19 (48%)	9 (41%)	7 (29%)	1.48E−01
Respiratory difficulty	8 (20%)	7 (32%)	5 (21%)	9.36E−01
Temperature (°C)	37.0±0.8	37.1±0.8	37.0±0.8	8.84E−01
Breathing	21.0±5.3	22.8±4.9	23.3±7.5	9.83E−02
Blood pressure				
Systolic pressure (mmHG)	129.0±18.3	129.5±14.8	142.0±22.4	5.56E−02
Diastolic pressure (mmHG)	76.0±11.9	78.6±10.1	79.4±13.5	1.89E−01
Tongue fur and pulse manifestations				
Reddish tongue	22 (55%)	12 (55%)	9 (38%)	1.75E−01
Yellow fur	22 (55%)	13 (59%)	7 (29%)	4.44E−02*
Stringy pulse	12 (30%)	6 (27%)	4 (17%)	3.71E−01
Greasy fur	13 (33%)	6 (27%)	2 (8%)	5.68E−02
TCM syndromes				
Syndrome of pathogenic qi lung invasion	16 (40%)	13 (59%)	6 (25%)	2.21E−01
Syndrome of phlegm-heat lung obstruction	15 (38%)	2 (9%)	5 (21%)	1.64E−01

Data are presented as mean±SD or median (IQR), *n* (%), or *n/N* (%), where *N* is the total number of patients in a group. *P* values were calculated via Mann–Whitney U test,  $\chi^2$  test, or Fisher's exact test as appropriate. *P* values were used to compare the discharge and death groups. Onset time means the earliest record of symptoms before admission. \* *P*<0.05, \*\* *P*<0.01.

biological products (e.g., albumin) were used in severe cases. In particular, large amounts of antishock drugs were used in the rescue phase of critical cases. However, except for a typical antiviral drug (i.e., arbidol), most other drugs were used for severe cases instead of for moderate cases. The use of some drugs, such as imipenem and cilastatin sodium, significantly differed between the two groups.

### Therapeutic characteristics of TCM herbal prescriptions

A total of 20 (6.8%) patients did not receive Chinese herbal

medicine, among whom 2 were in critical condition and not allowed to receive TCM therapy. EMR notes indicated that the remaining 18 cases (11 moderate and 7 severe) refused to take Chinese herbal medicine. The hospital stays of these 18 patients ranged from 5 days to 28 days. A total of 273 (93%) patients received 1176 herbal prescriptions (Table 7). Each prescription was prepared as a compound therapy that consisted of 16–18 herbs (Fig. 2A). A total of 256 (>95%) of the 269 survivors who were discharged or transferred received herbal prescriptions, whereas only 17 (71%) of the 24 deceased received herbal prescriptions instead (Table 7).

**Table 3** Laboratory findings based on the prognosis of severe cases before and after hospitalization treatment

Laboratory findings	Test time	Discharged (n = 40)	Transferred (n = 22)	Died (n = 24)
WBC ((3.5–9.5) × 10 <sup>9</sup> /L)	First	5.5 (4.5–7.7)	6.5 (3.8–7.6)	6.3 (3.4–8.8)
	Last	7.6 (4.4–8.8)	8.1 (5.0–12.7)	11.9 (6.9–12.7)
	<i>P</i> values	2.98E–01	3.96E–01	4.60E–02
Neutrophil count ((1.8–6.3) × 10 <sup>9</sup> /L)	First	4.1 (3.2–6.4)	5.4 (3.2–6.1)	4.4 (2.6–8.5)
	Last	5.4 (3.1–6.9)	6.1 (3.7–11.3)	10.3 (4.9–12.1)
	<i>P</i> values	6.50E–01	5.27E–01	6.43E–02
C-reactive protein (<3 mg/L)	First	45.1 (19.8–87.2)	37.5 (16.2–115.8)	81.6 (51–152.9)
	Last	3.1 (1.1–12.4)	34.60 (12.15–99.2)	72.3 (33–144.3)
	<i>P</i> values	2.99E–04**	6.64E–01	6.88E–01
Total cholesterol (<5.17 mmol/L)	First	4.1 (3.4–4.4)	3.5 (3.4–4.0)	4.0 (3.5–4.9)
	Last	5.6 (3.1–5.8)	3.7 (3.3–4.4)	3.4 (3.0–4.1)
	<i>P</i> values	3.89E–01	9.50E–01	5.12E–02
HDL (1.29–1.55 mmol/L)	First	0.99 (0.93–1.15)	0.95 (0.79–1.17)	1.01 (0.91–1.10)
	Last	0.95 (0.94–0.96)	0.90 (0.89–0.91)	0.77 (0.56–0.94)
	<i>P</i> values	4.81E–01	9.41E–01	4.00E–02*

Data are presented as median (IQR). *P* values were calculated via Mann–Whitney U test and used to compare the initial and final laboratory test results of each group during the hospitalization period. WBC, white blood cell count; HDL, high-density lipoprotein. \* *P*<0.05, \*\* *P*<0.01.

