BMJ Open Effects of tai chi and qigong on rehabilitation after COVID-19: a protocol for systematic review and metaanalysis

Zhe Zhang ¹ J G Ren, ¹ J L Guo, ² Lin An, ² Shuang Li, ² Z C Zhang, ² Yan Chen, ² Hui Liu.² Xiao Lei¹

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¹Department of Traditional Chinese Medicine, Affiliated Hospital of North Sichuan Medical College, Nanchong, Sichuan, China ²Department of Clinical Medicine of Traditional Chinese and Western Medicine, North Sichuan Medical College, Nanchong, Sichuan, China

Correspondence to

Dr Xiao Lei: 2424932797@qq.com

ABSTRACT

Introduction COVID-19 is a public health emergency of international concern, which is characterised by rapid and widespread transmission, high mortality and complications. Several studies have shown the benefits of tai chi and gigong for recovery after COVID-19; however, no meta-analysis has been reported. Therefore, the purpose of this study is to evaluate the efficacy and safety of tai chi and/or gigong on rehabilitation after COVID-19 through a systematic review and meta-analysis to provide a reference and basis for clinical application.

Methods and analysis This study will use the Cochrane Library, PubMed, Web of Science, Embase, China Knowledge Network, China Biomedical Literature Database, Chinese Scientific Journal Database and Wanfang Database. The time period is from the inception of the database to November 2021, with no language restrictions. Searches will be conducted using the subject terms "Taichi", "Qigong" and "COVID-19" plus free-text words. Articles will be screened and collected by two reviewers independently. Included studies will be assessed for quality using the Cochrane Risk of Bias Assessment Tool. Statistical analyses will be performed using the Revman V.5.3 software. The primary outcomes include 1-second forced expiratory volume and 1-second forced vital capacity, oxygen saturation, total white cell count and quality of life score. Secondary outcomes include time to remission of major symptoms, incidence of adverse events, clinical cure rate and mortality. Subgroup and sensitivity analyses will also be used to explore and interpret the heterogeneity. This protocol is written based on the guideline of the Preferred Reporting Items for Systematic Reviews and Meta-analyses Protocol. Ethics and dissemination Ethical approval and consent are unnecessary because no primary data will be

collected. The results will be disseminated through peerreviewed publications.

PROSPERO registration number CRD42021288962.

INTRODUCTION

In late 2019, a coronavirus disease was found in Wuhan, Hubei Province, China, and the pathogen was identified as novel COVID-19 in January 2020.² In January 2020, the WHO Director-General declared the novel

Strengths and limitations of this study

- Our accurate assessment may provide a new complementary therapy for COVID-19 rehabilitation that is derived from traditional Chinese mind-body exercises.
- The effectiveness and safety of tai chi and/or qigong on recovery after COVID-19 will be evaluated in this article. Also, the effects of different interventions on recovery from COVID-19 can be evaluated by subgroup analysis.
- It is not clear to us whether all patients had better adherence and whether there were uncontrolled or unmeasured confounding factors that could have biased the results.
- It is also unclear to us whether all studies differentiated between populations (age, sex, region), which may have produced selection bias.
- The time since the onset of acute COVID-19 and the clinical history of patients (ie, use of mechanical ventilation, sedation, etc) may be other potential sources of bias or variation among studies.

coronavirus outbreak a Public Health Emergency of International Concern, which was the highest level of alert.^{3 4} COVID-19 is a life-threatening infectious disease caused by SARS-CoV-2, whose clinical manifestations include fever, cough, dyspnoea, haemoptysis, headache, myalgia, diarrhoea, fatigue and decreased sense of smell.⁵ It affects not only the respiratory system but also the cardiovascular, renal, gastrointestinal, endocrine, neurological and musculoskeletal systems,⁶ and the elderly, obese individuals, and those with heart disease, immune-suppression, and pre-existing respiratory problems are more likely to develop severe forms of this disease.⁷ It is highly infectious and has a high mortality rate.8 The total number of confirmed COVID-19 cases worldwide as of 30 October 2021 is 245 373 039, including 4979 421 deaths.





