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Original Article

A Cohort Study on Traditional Chinese Medicine Syndrome Differentiation-based Treatment for Post-COVID-19 Syndrome

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Abstract

Background and objectives: Due to the lack of specific Western medicine therapies for post-coronavirus disease 2019 (COVID-19) syndrome in clinical practice, this study aimed to investigate the efficacy of traditional Chinese medicine (TCM) for post-COVID-19 syndrome using a cohort study design and to explore its clinical value in alleviating patients' symptoms and improving clinical outcomes.

Methods: In this cohort study, patients were divided into two groups according to clinical treatment. The control group received conventional Western medicine, and the treatment group received additional TCM syndrome differentiation–based treatment. Propensity score matching methods were used to reduce selection bias by equating groups based on observed covariates. Clinical data, including TCM symptom scores, the Short Form 36 Health Survey, clinical efficacy, and adverse events at Day 7, were collected. The primary outcome was the efficacy rate, defined by improvement at Day 7 compared with the Day 0 score. Data were processed and analyzed using SPSS 23.0 and R 4.5.0 software.

Results: A total of 434 patients were enrolled in the cohort, including 306 patients in the control group and 128 in the treatment group. After 1:1 matching, 94 matched pairs were analyzed. For the primary outcome, the effective rate in the treatment group was higher than that in the control group (30.8% vs. 17.2%; odds ratio (OR) = 2.17, 95% confidence interval (CI): 1.09–4.35, P = 0.003). After seven days of treatment, the TCM syndrome score improved more in the treatment group than in the control group (median difference (MD) = 2.00, 95% CI: 0.50–3.50, P = 0.009). Subgroup analyses showed generally favorable efficacy in the treatment group across subgroups, though not all reached statistical significance.

Conclusions: TCM syndrome differentiation–based therapy effectively relieves clinical symptoms in patients with post-COVID-19 syndrome.

Keywords: Long COVID; Traditional Chinese medicine; TCM; TCM syndrome; Clinical symptoms; Quality of life; Cohort study.

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Introduction

Coronavirus disease 2019 (COVID-19) is a highly contagious respiratory disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection.[1,2] SARS-CoV-2 can affect multiple systems, including the respiratory, circulatory, and digestive systems. Most infected individuals present with mild to moderate symptoms such as fever, cough, and fatigue; severe cases may develop dyspnea or even progress to acute respiratory distress syndrome.[1] Most COVID-19 patients enter the recovery

period after effective treatment, but they may still suffer from multisystem syndrome. For this syndrome, the World Health Organization (WHO) proposed the concept of "post-COVID-19 condition (long COVID)", which refers to a persistent multisystem disease that occurs three months after the initial SARS-CoV-2 infection, with symptoms lasting for at least two months and that cannot be explained by other diagnoses.[3–5] Common core symptoms include persistent fatigue, dyspnea, cognitive impairment, and chronic cough, with a long recovery period and complex pathogenesis.[5]

Multiple studies on post-COVID-19 patients have shown that long COVID patients often experience persistent respiratory symptoms (e.g., dyspnea and cough), physical symptoms (e.g., fatigue and post-exertional malaise), as well as various cognitive and autonomic dysfunctions.[6–8] Alleviating these long-term symptoms is crucial for treating "long COVID". At present, there is no specific Western medicine treatment for long COVID, and symptomatic support combined with lifestyle interventions is the main clinical approach.[9] The National Health Commission of China issued the Diagnostic and Treatment Protocol for Novel Coronavirus Infection (Trial Version 10),[10] which provides clear TCM syndrome differentiation and recommended prescriptions for the recovery period of COVID-19, providing a standardized basis for TCM clinical intervention. TCM syndrome differentiation–based treatment has the characteristics of individualization and holistic regulation and has shown potential value in the treatment of infectious disease syndromes.[11] This cohort study divided post-COVID-19 patients into intervention and control groups and applied the TCM-recommended prescriptions in Trial Version 10 for the recovery period, aiming to evaluate the short-term efficacy of standardized TCM syndrome differentiation–based treatment in relieving TCM symptoms and addressing the lack of clinical evidence on TCM for long COVID.

Materials and methods

Study subjects

This cohort study collected clinical cases from May 2023 to December 2024 at the outpatient department of our hospital. Patients were allocated to two cohorts based on clinical treatment preferences and medical decision-making. The treatment group received TCM syndrome differentiation-based treatment combined with Western medicine symptomatic treatment and lifestyle intervention, while the control group received only Western medicine symptomatic treatment and lifestyle intervention. Owing to clinical factors including patient voluntary withdrawal from intervention, loss to follow-up, and incomplete clinical data prior to the 7-day study endpoint, the final valid sample sizes were 128 cases in the treatment group and 306 cases in the control group. This imbalance was attributable to the nature of the clinical cohort study, in which some patients discontinued intervention, were lost to follow-up, or had incomplete data before completion of the 7-day study period. This study was conducted in accordance with the Declaration of Helsinki (2024 revision). Ethical approval was granted by the Ethics Committee of Guangdong Provincial Hospital of Chinese Medicine (approval number: ZF2023-037-01), and written informed consent was obtained from all participants prior to enrollment. This study was registered in the International Traditional Chinese Medicine Clinical Trial Registry (ITMCTR2025001974).