**Table 4** Associated clinical features for the prognosis of COVID-19

Variable	Coefficient	<i>P</i> values	LL	UL
<b>Baseline variables</b>				
Age (year)	0.753	0.002**	0.286	1.221
Gender (female/male)	0.173	0.042*	0.006	0.341
Clinical classification (moderate/severe)	0.856	<0.0001**	0.647	1.066
<b>Clinical variables (yes/no)</b>				
Cough	–0.14	0.115	–0.335	0.036
Chest tightness	0.013	0.894	–0.184	0.21
Wheezing	–0.06	0.525	–0.266	0.136
Fever	–0.08	0.354	–0.277	0.099
Fatigue	–0.23	0.01*	–0.413	–0.056
Insomnia	0.038	0.718	–0.173	0.251
Reduced appetite	–0.19	0.066	–0.405	0.013
Coughing of phlegm	0.329	0.006**	0.094	0.564
Dry cough	–0.07	0.47	–0.289	0.134
Respiratory difficulty	–0.02	0.873	–0.294	0.25
Throat discomfort	–0.10	0.487	–0.401	0.191
White sputum	0.276	0.111	–0.064	0.616
Headache	–0.13	0.429	–0.463	0.197
Palpitation	–0.11	0.456	–0.431	0.194
Diarrhea	0.066	0.68	–0.252	0.386
Loose stool	0.053	0.765	–0.296	0.402
Bitter taste in mouth	–0.24	0.303	–0.698	0.218
Vertigo	–0.36	0.061	–0.74	0.017
Dry mouth	0.162	0.514	–0.327	0.652
Limb pain	0.222	0.283	–0.185	0.631
Hypertension	–0.09	0.3	–0.161	0.52
Diabetes mellitus	–0.06	0.393	–0.309	0.122
Coronary heart disease	0.179	0.584	–0.301	0.17
Cerebral infarction	0.758	0.001**	0.308	1.209
Reddish tongue	–0.09	0.221	–0.352	0.082

Variable	Coefficient	P values	(Continued)	
			LL	UL
Pink tongue	-0.10	0.701	-0.566	0.381
Deep red tongue	-0.04	0.608	-0.252	0.43
Pale tongue	-0.09	0.929	-0.263	0.24
Dull tongue	-0.11	0.619	-0.446	0.266
Yellow fur	-0.31	0.042**	-0.616	-0.011
Greasy fur	-0.13	0.29	-0.113	0.376
Thin fur	-0.01	0.605	-0.517	0.302
White fur	-0.26	0.529	-0.301	0.155
Thick fur	-0.01	0.652	-0.618	0.388
Wiry pulse	-0.07	0.087	-0.573	0.039
Slippery pulse	0.131	0.913	-0.283	0.253
Rapid pulse	0.155	0.248	-0.109	0.42
Floating pulse	0.088	0.093	-0.046	0.592
Thready pulse	0.273	0.841	-0.517	0.421
Syndrome of pathogenic qi lung invasion	-0.26	0.946	-0.415	0.444
Syndrome of phlegm-heat lung obstruction	-0.02	0.033*	-0.501	-0.021
Syndrome of stagnant and jamming wind-heat	-0.07	0.864	-0.266	0.223
Syndrome of wind-heat weifen invasion	0.014	0.925	-0.445	0.405

LL, lower limit; UL, upper limit; including all variables with more than 10 patients. \*  $P < 0.05$ , \*\*  $P < 0.01$ .

**Table 5** Clinical therapies for moderate and severe COVID-19 cases

Medicine	Total (n = 293)	Moderate (n = 207)	Severe (n = 86)	P values
Antibiotics	258 (88%)	175 (85%)	83 (97%)	7.83E-03**
Moxifloxacin	232 (79%)	152 (73%)	80 (93%)	1.69E-04**
Cefoperazone	91 (31%)	42 (20%)	49 (57%)	2.19E-09**
Imipenem and cilastatin sodium	49 (17%)	7 (3%)	42 (49%)	1.12E-19**
Antivira	247 (84%)	171 (83%)	76 (88%)	2.17E-01
Arbidol	199 (68%)	143 (69%)	56 (65%)	5.83E-01
Ribavirin	56 (19%)	38 (18%)	18 (21%)	6.27E-01
Interferon	52 (18%)	33 (16%)	19 (22%)	2.40E-01
Digestive system drugs	190 (65%)	117 (57%)	73 (85%)	3.65E-06**
Omeprazole	79 (27%)	42 (20%)	37 (43%)	1.42E-04**
Pantoprazole	78 (27%)	45 (22%)	33 (38%)	5.52E-03**
TCM patent prescription	184 (63%)	112 (54%)	72 (84%)	1.79E-06**
Baicalin	52 (18%)	19 (9%)	33 (38%)	1.59E-08**
Xue Bi Jing injection	46 (16%)	13 (6%)	33 (38%)	7.81E-11**
Glucocorticoids	135 (46%)	68 (33%)	67 (78%)	1.84E-12**
Methylprednisolone	116 (40%)	51 (25%)	65 (76%)	7.00E-16**
Nutrition support	134 (46%)	69 (33%)	65 (76%)	3.83E-11**
Potassium chloride	61 (21%)	28 (14%)	33 (38%)	5.79E-06**
Biological products	127 (43%)	64 (31%)	63 (73%)	2.75E-11**
Human albumin	61 (21%)	20 (10%)	41 (48%)	3.19E-12**
Antitussive and antiasthmatic	126 (43%)	74 (36%)	52 (60%)	9.97E-05**
Ambroxol	52 (18%)	23 (11%)	29 (34%)	1.55E-05**
Vitamins	111 (38%)	61 (29%)	50 (58%)	4.09E-06**
Vitamin C	68 (23%)	35 (17%)	33 (38%)	1.30E-04**
Antipyretic analgesic	84 (29%)	44 (21%)	40 (47%)	1.34E-05**
Diclofenac sodium	44 (15%)	24 (12%)	20 (23%)	1.85E-02*
Anticoagulant	76 (26%)	35 (17%)	41 (48%)	4.46E-08**
Heparin	69 (24%)	32 (15%)	37 (43%)	1.54E-06**
Antihypertensive agent	67 (23%)	36 (17%)	31 (36%)	5.35E-04**