Studies have demonstrated that physical activity is one of the important ways of rehabilitation for patients with COVID-19. Physical exercise can enhance physical fitness (including lung function and cardiovascular function) and improve the immune system's ability to defend against COVID-19. 11 12 Sun et al 13 pointed out that pulmonary rehabilitation could not only reduce inflammatory indicators such as neutrophil percentage, C reactive protein (CRP) and procalcitonin in patients with COVID-19, but also improve cough and dyspnoea symptoms, and improve the quality of life and psychological status of patients.

Tai chi and qigong are physical and mental exercises with a Chinese history of several thousand years. ^{14 15} The practice of tai chi and qigong can improve pulmonary function, relieve symptoms such as dyspnoea and cough, regulate the function of the body's immune system and inflammatory marker response, improve quality of life and psychological well-being, reduce anxiety and depression, and shorten the length of hospital stay in patients with COVID-19. ^{10 16–18} Therefore, our aim is to conduct a meta-analysis to study the effects of tai chi and/or qigong on COVID-19, to provide an assessment of its safety and efficacy, and to provide a clinical treatment method and evidence for the rehabilitation of patients with COVID-19.

MATERIALS AND METHODS

This protocol was registered at PROSPERO with the registration number CRD42021288962, and was written based on the guideline of the Preferred Reporting Items for Systematic Reviews and Meta-analyses Protocol. ¹⁹

Criteria for included studies

Types of studies

Only published randomised controlled trials (RCTs) investigating the effect of tai chi and/or qigong on COVID-19 will be included in the full review. There are no restrictions on language or publication status. Relevant non-randomised controls, reviews and individual cases will be excluded.

Types of participants

Patients who were diagnosed with COVID-19 will be included. In addition, there are no restrictions on gender, age or nationality.

Types of intervention

The experimental group practised tai chi and/or qigong as an intervention, while the control group did not limit the intervention. Control interventions will include: no treatment, placebo and other interventions (eg, herbal medicine, acupuncture, massage, cupping therapy, western medicine).

Types of outcomes Primary outcomes

1. One-second forced expiratory volume and 1-second forced vital capacity.

- 2. Blood oxygen saturation and total white cell count.
- 3. 3.scores on quality of life using validated instruments such as SF-36, NHP, WHO QOS scale (WHOQOL-100) and QOS index (QL).

Secondary outcomes

- 1. The time of when main symptoms (including fever, asthenia, cough disappearance rate and temperature recovery time) disappear.
- 2. Negative COVID-19 result rates on two consecutive occasions (not on the same day).
- 3. CT image improvement.
- 4. Average hospitalisation time, occurrence rate of common type to severe form, clinical cure rate and mortality.
- 5. Safety from the incidence of adverse events (bleeding, pain, haematoma, syncope, etc).

Information sources and search strategy

We will carry out a literature search in Cochrane Library, Web of Science, PubMed, Embase, China Biomedical Literature Database, China Knowledge Network, China Science and Technology Journal Database and Wanfang Database. The time period is from the inception of the database to November 2021, with no language restrictions. The search will be performed using the subject terms plus free-text words; Chinese searches will use the Chinese translation of the search terms. The suggested search syntax on PubMed is summarised in table 1.

Search strategy

Electronic searches

The literature search and screening will be performed independently by two authors (JLG and LA). First, duplicate literature will be excluded and an initial screening will be performed based on the title and abstract. Then, the literature that meets the criteria is screened by reading the full text. If there is disagreement, it should be discussed or submitted to a third person (XL) for evaluation. The EndNote software is used for literature management and the reasons for exclusion should be recorded in the excluded studies. Figure 1 illustrates the literature screening process used in this study.

Data extraction and management

Two authors (ZCZ and SL) will independently generate a table to complete the data extraction. The data extraction table includes the name of the first author, year of publication, follow-up, sample size, interventions, outcomes, allocation concealment, randomisation, selective reporting, blinding, completeness of outcome data and subject characteristics (age, sex, duration of disease and literacy). If the results of data extraction differed, they will be discussed or submitted to a third person (XL) for adjudication. If the required data are lacking, the authors of the article would be contacted to obtain relevant information; and if data are still not available, studies with missing data would be excluded.