Sample size justification

The expected effective rates, with 30% in the treatment group and 15% in the control group, were obtained from a preliminary small sample pilot study investigating TCM intervention for long COVID, which was performed by our research team. Based on the sample size calculation formula for two independent groups, a two-sided type I error rate $\alpha = 0.05$ and a type II error rate $\beta = 0.2$ were applied. Under these settings, the minimum sample size required for each group was estimated to be 88 cases.

Patient flow

A total of 456 patients were screened. Among them, 22 patients were excluded, including 10 with severe cardiovascular and respiratory diseases, 6 with allergy to TCM ingredients, 4 receiving TCM for COVID-19 treatment, and 2 with impaired expression and communication ability. In total, 434 patients were finally enrolled.

Following 1:1 propensity score matching with a caliper value of 0.2, 94 matched pairs were included in the final analysis. A total of 246 unmatched cases were excluded, including 122 with extreme propensity scores, 78 lost to follow-up, and 46 with incomplete clinical data. A participant flow diagram was provided in accordance with the RECORD statement requirements for cohort studies (Fig. 1).

Diagnostic criteria

According to the 2022 WHO official definition of post-COVID-19 syndrome (long COVID)[5]: the condition occurs three months after the initial SARS-CoV-2 infection, with symptoms lasting for at least two months, cannot be explained by other diagnoses, and has core symptoms that include persistent fatigue, dyspnea, cognitive dysfunction, chronic cough, etc.

Inclusion criteria

All of the following criteria must be satisfied: 1) Meeting the WHO diagnostic criteria for long COVID (symptom onset ≥3 months after SARS-CoV-2 infection, duration ≥2 months); 2) Aged 18–80 years; 3) Normal expression and communication ability, and ability to cooperate with the completion of treatment and follow-up assessments; 4) The enrolled patients provided written informed consent themselves; 5) Complete clinical and follow-up data.

Exclusion criteria

Participants meeting any of the following were excluded: 1) Patients with severe respiratory or cardiovascular diseases or malignant tumors; 2) Patients with mental illnesses or currently taking sedatives, anti-anxiety drugs, etc.; 3) Patients allergic to TCM ingredients; 4) Patients currently taking TCM for COVID-19 treatment.

Elimination criteria

Patients incorrectly included who did not meet the inclusion criteria and patients with no data records after entering the study.

Dropout criteria

Patients who discontinued the study due to severe adverse events and patients who voluntarily withdrew due to ineffective treatment or personal reasons.

Treatments and grouping

Cohort assignment basis

Patients were assigned to treatment or control cohorts based on clinical treatment preference and joint decision-making between patients and attending physicians: patients who opted for TCM combined with Western medicine were included in the treatment

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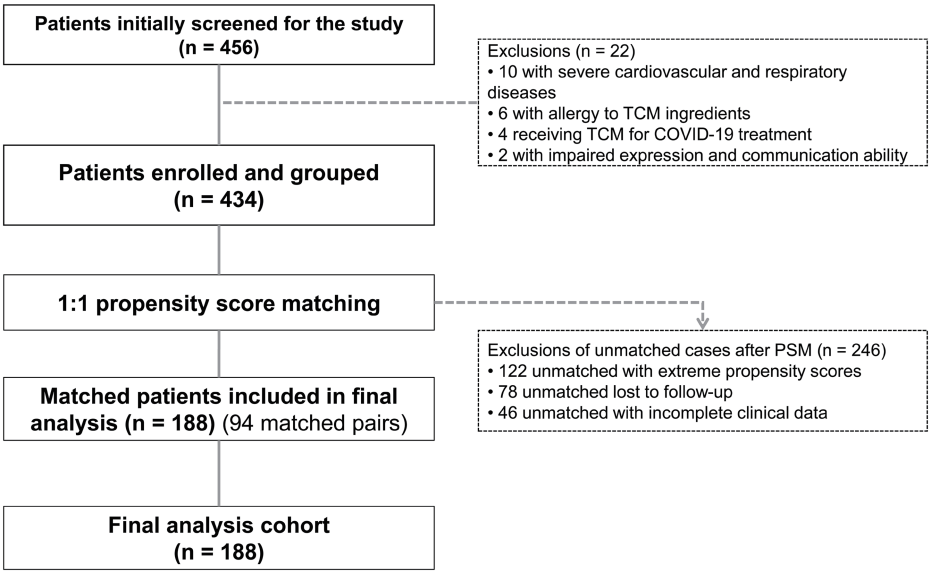

Fig. 1. The flow diagram of the study. COVID-19, coronavirus disease 2019; TCM, traditional Chinese medicine.

group, and patients who only accepted Western medicine treatment were included in the control group.