(Continued)

Medicine	Total ( <i>n</i> = 293)	Moderate ( <i>n</i> = 207)	Severe ( <i>n</i> = 86)	<i>P</i> values
Amlodipine	31 (11%)	14 (7%)	17 (20%)	2.77E-03**
Immunomodulator	62 (21%)	28 (14%)	34 (40%)	6.93E-07**
Thymosin	57 (19%)	24 (12%)	33 (38%)	5.18E-07**
Antidiabetic	51 (17%)	21 (10%)	30 (35%)	3.66E-07**
Acarbose	29 (10%)	15 (7%)	14 (16%)	2.97E-02*
Insulin	28 (10%)	5 (2%)	23 (27%)	1.49E-09**
Antishock	22 (8%)	0 (0%)	22 (26%)	2.30E-13**
Epinephrine	19 (6%)	0 (0%)	19 (22%)	1.62E-11**
Lobeline hydrochloride	12 (4%)	0 (0%)	12 (14%)	2.30E-07**
Prognosis				
Discharged	238 (81%)	198 (96%)	40 (47%)	
Transferred	31 (11%)	9 (4%)	22 (26%)	
Died	24 (8%)	0 (0%)	24 (28%)	

Including drugs with statistical significance (*P* values <0.01) and top 20 drugs sorted by the number of patients in the total group. Data are presented as *n* (%) or *n/N* (%), where *N* is the total number of patients in group. *P* values were calculated via  $\chi^2$  test or Fisher's exact test. *P* values were used to compare the moderate and severe groups. \* *P*<0.05, \*\* *P*<0.01.

**Table 6** Clinical therapies sorted by the prognosis of severe cases

Medicine	Discharged ( <i>n</i> = 40)	Transferred ( <i>n</i> = 22)	Died ( <i>n</i> = 24)	<i>P</i> values
Antibiotics	38 (95%)	22 (100%)	23 (96%)	6.47E-01
Moxifloxacin	37 (93%)	21 (95%)	22 (92%)	7.18E-01
Cefoperazone	19 (48%)	15 (68%)	15 (63%)	2.44E-01
Imipenem and cilastatin sodium	14 (35%)	13 (59%)	15 (63%)	3.24E-02*
Antivira	34 (85%)	21 (95%)	21 (88%)	9.26E-01
Arbidol	24 (60%)	14 (64%)	18 (75%)	2.21E-01
Glucocorticoids	30 (75%)	18 (82%)	19 (79%)	7.03E-01
Methylprednisolone	28 (70%)	18 (82%)	19 (79%)	4.21E-01
TCM patent prescription	29 (73%)	20 (91%)	23 (96%)	2.30E-02*
Xue Bi Jing injection	12 (30%)	7 (32%)	14 (58%)	2.55E-02*
Antihypertensive agent	15 (38%)	7 (32%)	9 (38%)	1.00E+00
Antishock	0 (0%)	1 (5%)	21 (86%)	3.85E-12**
Epinephrine	0 (0%)	0 (0%)	19 (79%)	4.87E-12**