Table 1	PubMed example of literature search strategy
Search number	Query
#1	"Qigong" [Mesh]
#2	Qigong [tiab] OR Ch'i Kung [tiab]
#3	#1 0R #2
#4	"Tai Ji"[Mesh]
#5	Tai-ji [tiab] OR Tai Chi [tiab] OR Chi, Tai [tiab] OR Tai Ji Quan [tiab] OR Ji Quan, Tai [tiab] OR Quan, Tai Ji [tiab] OR Taiji [tiab] OR Taijiquan [tiab] OR T'ai Chi [tiab] OR Tai Chi Chuan [tiab]
#6	#4 OR #5
#7	#3 OR #6
#8	"COVID 19"[Mesh]
#9	COVID Virus Disease [tiab]OR COVID 19 Virus Disease [tiab] OR COVID Virus Diseases [tiab] OR Disease, COVID Virus OR Virus Disease, COVID [tiab] OR COVID Virus Infection [tiab] OR COVID 19 Virus Infection [tiab] OR Infection, COVID Virus Infection, COVID [tiab] OR 2019-nCoV Infection [tiab] OR 2019-nCoV Infection [tiab] OR 2019-nCoV Infection [tiab] OR Coronavirus Disease-19 [tiab] OR Coronavirus Disease 19 [tiab] OR 2019 Novel Coronavirus Disease [tiab] OR 2019-nCoV Disease [tiab] OR 2019-nCoV Disease [tiab] OR 2019-nCoV Disease [tiab] OR 2019-nCoV Disease [tiab] OR Disease, 2019-nCoV [tiab] OR COVID [tiab] OR Coronavirus Disease 2019 [tiab] OR Disease 2019, Coronavirus [tiab] OR SARS Coronavirus 2 Infection [tiab] OR SARS-CoV-2 Infection [tiab] OR COVID Pandemic [tiab] OR COVID 19 Pandemic [tiab] OR COVID Pandemics [tiab] OR Pandemic [tiab] OR COVID [tiab]
#10	#8 OR #9
#11	#7 AND #10

Assessment of risk of bias in included studies

Two authors (JLG and LA) will assess the quality of the included studies using the assessment tools described in the Cochrane Handbook for Systematic Reviews of Interventions.²⁰ All studies will be assessed as low, unclear or high risk of bias in the following six areas:

1. Machine allocation method.

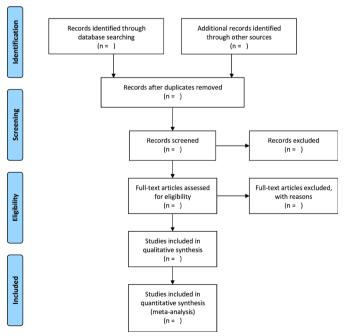


Figure 1 Flow chart of the systematic review.

- 2. Allocation protocol concealment.
- 3. Blinding of study subjects, treatment protocol implementers and study outcome measures.
- 4. Incomplete outcome data.
- 5. Selective reporting of study results.
- 6. 'Other' issues.

If there is a disagreement, they will discuss it or refer it to a third party (XL).

Data analysis and synthesis

Data analysis will be performed using the Review Manager V.5.3 software provided by Cochrane Collaboration (www. cochrane.org). The Q-test and I^2 statistic will be used to assess the heterogeneity of the included studies. The relative risk will be used to analyse dichotomous risk. The fixed-effects model will be used to combine the data if the statistical heterogeneity is low (p \geq 0.1 and $I^2\leq$ 25%), or a random-effects model will be used if the statistical heterogeneity is high (p<0.1 and $I^2>$ 50%). The mean difference (MD) with 95% CI will be used for the continuous variables, and standardised MD and 95% CI will be used for the continuous variables if the units are different.

Subgroup analysis

If the included studies show obvious clinical heterogeneity, subgroup analysis will be conducted according to clinical characteristics. In this study, we will conduct subgroup analysis according to the gender and age of patients, country, type of tai chi or qigong, and so on.



Sensitivity analysis

This study will carry out sensitivity analysis by changing the effect indicators and statistical model, and deleting each included study one by one to verify the stability of the study results. If different conclusions are reached, the results of the meta-analysis are carefully obtained by discussion between the two authors (ZZ and JGR) or by evaluation by a third person (XL).

Assessment of reporting biases

If more than 10 articles are included,²² the presence of reporting bias can be assessed by the symmetry of the funnel plot.

Patient and public involvement

Patients or members of the public were not involved in the design of this study.