Control cohort

The control group received conventional Western medicine symptomatic treatment for the recovery period of COVID-19 infection combined with standardized lifestyle intervention. Specific and operational Western medicine therapies included: 1) Targeted symptomatic management for respiratory and systemic symptoms (e.g., antiasthmatic, antitussive and expectorant, and analgesic drugs); 2) Standardized treatment for underlying diseases (e.g., hypertension, diabetes) in accordance with clinical guidelines; 3) Lifestyle intervention: maintaining regular sleep, adequate water intake, slow eating, balanced nutrition, and appropriate gentle exercise (e.g., walking, tai chi). The treatment course was seven consecutive days.

Treatment cohort

The treatment group received TCM syndrome differentiation-based treatment combined with the same specific Western medicine symptomatic treatment and lifestyle intervention as the control group, in accordance with the Diagnostic and Treatment Protocol for Novel Coronavirus Infection issued by the National Health Commission of China.[10] The treatment course was seven consecutive days, and the specific, operational TCM syndrome differentiation types, clinical manifestations, herbal compositions, and doses were as follows:

Lung-Spleen Qi Deficiency Syndrome

Clinical manifestations: Shortness of breath, lassitude and fatigue, poor appetite with nausea and vomiting, stuffiness and fullness in the abdomen, weak defecation, and loose and unsmooth stool. Pale, enlarged tongue with white, greasy coating.

Recommended prescription: Rhizoma Pinelliae Preparata 9 g, Pericarpium Citri Reticulatae 10 g, Radix Codonopsis 15 g, Radix Astragali Preparata 30 g, Rhizoma Atractylodis Macrocephalae Stir-fried 10 g, Poria cocos 15 g, Herba Pogostemonis 10 g, Fructus Amomi 6 g (decocted later), and Radix Glycyrrhizae 6 g.

Qi-Yin Deficiency Syndrome

Clinical manifestations: Fatigue, shortness of breath, dry mouth and thirst, palpitations, excessive sweating, poor appetite, and dry cough with little phlegm. Red tongue with less fluid, and a thready or weak and forceless pulse.

Recommended prescription: Radix Adenophorae Tetraphyllae 10 g, Radix Glehniae 10 g, Radix Ophiopogonis 15 g, Radix Panacis Quinquefolii 6 g, Fructus Schisandrae Chinensis 6 g, Gypsum Fibrosum 15 g, Herba Lophatheri 10 g, Folium Mori 10 g, Rhizoma Phragmitis 15 g, Radix Salviae Miltiorrhizae 15 g, and Radix Glycyrrhizae 6 g.

Cold Fluid Stagnating in the Lung Syndrome

Clinical manifestations: Pruritic cough, or paroxysmal cough, irritative cough, nocturnal cough, aggravated by cold, induced by allergy, white phlegm difficult to expectorate, white and greasy fur, and a string-like and tight pulse.

Recommended prescription: Rhizoma Belamcandae 9 g, Herba Ephedrae Preparata 6 g, Rhizoma Zingiberis 15 g, Radix Asteris 30 g, Flos Farfarae 30 g, Fructus Schisandrae Chinensis 15 g, Rhizoma Pinelliae Preparata 9 g, Radix Peucedani 15 g, Radix Stemonae 15 g, Fructus Perillae 9 g, Semen Lepidii et Descurainiae 15 g, and Bulbus Fritillariae Cirrhosae Powder 3 g (taken with boiled water).

TCM medication administration method: All selected Chinese medicinal herbs were decocted with an appropriate amount of clear water. One dose per day was decocted into a medicinal preparation and taken warm twice a day (morning and evening) for seven consecutive days. No other TCM therapies (acupuncture, moxibustion, proprietary Chinese medicine) or concurrent unapproved therapies were used in either cohort during the study period.

Syndrome differentiation quality control: TCM syndrome differentiation was independently completed by two deputy chief physicians or above specializing in TCM internal medicine, based on the four basic diagnostic methods including inspection, auscultation and olfaction, inquiry, and palpation. Inter-rater consistency was evaluated using the Kappa coefficient. A Kappa value of 0.82 with $P < 0.001$ indicated good consistency. For discordant cases, the final syndrome

type was determined by discussion between the two physicians or by arbitration by a third chief physician of TCM. No other TCM therapies (acupuncture, moxibustion, proprietary Chinese medicine) were used in this study to ensure the uniformity of the intervention.