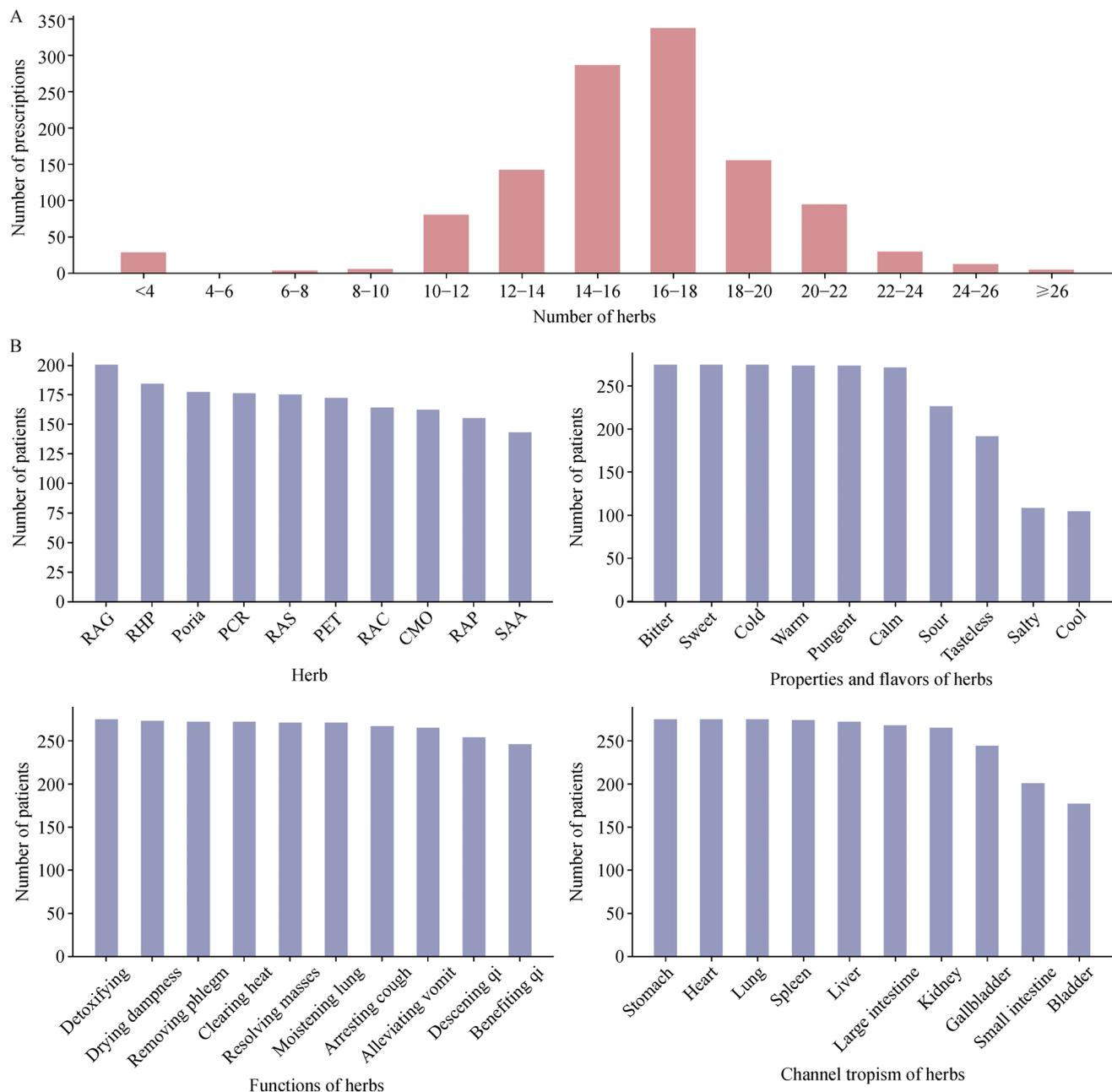
Data are presented as *n* (%) or *n/N* (%), where *N* is the total number of patients in group. *P* values were calculated by using  $\chi^2$  test or Fisher's exact test. *P* values were used to compare the discharged and death groups. \* *P*<0.05, \*\* *P*<0.01.

**Table 7** Prognosis of patients treated with herbal prescriptions

Prognosis	Disease conditions (Number of patients treated with herb prescriptions/number of patients)		
	Moderate ( <i>N</i> = 207)	Severe ( <i>N</i> = 86)	Total ( <i>N</i> = 293)
Discharged ( <i>n</i> = 238)	187/198 (94%)	39/40 (98%)	226/238 (95%)
Transferred ( <i>n</i> = 31)	9/9 (100%)	21/22 (95%)	30/31 (97%)
Died ( <i>n</i> = 24)	0/0	17/24 (71%)	17/24 (71%)
Total ( <i>n</i> = 293)	196/207 (95%)	77/86 (90%)	273/293 (93%)

In the TCM clinical setting of COVID-19, personalized herbal prescriptions remained regular therapeutic solutions for treatment. From our data, we found that 290 distinct herbs were used for COVID-19 treatment. Most of the herbs in these prescriptions had pharmacological effects (from TCM pharmacological perspectives) of clearing heat and detoxifying (e.g., Radix Scutellariae and Pericarpium Trichosanthis) and dampening phlegm (e.g., Rhizoma

Pinellia and Pericarpium Citri Reticulatae). These herbs had bitter or sweet properties and flavors. Despite the concept of holism that permeates all fields of TCM, including physiology, pathology, diagnosis, syndrome differentiation, and treatment, these therapies emphasized the upper energizer (heart and lung channel) and middle energizer (stomach and spleen channel) (Fig. 2B). Here, we showed and compared the partial results of herbal



**Fig. 2** Therapeutic characteristics of TCM herbal prescriptions. (A) Distributions of 1176 prescription-related herbs for 273 patients; (B) top 10 herbs and related features sorted by the number of patients. RAG, Radix Glycyrrhizae; RHP, Rhizoma Pinellia; PCR, Pericarpium Citri Reticulatae; RAS, Radix Scutellariae; PET, Pericarpium Trichosanthis; RAC, Radix Codonopsis; CMO, Cortex Magnoliae Officinalis; RAP, Radix Platycodonis; SAA, Semen Armeniacae Amarum.

therapies between moderate and severe cases (Tables 8 and 9).

Furthermore, we presented the top 10 herb combinations (Table 10) among the 1176 herb prescriptions to detect combination regularities (e.g., the frequently used herb combinations in TCM compound therapies) for the treatment of COVID-19 disease. The results showed that herb pairs, such as Semen Trichosanthis and Poria, Pericarpium Trichosanthis and Rhizoma Pinellia, and Pericarpium Citri Reticulatae and Radix Glycyrrhizae,

were frequently prescribed for the treatment of patients with COVID-19.