Ethics and dissemination

Ethical approval and consent are unnecessary because no primary data will be collected. The results will be disseminated through peer-reviewed publications.

DISCUSSION

COVID-19 is characterised by rapid and widespread transmission, high mortality and complications, 23-25 which seriously threatens the public's physical and mental health.²⁶ Indu *et al*²⁷ showed that married women during COVID-19 epidemic and confinement may be prone to depression, anxiety and stress, and even serious domestic violence. A total of 49650 patients from 21 studies were pooled and analysed, ²⁸ indicating that the combined prevalence rates of post-traumatic stress disorder, depression and anxiety in COVID-19 survivors were 18%, 12%, and 17%, respectively, and that the prevalence of major depression and anxiety was higher. COVID-19 survivors' social functioning, role physical and role emotional health domains all decreased. Also, COVID-19 frontline healthcare workers were prone to stress, anxiety and depression. In Jordan, a survey of 225 young female healthcare workers found that 46.2% of them had low levels of stress, 53.8% had high levels of stress, 52.9% reported high levels of anxiety and 66.2% had high levels of depression.²⁹ In India, out of 315 healthcare workers, 28.5% felt moderate to severe depression, 31% felt anxiety and 18.4% felt stress.³⁰ Among patients who recovered from COVID-19, some remain severely impaired physically and psychologically,³¹ and face reduced quality of life, anxiety, insomnia, depression and difficulty recovering in the short term.^{32–34}

Exercise training is helpful in the rehabilitation of patients with COVID-19. Tai chi and qigong can be helpful in the recovery of patients with COVID-19. It is found that tai ${\rm chi}^{16}$ can reduce inflammatory indicators such as TNF- α , interleukin 6 and CRP, which can be used as an adjuvant therapy for COVID-19. It is also found that there was significant improvement in respiratory muscle strength and function in 33 patients recovering

from COVID-19 after 4 weeks of intervention using traditional Chinese qigong 'Liuzijue'. ¹⁰ The mean increase in maximal inspiratory pressure was 13.46 ± 20.06 cmH₂O (p<0.001), the mean increase in peak inspiratory flow was 0.74 ± 0.58 L/s (p<0.001) and the mean increase in diaphragm movement in deep breathing was 0.57 ± 1.18 ; and it also improves the patient's quality of life, restores physical function, and reduces anxiety and depression symptoms. Therefore, we will evaluate the efficacy and safety of tai chi and/or qigong on rehabilitation after COVID-19.

This study consisted of several aspects: first, the search strategy and inclusion and exclusion criteria are determined; then, all eligible RCTs are screened; immediately after, data extraction, data analysis and processing, and analysis by heterogeneity test, subgroup analysis, and sensitivity analysis are performed; finally, conclusions are obtained from the analysis.

However, there are limitations to this study. It is not clear to us whether all patients had better adherence and whether there were uncontrolled or unmeasured confounding factors that could have biased the results. It is also unclear to us whether all studies differentiated between populations (age, sex, region), which may have produced selection bias. The time since acute COVID-19 onset and the clinical history of these patients (ie, use of mechanical ventilation, sedation, etc) are other potential sources of bias or variation among studies. The results of this meta-analysis may be affected if studies did not include a sufficient number of high-quality RCTs.

CONCLUSION

This systematic review will assess and summarise the efficacy and safety of tai chi and/or qigong on rehabilitation after COVID-19, and the effect of different interventions on the rehabilitation of patients with COVID-19 could also be assessed by subgroup analysis. What is more, our accurate assessment may provide a new complementary therapy for the rehabilitation of patients with COVID-19, which is derived from the Chinese tradition of mind-body exercises.

Contributors ZZ and JGR contributed equally to this study. ZZ conceived the study and developed the first framework of the manuscript. ZZ and JGR drafted the manuscript, and JLG and LA were involved in the development of the search strategy. ZCZ and SL will read the full text of the study and extract the data and perform data synthesis. YC and HL assessed the quality of the included studies. If there is any disagreement, XL will arbitrate. The manuscript was revised by XL. All the authors read and approved the final manuscript.

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Competing interests None declared.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Patient consent for publication Not required.

Provenance and peer review Not commissioned; externally peer reviewed.

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ORCID iD

Zhe Zhang http://orcid.org/0000-0002-1852-2822

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