Observation indicators

Primary outcome measure

The total effective rate of TCM symptom improvement was defined as the primary outcome of this study and calculated using the nimodipine method, a validated approach for assessing therapeutic efficacy of TCM syndromes in respiratory diseases. The therapeutic index was first calculated using the formula: Therapeutic index (%) = (Baseline TCM syndrome score - Post-treatment TCM syndrome score) / Baseline TCM syndrome score × 100%. Based on the therapeutic index, the efficacy was stratified into four grades with clear definitions:

- Ineffective: Therapeutic index < 25%;
- Effective: 25% ≤ Therapeutic index < 45%;
- Markedly effective: 45% ≤ Therapeutic index < 90%;
- Cure: Therapeutic index ≥ 90%. Total effective rate (%) = (Number of effective cases + Number of markedly effective cases + Number of cured cases) / Total number of cases × 100%.

TCM syndrome scores were assessed at baseline and on Day 7 post-treatment by trained assessors blinded to cohort allocation.

Secondary outcome measures

TCM syndrome scores: A 25-item TCM syndrome scale was adopted (Supplementary Table 1), covering primary, secondary, and general symptoms. Each item was scored 0 (asymptomatic), 2 (mild), 4 (moderate), or 6 (severe), with a total score range of 0 to 150, and was linearly converted to a range of 0 to 75 for efficacy analysis. Higher scores indicated more severe symptoms. Scores were collected at baseline and Day 7 post-treatment, and the score change from baseline to post-treatment was calculated. Outcome assessors were blinded to group allocation. The 25-item TCM syndrome scale was developed by our research team for this study, based on established TCM diagnostic criteria for respiratory conditions and the Diagnostic and Treatment Protocol for Novel Coronavirus Infection. This scale has not undergone formal external validation; its items cover primary, secondary, and general symptoms relevant to post-COVID-19 TCM syndrome patterns (Supplementary Table 1).

The Short Form 36 Health Survey (SF-36): The Chinese version of the SF-36 scale was used,[12–14] which includes eight core dimensions. These dimensions are physical functioning, role limitations due to physical health, bodily pain, general health, vitality, social functioning, role limitations due to emotional problems, and mental health. The scale also contains one single-item health transition measure that is not included in total score calculation.

Scoring method: Each dimension contains 2–10 items, with different weights assigned to individual items based on the scale's standard scoring manual. First, the raw score of each dimension was calculated by summing the weighted scores of its constituent items; then, the raw score was linearly transformed to a standardized score ranging from 0 to 100 using the scale's conversion formula. A higher standardized score indicates better health-related quality of life. The total quality of life score was calculated as the average of the eight core dimension standardized scores (ranging from 0 to 100). Scores were assessed at baseline (Day 0) and 7 days after treatment (Day 7), and the score change was computed as Day 7 standardized total score minus Day 0 standardized total score. A positive value reflects an improvement in quality of life. The assessors were blinded to patient grouping.

Safety evaluation

A dedicated researcher who was blinded to the patient group allocation was responsible for daily safety monitoring throughout the 7-day treatment period. Safety monitoring consisted of active telephone follow-up conducted once every two days to solicit adverse reactions, as well as outpatient reexamination performed on Day 7 for physical examination and symptom assessment. Patients were instructed to report any adverse reactions promptly, including nausea, vomiting, abdominal pain, diarrhea, headache, and rash, among others. The safety monitoring records included the occurrence time, duration, severity, and handling measures of adverse reactions.

Missing data handling

The complete case analysis method was adopted in this study. Cases with missing key outcome indicators, including TCM symptom scores and efficacy evaluation, were excluded from the final statistical analysis, with a total of 46 cases excluded.

Statistical analysis

Statistical analysis was performed using SPSS (version 23.0) and R software (version 4.5.0). 1:1 PSM was conducted, with a caliper value of 0.2, to further balance the baseline covariates of the matched groups. Baseline balance assessment: Both *P*-values and standardized mean differences (SMD) were used to evaluate baseline balance between groups.

Count data were expressed as frequencies or percentages and analyzed using the *Chi*-square test or Fisher's exact test. Quantitative data conforming to normal distribution and homogeneity of variance were expressed as mean ± standard deviation; paired-sample *t*-tests were used for intragroup comparisons, and independent-sample *t*-tests for intergroup comparisons. If they did not conform to normal distribution, they were expressed as [M (Q1, Q3)]; Wilcoxon signed-rank tests were used for intragroup comparisons, and Mann-Whitney U tests for intergroup comparisons. Rank sum tests were used for ranked data. Logistic regression model optimization: Sparse variables (n ≤ 1, such as vitiligo and Hashimoto's thyroiditis) were excluded from the logistic regression analysis to avoid quasi-complete separation. Sensitivity analysis was performed by excluding patients with hypertension (an imbalanced baseline index) to verify the stability of the results. A *P*-value < 0.05 was considered statistically significant. All statistical results were expressed as *P*-values with specific numerical values, and 95% confidence intervals (CI) were attached to core effect sizes (odds ratio and mean difference).