We modeled herb combinations as a network and applied complex network analysis to identify the core herb combinations from these prescriptions (Fig. 3). The outcome was consistent with the results from association rule mining. The core combinations were confirmed to have the pharmacological effects of detoxification, phlegm removal, and dampness drying in COVID-19 treatment.

**Table 8** Differences between the herb therapies received by moderate and severe cases of COVID-19

Herb	Total ( <i>n</i> = 293)	Moderate ( <i>n</i> = 207)	Severe ( <i>n</i> = 86)	<i>P</i> values
Radix Glycyrrhizae	200 (68%)	143 (69%)	57 (66%)	6.80E-01
Rhizoma Pinellia	184 (63%)	137 (66%)	47 (55%)	8.41E-02
Poria	177 (60%)	129 (62%)	48 (56%)	3.59E-01
Pericarpium Citri Reticulatae	176 (60%)	130 (63%)	46 (53%)	1.51E-01
Radix Scutellariae	175 (60%)	117 (57%)	58 (67%)	9.02E-02
Pericarpium Trichosanthis	172 (59%)	124 (60%)	48 (56%)	5.18E-01
Radix Codonopsis	164 (56%)	127 (61%)	37 (43%)	4.54E-03**
Cortex Magnoliae Officinalis	162 (55%)	115 (56%)	47 (55%)	8.98E-01
Radix Platycodonis	155 (53%)	121 (58%)	34 (40%)	4.54E-03**
Semen Armeniacae Amarum	143 (49%)	100 (48%)	43 (50%)	7.99E-01
Rhizoma Anemarrhenae	99 (34%)	62 (30%)	37 (43%)	4.15E-02*
Fructus Schisandrae Chinensis	75 (26%)	62 (30%)	13 (15%)	8.11E-03**
Fructus Forsythiae	68 (23%)	41 (20%)	27 (31%)	4.75E-02*
Radix Notoginseng	55 (19%)	46 (22%)	9 (10%)	2.11E-02*
Semen Coicis	47 (16%)	27 (13%)	20 (23%)	3.62E-02*

Including the top10 herbs sorted on the basis of the number of patients and other five herbs with statistical significance. Data are presented as *n* (%) or *n/N* (%), where *N* is the total number of patients in a group. *P* values were calculated via  $\chi^2$  test or Fisher's exact test and used to compare moderate and severe groups. \* *P*<0.05, \*\* *P*<0.01.

**Table 9** Herb therapies sorted on the basis of the prognosis of patients with severe COVID-19

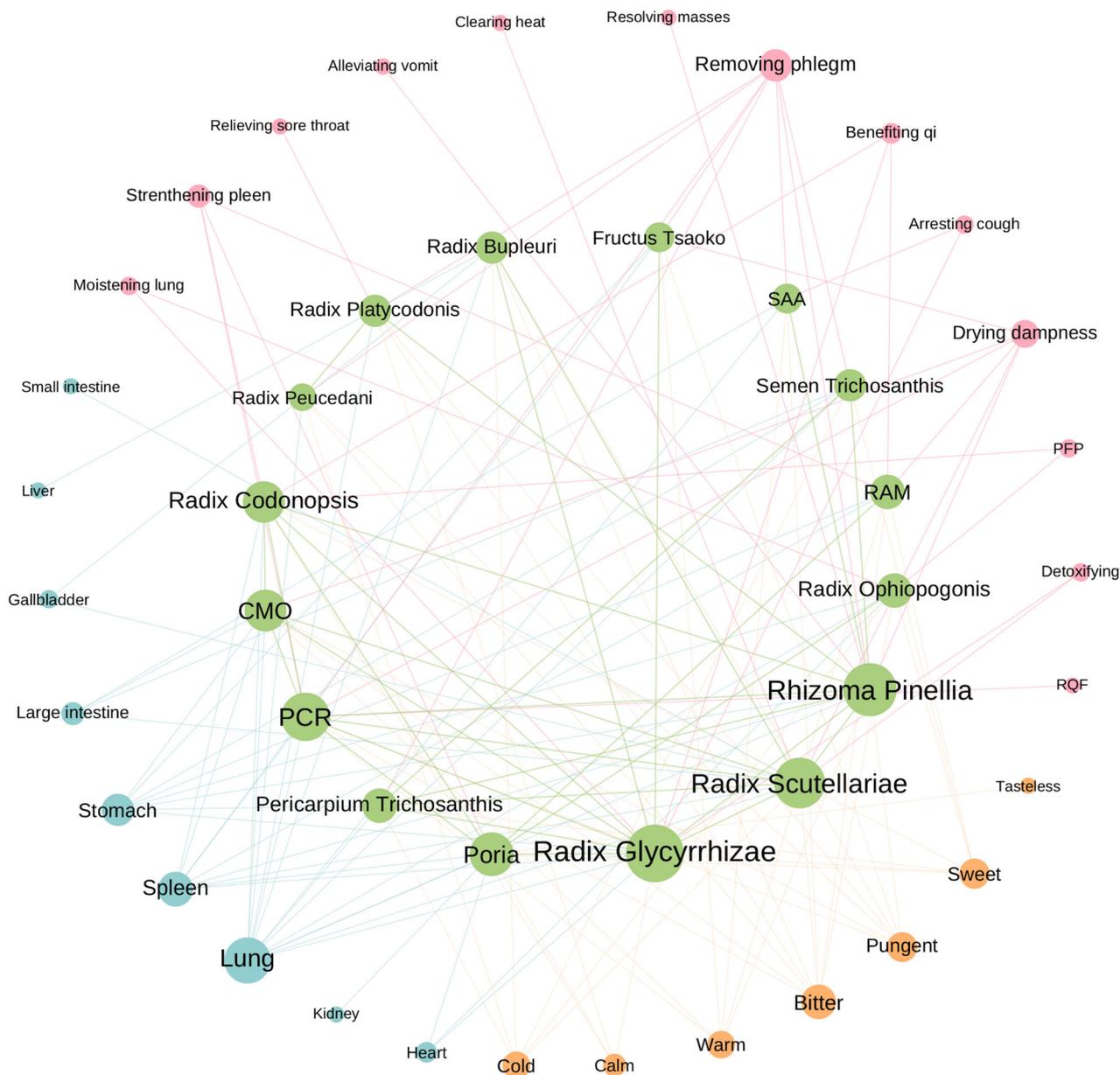
Herb	Discharged ( <i>n</i> = 40)	Transferred ( <i>n</i> = 22)	Died ( <i>n</i> = 24)	<i>P</i> values
Radix Scutellariae	29 (73%)	16 (73%)	13 (54%)	1.77E-01
Radix Glycyrrhizae	30 (75%)	15 (68%)	12 (50%)	5.81E-02
Pericarpium Trichosanthis	29 (73%)	8 (36%)	11 (46%)	6.06E-02
Poria	30 (75%)	10 (45%)	8 (33%)	1.54E-03**
Rhizoma Pinellia	31 (78%)	6 (27%)	10 (42%)	6.61E-03**
Cortex Magnoliae Officinalis	23 (58%)	11 (50%)	13 (54%)	8.01E-01
Pericarpium Citri Reticulatae	24 (60%)	15 (68%)	7 (29%)	2.15E-02*
Semen Armeniacae Amarum	26 (65%)	10 (45%)	7 (29%)	9.26E-03**
Rhizoma Anemarrhenae	21 (53%)	10 (45%)	6 (25%)	3.89E-02*
Rhizoma Atractylodis Macrocephalae	22 (55%)	10 (45%)	5 (21%)	9.37E-03**
Radix Codonopsis	21 (53%)	10 (45%)	6 (25%)	3.89E-02*
Radix Bupleuri	19 (48%)	10 (45%)	7 (29%)	1.92E-01
Fructus Tsaoko	18 (45%)	7 (32%)	10 (42%)	1.00E+00
Radix Ophiopogonis	21 (53%)	10 (45%)	4 (17%)	7.45E-03**
Herba Pogostemonis	18 (45%)	9 (41%)	7 (29%)	2.91E-01