Results

Baseline characteristics

A total of 456 patients were initially screened. Among them, 22 patients were excluded, including 10 with severe cardiovascular and respiratory diseases, 6 with allergy to TCM ingredients, 4 receiving TCM for COVID-19 treatment, and 2 with impaired expression and communication ability. A total of 434 patients were finally included and allocated into groups, with 306 patients in the control group and 128 patients in the treatment group. Propensity score matching was performed on the enrolled cohort to further balance confounding factors, and 94 matched patient pairs were included in the analysis. The probability density analysis charts before and after matching are presented in Supplementary Figure 1. Baseline balance was evaluated by both *P*-values and SMD: most

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Table 1. General characteristics of patients after matching

Variables	Total (n = 188)	Control group (n = 94)	Treatment group (n = 94)	*P*
Age, [Median (IQR)]	40.50 (29.00, 51.00)	40.50 (29.00, 56.00)	41.00 (28.25, 50.00)	0.654
Sex, n (%)				0.301
Male	44 (23.40)	19 (20.21)	25 (26.60)	
Female	144 (76.60)	75 (79.79)	69 (73.40)	
Absence of underlying disease, n (%)				0.013
No	33 (17.55)	10 (10.64)	23 (24.47)	
Yes	155 (82.45)	84 (89.36)	71 (75.53)	
Hepatopathy, n (%)				0.244
No	185 (98.40)	94 (100.00)	91 (96.81)	
Yes	3 (1.60)	0 (0.00)	3 (3.19)	
Hypertension, n (%)				0.047
No	170 (90.43)	89 (94.68)	81 (86.17)	
Yes	18 (9.57)	5 (5.32)	13 (13.83)	
Hyperlipidemia, n (%)				0.129
No	184 (97.87)	94 (100.00)	90 (95.74)	
Yes	4 (2.13)	0 (0.00)	4 (4.26)	
Diabetes, n (%)				1.000
No	184 (97.87)	92 (97.87)	92 (97.87)	
Yes	4 (2.13)	2 (2.13)	2 (2.13)	
Lung Qi Deficiency, n (%)				1.000
No	6 (3.19)	3 (3.19)	3 (3.19)	
Yes	182 (96.81)	91 (96.81)	91 (96.81)	
Other TCM syndrome, n (%)				1.000
No	182 (96.81)	91 (96.81)	91 (96.81)	
Yes	6 (3.19)	3 (3.19)	3 (3.19)	

Data are presented as numbers or medians. IQR, interquartile range.

covariates (gender, age, diabetes, *Lung Qi* Deficiency, etc.) had SMD < 0.1, indicating good balance, while "absence of underlying disease" ($P = 0.013$, SMD = 0.32) and hypertension ($P = 0.047$, SMD = 0.25) had SMD > 0.1, indicating residual imbalance. All enrolled patients had normal expression and communication ability and completed the informed consent process.

The baseline data of the two groups are presented in Table 1 for the matched cohort and in Supplementary Table 2 for the cohort before propensity score matching. Analysis of the 246 unmatched patients showed that their baseline characteristics, including age, communication ability, and syndrome types, were consistent with those of the matched sample, with all covariates having $P > 0.05$. Exclusion of these unmatched patients did not significantly affect the study results.

Outcome measurements and efficacy analysis

Primary outcome

After propensity score matching, the total effective rate was 30.85% (29/94) in the treatment group and 17.02% (16/94) in the control group, with the treatment group significantly higher than the control group (OR = 2.17, 95% CI: 1.09–4.35, $P = 0.003$) (Table 2). No cure cases were found in either group, whereas there were 10 cases (10.64%) of marked effectiveness in the treatment group (0 in the control group), and 19 cases (20.21%) of effectiveness in the treatment group (vs. 16 cases [17.02%] in the control group). The three TCM syndrome types in the treatment group all showed symptomatic improvement, with the highest effective rate in *Lung–Spleen Q*i Deficiency Syndrome (32.14%).

Secondary outcome

After matching, the median change in TCM syndrome scores (converted to a 0–75 scale) was 3.00 (0.25, 5.75) in the treatment group and 1.00 (0.00, 4.00) in the control group, with a significant intergroup difference ($P = 0.009$) (Table 3). The median change in the SF-36 standardized total score was 2.00 (−2.30, 5.00) in the treatment group and 0.00 (−2.75, 4.00) in the control group, with no significant intergroup difference ($P = 0.268$) (Table 3).

Screening factors associated with primary outcome

Univariate binary logistic analysis

Sparse variables (n ≤ 1) were excluded from the analysis to avoid

Table 2. Clinical efficacy of the two groups after matching

Variables	Total (n = 188)	Control group (n = 94)	Treatment group (n = 94)	*P*
Efficacy, n (%)				0.003
Ineffective	143 (76.06)	78 (82.98)	65 (69.15)	
Effective	35 (18.62)	16 (17.02)	19 (20.21)	
Markedly effective	10 (5.32)	0 (0.00)	10 (10.64)	
Total effective rate (%)		17.2%	30.85%	

quasi-complete separation. After propensity score matching, statistically significant differences were observed in the change in TCM syndrome scores (OR = 13.45, 95% CI: 3.63–49.81, $P < 0.001$), absence of underlying diseases (OR = 0.40, 95% CI: 0.18–0.89, $P = 0.025$), hypertension (OR = 3.72, 95% CI: 1.38–10.06, $P = 0.010$), and diabetes (OR = 10.14, 95% CI: 1.03–100.08, $P = 0.047$) (Table 4).

Multivariate binary logistic analysis

Variables with statistical significance in the univariate analysis were included in the multivariate binary logistic analysis, and the results showed that the change in TCM syndrome scores was the only independent influencing factor for clinical efficacy (OR = 15.49, 95% CI: 3.80–63.17, $P < 0.001$) (Table 5). Absence of underlying diseases, hypertension, and diabetes had no significant predictive value for efficacy ($P > 0.05$). Different TCM syndrome types had no significant impact on the total effective rate ($P > 0.05$).

Sensitivity analysis

To address the residual baseline imbalance in hypertension ($P = 0.047$), 18 patients with hypertension were excluded in the sensitivity analysis (170 patients remaining: 81 in the treatment group and 89 in the control group). The total effective rate of TCM symptom improvement was 28.40% (23/81) in the treatment group and 14.61% (13/89) in the control group, with a statistically significant intergroup difference (OR = 2.32, 95% CI: 1.08–4.96, $P = 0.044$). The median change in TCM syndrome scores was 3.00 (0.00, 5.00) in the treatment group and 1.00 (0.00, 4.00) in the control group ($P = 0.006$). These results confirmed the stability of the study findings, which were not affected by the residual baseline imbalance in hypertension.

Subgroup analysis

Subgroup analysis showed that the treatment group had better efficacy than the control group in most subgroups, with some differences reaching statistical significance ($P < 0.05$) (Fig. 2).

Safety evaluation

No adverse events were reported in either group during the 7-day treatment period. This finding indicates acceptable short-term safety of the integrated TCM and Western medicine regimen as well as the Western medicine-only regimen in this study population. However, this observation does not indicate that TCM alone, Western medicine alone, or their combination are completely free of adverse effects in all circumstances. In addition, the absence of adverse events does not imply that the guideline-based treatment regimen is ineffective.

Discussion

This cohort study adopted the standardized TCM-recommended prescriptions from the Diagnostic and Treatment Protocol for Novel Coronavirus Infection for the recovery period,[11] and found that TCM syndrome differentiation-based treatment combined with Western medicine symptomatic treatment and lifestyle intervention can significantly improve TCM symptoms in patients with post-COVID-19 syndrome within seven days. The total effective rate of the treatment group was 30.85%, which was significantly higher than that of the group receiving Western medicine symptomatic treatment combined with lifestyle intervention (17.20%). This result is consistent with the 17–60% total effective rate range of TCM syndrome differentiation-based treatment for long COVID reported in previous clinical studies,[12,13] further confirming the stable short-term efficacy of standardized TCM intervention in alleviating post-COVID-19–related symptoms. All three TCM syndrome types (*Lung-Spleen Qi* Deficiency, *Qi-Yin* Deficiency, and *Cold Fluid Stagnating* in the Lung) showed obvious symptomatic improvement, indicating the universality of the standardized TCM prescriptions in Trial Version 10 for the recovery period of long COVID. The change in TCM syndrome scores was the only independent influencing factor for clinical efficacy, indicating that the improvement of TCM symptoms is closely related to the therapeutic effect.