Including the top15 herbs sorted by the number of total patients. *P* values were used to compare the discharged and death groups. Data are presented as *n* (%) or *n/N* (%), where *N* is the total number of patients in each group. *P* values were calculated by using  $\chi^2$  test or Fisher's exact test. *P* values were used to compare the discharged and death groups. \* *P*<0.05, \*\* *P*<0.01.

**Table 10** Top 10 herb combinations in COVID-19 TCM herbal prescriptions

Herb name	Herb name	Confidence	Frequency
Poria	Semen Trichosanthis	0.74	434
Semen Trichosanthis	Poria	0.95	434
Pericarpium Trichosanthis	Rhizoma Pinellia	0.78	398
Pericarpium Citri Reticulatae	Radix Glycyrrhizae	0.71	398
Radix Codonopsis	Pericarpium Citri Reticulatae	0.82	393
Pericarpium Citri Reticulatae	Radix Codonopsis	0.71	393
Radix Scutellariae	Radix Glycyrrhizae	0.79	388
Radix Codonopsis	Radix Glycyrrhizae	0.76	363
Pericarpium Trichosanthis	Semen Trichosanthis	0.70	358
Semen Trichosanthis	Pericarpium Trichosanthis	0.96	358

Detected via association rules with support >0.3. The frequency indicates the number of herb pairs that co-occurred in prescriptions.



**Fig. 3** Core herbs for COVID-19 treatment and their characteristics. This network shows the core herb combinations in TCM prescriptions. It is organized into four different types of nodes: the green nodes represent TCM herbs, and the pinkish blue and orange nodes correspond to the core pharmacological effects, channel tropisms, and flavor of the herbs. Node size reflects the degree value (a high degree is represented by a large node). PCR, Pericarpium Citri Reticulatae; CMO, Cortex Magnoliae Officinalis; SAA, Semen Armeniacae Amarum; RQF, Regulating qi flow; PFP, Rhizoma Atractylodis Macrocephalae; RAM, Rhizoma Atractylodis Macrocephalae.

### Therapeutic characteristics of therapies before admission

We extracted the mentions of therapies in the text records of EMR admission notes to investigate the therapeutic profiles of patients with COVID-19 before admission. We identified 285 (97%) patients with discomfort and found

that 172 (59%) patients were treated with drugs before admission (Table 11). Most of the patients received therapies with antibiotics (138) or antivirals (122). A total of 89 (30%) patients were treated with TCM patent medicine. Among these patients, 69 (78%) received Lianhuaqingwen capsule, which has a function of clearing heat and toxic materials. We observed that 83 symptoms (e.g., fever, cough, and fatigue) occurred before admission.