Subgroup analyses revealed favorable trends in most subgroups, although statistical significance was not reached in some subgroups (e.g., age ≥ 65 years, female, hypertension). This finding is consistent with the trend of our previous meta-analysis on integrated traditional Chinese and Western medicine for acute COVID-19: the previous study showed that integrated medical treatment had stable and significant therapeutic advantages over conventional Western medicine alone across different subgroups stratified by treatment duration, COVID-19 severity, and risk of bias, with consistent efficacy regardless of subgroup stratification.[14] The two studies together confirm that TCM syndrome differentiation-based combined treatment has stable efficacy throughout the entire

Table 3. Differences in TCM syndrome scores and SF-36 scores after matching between the two groups

Variables	Total (n = 188)	Control group (n = 94)	Treatment group (n = 94)	*P*
TCM syndrome score difference, [Median (IQR)]	2.00 (0.00, 5.00)	1.00 (0.00, 4.00)	3.00 (0.25, 5.75)	0.009
SF-36 score difference, [Median (IQR)]	0.00 (−2.55, 5.00)	0.00 (−2.75, 4.00)	2.00 (−2.30, 5.00)	0.268

IQR, interquartile range; TCM, traditional Chinese medicine; SF-36, Short Form 36 Health Survey.

Table 4. Results of univariate binary logistic regression analysis for factors associated with TCM syndrome score improvement after propensity score matching

Variables	β	S.E	OR (95% CI)	*P*
Age	−0.02	0.01	0.98 (0.96–1.01)	0.174
Differences in TCM symptoms	2.60	0.67	13.45 (3.63–49.81)	<0.001
SF-36 difference	−0.02	0.02	0.98 (0.95–1.02)	0.362
Sex				
Male			1.00 (Reference)	
Female	0.26	0.42	1.30 (0.57–2.95)	0.537
Absence of underlying disease				
0			1.00 (Reference)	
1	−0.92	0.41	0.40 (0.18–0.89)	0.025
Hepatopathy				
0			1.00 (Reference)	
1	−14.43	840.27	0.00 (0.00–Inf)	0.986
Hypertension				
0			1.00 (Reference)	
1	1.31	0.51	3.72 (1.38–10.06)	0.010
Hyperlipemia				
0			1.00 (Reference)	
1	1.19	1.02	3.28 (0.45–23.98)	0.242
Diabetes mellitus				
0			1.00 (Reference)	
1	2.32	1.17	10.14 (1.03–100.08)	0.047
Lung Qi Deficiency				
0			1.00 (Reference)	
1	−0.48	0.88	0.62 (0.11–3.50)	0.587
Other TCM syndrome				
0			1.00 (Reference)	
1	0.48	0.88	1.62 (0.29–9.13)	0.587

CI, confidence interval; OR, odds ratio; S.E., standard error; TCM, traditional Chinese medicine.

Table 5. Results of multivariate binary logistic regression analysis for independent factors influencing TCM syndrome score improvement

Variables	β	S.E	OR (95% CI)	*P*
Differences in TCM symptoms	2.74	0.72	15.49 (3.80–63.17)	<0.001
Absence of underlying disease				
0			1.00 (Reference)	
1	−2.26	1.84	0.10 (0.00–3.86)	0.220
Hypertension				
0			1.00 (Reference)	
1	0.30	2.19	1.35 (0.02–97.85)	0.892
Diabetes mellitus				
0			1.00 (Reference)	
1	−3.08	5.82	0.05 (0.00–4,162.76)	0.597

CI, confidence interval; OR, odds ratio; S.E., standard error; TCM, traditional Chinese medicine.

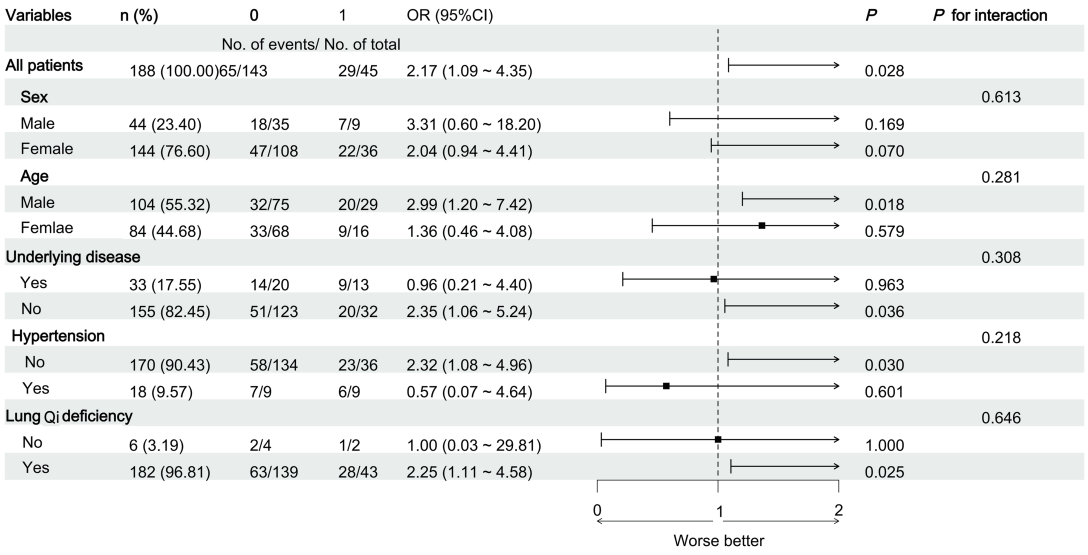

Fig. 2. Subgroup analysis and forest plot of the results. CI, confidence interval; OR, odds ratio.

course of COVID-19, spanning from the acute stage to the recovery stage, and can maintain a consistent symptomatic relief effect in different patient subgroups. At present, there are few published studies focusing on the subgroup efficacy of TCM treatment for long COVID stratified by demographic characteristics such as age and gender. The results of this study supplement clinical evidence in this field, suggesting that this standardized TCM regimen has good population adaptability for long COVID patients.

The significant improvement in TCM symptom scores was not accompanied by a corresponding difference in the SF-36 standardized total scores (P = 0.268). This finding may be attributed to three main factors. First, the 7-day short-term intervention only relieved specific TCM symptoms, whereas long COVID is a chronic condition requiring longer follow-up to improve overall quality of life[1,8]; second, the SF-36 is a general quality-of-life scale that is less sensitive to targeted relief of specific symptoms[15]; third, the improved TCM symptoms are mainly localized to the respiratory and digestive systems, with limited impact on the multidimensional health status assessed by the SF-36.

Limitations

This study has several limitations: the follow-up period was only seven days, making it impossible to assess mid- to long-term efficacy and symptom recurrence; it was a single-center study with residual baseline imbalance in hypertension and the absence of underlying disease in some participants; the TCM syndrome scale used in this study was developed for this specific research context and has not undergone formal external validation or establishment of a minimal clinically important difference, which may affect the precision and generalizability of symptom scoring; and it lacked objective lung function data. The absence of objective lung function measurement limited the comprehensive evaluation of the therapeutic effect of TCM on respiratory function improvement in patients with long COVID; therefore, the conclusions of this study should be interpreted with caution, and over-interpretation of the efficacy should be avoided. The study was retrospectively registered, which may affect the rigor of the study reporting. In addition, the safety evaluation was limited to a 7-day observation period; the long-term safety of combined TCM and Western medicine treatment remains to be further observed.

Future directions

Future studies should conduct large-sample, multicenter randomized controlled trials with longer follow-up to verify the mid- to long-term efficacy of TCM syndrome differentiation-based treatment, collect objective indicators such as lung function to comprehensively evaluate therapeutic effects, explore the underlying mechanisms through basic experiments, and adopt more rigorous study designs, including prospective registration and double-blind, placebo-controlled designs, to improve the quality of evidence.

Conclusions

In this single-center cohort study, standardized TCM syndrome differentiation-based treatment from the Diagnostic and Treatment Protocol for Novel Coronavirus Infection, combined with conventional Western medicine symptomatic treatment and lifestyle intervention, effectively relieved TCM symptoms in adult patients aged 18–80 years with post-COVID-19 syndrome after seven days of intervention, with favorable short-term efficacy and good safety. The change in TCM syndrome scores was the only independent influencing factor for clinical efficacy, and the stability of the study results was fully verified by sensitivity analysis. This study provides clinical evidence for the short-term standardized application of TCM syndrome differentiation-based treatment in the clinical management of post-COVID-19 syndrome.

Supporting information

Supplementary material for this article is available at https://doi.org/10.14218/FIM.2026.00001.

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Conflict of interest

The authors declared that there is no conflict of interest in the authorship and publication of this contribution.

Author contributions

Designed the study and finalized the manuscript (RY, QL), collected information and constructed the dataset (MJ, YT, JQ, DZ), completed the first version of the manuscript (MJ, QL), and finished the manuscript corrections (QL, RY, QyL, YG, QD, XX). All authors read, revised, and approved the final manuscript.

Ethical statement

This study was conducted in accordance with the Declaration of Helsinki (2024 revision). Ethical approval was granted by the Ethics Committee of Guangdong Provincial Hospital of Chinese Medicine (approval number: ZF2023-037-01), and written informed consent was obtained from all participants prior to enrollment. This study was retrospectively registered in the International Traditional Chinese Medicine Clinical Trial Registry (ITMCTR2025001974). As this study was initiated as a routine clinical practice-driven pragmatic study, the registration was performed retroactively after study initiated, with all ethical requirements fully implemented before patient enrollment.

Data sharing statement

This study involves human participants, and the sharing of relevant research data is restricted due to ethical constraints, which limits complete and free public access to the raw data. Researchers who intend to apply for access to the study data may send a data application with a detailed justification to the email address: qliu15@gzucm.edu.cn.

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