**Table 11** Therapeutic characteristics of preadmission therapies

Medicine	Patient number	Percentage ( <i>n</i> = 293)
Antibiotics	138	47%
Moxifloxacin	101	34%
Cephalosporin	48	16%
Levofloxacin	16	5%
Amoxicillin	12	4%
Antivirals	122	42%
Oseltamivir	79	27%
Arbidol	61	21%
Chinese patent medicine	89	30%
Lianhuaqingwen capsule	69	24%
Biological products	14	5%
Immunoglobulin	13	4%

Among the symptoms shown by the 94 pretreated patients, 51 had temporal outcomes (e.g., symptom disappearance) after preadmission treatment.

We found that the related symptoms relieved by the top 3 frequently used Western medical drugs before admission, namely, moxifloxacin (101 cases), oseltamivir (79 cases), and arbidol (61 cases), were fever (30%–40% partial relief rate (PRR)), fatigue and dry cough (20%–45% PRR), and cough (10%–20% PRR). However, these drugs rarely reduced the severity of chest tightness, palpitation, and wheezing. The related symptoms that could be relieved by the top Chinese patent medicine, Lianhuaqingwen capsule (69 cases), were fatigue (43% PRR), fever (38% PRR), dry cough (25% PRR), coughing (20% PRR), and wheezing (18% PRR) (Table 12).

## Discussion

Fully elucidating the patterns of the epidemiological and clinical features of COVID-19 is necessary to control, prevent, and treat this disease. TCM practitioners mainly investigate the patterns of symptom phenotypes for disease diagnosis and treatment. Therefore, obtaining the detailed TCM descriptions of patients with COVID-19 in terms of symptoms and tongue and pulse manifestations will help elucidate the clinical groups of patients with COVID-19. In addition, given the absence of proven evidence for the effectiveness of antiviral and antibiotic drugs [16–19], TCM herb prescriptions are a feasible clinical choice for COVID-19 treatment especially because they have been successfully used to treat SARS, a coronavirus-induced disease that is similar to COVID-19 [20–24]. In this retrospective study, we reported the clinical features of COVID-19 from the perspectives of TCM and Western medicine and further investigated related clinical therapies. In contrast to the cases that were included in previous studies [25–27], the 293 COVID-19 cases included in our analysis originated solely from a TCM hospital in Wuhan,

**Table 12** Symptoms of preadmission medication cases with improvement

Medicine and symptom	Patient number	Patient number (relieved)	Partial relief rate
<b>Moxifloxacin</b>			
Fever	63	27	43%
Coughing	36	7	19%
Chest tightness	25	1	4%
Wheezing	25	2	8%
Dry cough	10	2	20%
Fatigue	9	4	44%
Diarrhea	9	2	22%
Palpitation	4	0	0%
Dry mouth	4	0	0%
Throat discomfort	2	0	0%
<b>Oseltamivir</b>			
Fever	44	13	30%
Coughing	29	3	10%
Wheezing	19	0	0%
Chest tightness	17	0	0%
Diarrhea	8	0	0%
Dry cough	7	0	0%
Fatigue	7	2	29%
Palpitation	5	0	0%
Throat discomfort	3	0	0%
Dry mouth	2	0	0%
<b>Arbidol</b>			
Fever	30	12	40%
Coughing	21	4	19%
Chest tightness	17	3	18%
Wheezing	17	4	24%
Diarrhea	7	1	14%
Dry cough	7	3	43%
Fatigue	7	3	43%
Palpitation	3	0	0%
Throat discomfort	2	0	0%
Dry mouth	2	0	0%
<b>Lianhuaqingwen capsule</b>			
Fever	39	15	39%
Coughing	25	5	20%
Chest tightness	18	2	11%
Wheezing	17	3	18%
Dry cough	12	3	25%
Diarrhea	7	0	0%
Fatigue	7	3	43%
Palpitation	4	0	0%
Dry mouth	2	0	0%
Throat discomfort	1	0	0%

where patients tended to be in severe condition and were elderly (57 years old on average). The long symptom onset time (10 days on average) before admission resulted in the

overloading of hospitals in Wuhan during late January and the entirety of February. A total of 61% of the patients had different types of comorbidities, and the comorbidity rate of the 207 moderate cases approached 52%. However, all the moderate cases were successfully treated, and most of these patients were discharged within 2 weeks. Among the remaining 86 severe cases, 40 were finally discharged successfully, and 24 died during treatment. The results showed that elderly male patients (73 years on average for death cases) with a high rate of disease comorbidity tended to have poor prognosis. The top frequently occurring symptoms were coughing, wheezing, chest tightness, fever, and insomnia. TCM-specific manifestations, such as yellow fur, might be a preventive TCM phenotype marker for good prognosis. Furthermore, most of the clinical findings from laboratory tests, such as white blood cell and lymphocyte counts, that were identified as risk factors for severe COVID-19 in our study were consistent with those reported in previous studies [28,29]. However, we found that triglycerides and total cholesterol were exceptions: the baseline levels of triglycerides and total cholesterol were higher in moderate cases than in severe cases but did not exceed their normal ranges. This result would be insightful for further biomedical investigations given that previous studies have shown that liver function and lipid levels are often related to viral infections in hepatitis B-related cirrhosis [30]. Cholesterol has critical functions in infection by several types of coronaviruses, such as type-I feline coronavirus [31,32].

Although regularly used drugs, such as methylprednisolone and moxifloxacin, have been widely applied to treat severe cases, reliable evidence for their effectiveness does not exist [16]. Therefore, screening potentially effective drugs for COVID-19 treatment is important. Among the 273 patients who used herbal prescriptions, 256 were discharged or transferred (i.e.,  $17/273 = 6.2\%$  death rate for all cases and  $17/77 = 22\%$  death rate for severe cases). Among the remaining 20 patients who did not use herbal prescriptions, 13 survived ( $7/20 = 35\%$  death rate for all cases and  $7/9 = 77.7\%$  death rate for severe cases). These results hinted at the potential effectiveness of herbal prescriptions. Therefore, these prescriptions should be further studied in well-designed clinical trials. Our data covered a period of 1.5 months commencing from mid-January, during which the national guideline for COVID-19 treatment was still being developed. Frontline TCM practitioners developed optimal personalized prescriptions for patients with COVID-19. As a result, nearly 300 distinct herbs were used at that time. The results showed that common herbs and their combinations were practically prescribed for COVID-19 treatment. These common herbs and their related combinations, such as *Poria*, *Pericarpium Trichosanthis* and *Radix Scutellariae*, *Pericarpium Tricho-*

*santhis*, and *Radix Codonopsis* and *Fructus Forsythiae*, have been included in the suggested prescriptions in the latest national guideline of COVID-19 [33]. The pharmacological effects of these herbs in removing phlegm, clearing heat, and arresting cough were useful in combating cough, fever, phlegm, and COVID-19-related complications. Moreover, the herbs, such as *Radix Ophiopogonis*, *Poria*, *Rhizoma Pinellia*, and *Rhizoma Atractylodis Macrocephalae*, possibly contributed to the good prognosis of severe cases. The underlying pharmacological mechanisms of these herbs and their related prescriptions for COVID-19 treatment have been active research topics in recent months [34]. We found that the three popularly used drugs, namely moxifloxacin, oseltamivir, and abidol, and one Chinese patent medicine (i.e., Lianhuaqingwen capsule) provided some degree of symptom (e.g., fever and dry cough) relief. However, these drugs rarely relieved most symptoms, such as chest tightness, palpitation, and wheezing, related to severe conditions. Western drugs were given to patients who stayed in-hospital, and 238 (81.2%) cases were finally discharged. The results indicated the effectiveness of TCM herbal prescriptions in the integrative treatment of COVID-19.

Our study has several limitations. First, given that the causative pathogen had just been identified at the time of admission, the diagnoses of most of the 293 patients were confirmed to be positive on the basis of the presence of SARS-CoV-2 nucleic acid. However, 102 cases still lacked viral RNA detective data. Second, this study involved a modest set of cases of hospitalized patients. Therefore, the laboratory test results, especially the multiple test comparisons, statistical test results, and *P* values obtained in this work, should be interpreted with caution because of the limited number of cases. Third, 31 patients were transferred to designated hospitals for mixed reasons, including management reasons in the early days of the pandemic and condition aggravation. Therefore, assessing the prognoses of these cases is difficult. Finally, this study mainly focused on the clinical features of the real-world manifestations and therapeutic characteristics of the integrated treatment of 293 COVID-19 cases in a clinical environment in Wuhan, China. Carefully designed clinical trials are required to filter out potential confounders to validate the correlations between the clinical features and prognosis of COVID-19 that may have clinical implications. Furthermore, due to complicated interactions among clinical features (e.g., symptoms and comorbidities) [35,36] and associations between phenotypes and genotypes, the exploration of the correlations between clinical phenotype networks and prognosis by COVID-19 clinical management is promising [37–39] to identify the precise patient subgroups [40,41] with possibly high mortality or good prognosis.

## Conclusions

We described the clinical features and therapeutic characteristics of 293 COVID-19 inpatient cases in Wuhan. These cases were treated via the integration of TCM herbal prescriptions and Western medicine. Our results reconfirmed several well-recognized risk factors, such as age, gender (male), and comorbidities, and provided novel laboratory indications (e.g., cholesterol) and TCM-specific phenotype markers (e.g., dull tongue) that were relevant to COVID-19 infections and prognosis. Furthermore, we proposed a TCM symptom profile on the basis of nearly 300 COVID-19 cases. This profile would provide some important insights into TCM pathological studies. We identified frequently used herbs and their combinations from 1176 TCM prescriptions, which reflected the treatment principles of TCM for COVID-19 infections. Lastly, we found that 59% of patients received some form of treatment, including antivirals, antibiotics, and Chinese patent medicine, before admission. These might have some effects on COVID-19 symptoms, such as fever and dry cough.

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## Compliance with ethics guidelines

Zixin Shu, Yana Zhou, Kai Chang, Jifen Liu, Xiaojun Min, Qing Zhang, Jing Sun, Yajuan Xiong, Qunsheng Zou, Qiguang Zheng, Jinghui Ji, Josiah Poon, Baoyan Liu, Xuezhong Zhou, and Xiaodong Li declare that they have no conflict of interest. This study was approved by the ethics review board of Hubei Provincial Hospital of Traditional Chinese Medicine (HBZY2020-C01-01). Written consent was waived due to the retrospective nature. This study was reported according to STROBE (The Strengthening the Reporting of Observational Studies in Epidemiology).

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