Efficacy of Dao Yin in patients with 2019 novel coronavirus pneumonia: study protocol for a randomized controlled trial

Shuaipan Zhang
Yue yang Hosipital of Interate Medicine Shanghai University of Traditional Chinese Medicine
Zhizhen Lv
Shanghai University of Traditional Chinese Medicine
Qingguang Zhu (zhuqingguang@162.com)
Inisitute of Tuina,Shanghai University of Traditional Chinese Medicine
Wuquan Sun
Shanghai University of Traditional Chinese Medicine Yueyang Hospital of Integrated Traditional Chinese Medicine and Western Medicine Department of Tuina
Fei Yao
Shanghai University of Traditional Chinese Medicine
Lei Fang
Shanghai University of Traditional Chinese Medicine
Lingjun Kong
Institute of Tuina,Shanghai institute of Tradition Chinese Medicine
Yanbin Cheng
Insitute of Tuina ,Shanghai Univerity of traditional Chinese Medicine
Zhiwei Wu
Shanghai University of Traditional Chinese Medicine Yueyang Hospital of Integrated Traditional Chinese Medicine and Western Medicine Department of Tui
Min Fang (fangmin19650510@163.com)
Institute of Tuina,Shanghai Institute of Traditional Chinese Medicine,Shanghhai 200437,China;Shanghai University of Traditional Chinese Medicine,Shanghai201203China

---

Study protocol

Keywords: 2019-nCoV pneumonia, Dao Yin, Conventional therapy, Randomized controlled trial

Posted Date: March 4th, 2020

DOI: https://doi.org/10.21203/rs.3.rs-15947/v1

Abstract

Background The epidemic of 2019 novel coronavirus (2019-nCoV) pneumonia has become a focused public health event in world. The authorities have taken prompt medical action in China, which contained strict isolation measures and potential symptomatic supportive care. Dao Yin, a traditional Chinese exercise, combines limb movements and breathing exercises. Previous researches showed that it can activate the immune system and improve the lung function and the mental state of patients. Therefore, there may be a potential effect of Dao Yin on the physical and mental health of patients with 2019-nCoV. The aim of this trail is to verify whether conventional therapy plus Dao Yin could show better effects for 2019-nCoV than conventional therapy alone.

Methods/design The study is a multicenter randomized controlled trial with parallel-group design including two intervention groups: a conventional therapy group and a conventional therapy plus Dao Yin group. A total of 186 eligible participants will be randomly assigned to the groups in a 1:1 ratio. The routine treatment of the two groups is performed daily according to guideline, and Dao Yin is performed once a day until the patient is out of the hospital. The primary outcome is the Length of Hospital Stay (LHS). Secondary outcomes include the vital signs, respiratory symptoms, questionnaire of mental health and the quantity of immune cells. The outcomes will be assessed at five points including the baseline, 3th, 6th, 9th day during hospitalization and the discharge day. The significance level is 5%. This study will focus on the value of a conventional therapy plus Dao Yin as the treatment for 2019-nCoV and will explore any potential connection among the outcomes.

Discussion This study may evaluate the efficacy of conventional therapy plus Dao Yin for 2019-nCoV, which can contribute to provide a solid evidence of Dao Yin therapy for the nationwide emergence.

Trial registration: Chinese Clinical Trial Registry, ChiCTR2000029978 Registered on 18 February 2020.

Background

Early in December 2019, an unknown acute respiratory disease appeared in Wuhan city, Hubei province, China[1]. A new coronavirus was isolated by high-throughput sequencing, and was currently named 2019 novel coronavirus (2019-nCoV)—infected pneumonia [2]. The World Health Organization (WHO) defines this pneumonia as an international emergency. A study has further demonstrated human-to-human reliability, with infectious diseases with a low median incubation period of 3 days and relatively low relative mortality[3, 4]. The clinical symptoms of the disease are not specific. Fever and cough are common symptoms. The chest computed tomography (CT) showed multiple ground glass shadows, which could further develop into hypoxia, causing shock, sepsis, and even death. Diagnosis is based on the provisional guidelines of WHO [5, 6]. As of February 14, 2020, the number of confirmed diagnoses nationwide has reached 63836, the number of deaths was 1,381, and the number of suspected case was 10109[7]. People without good immunity are susceptible to the infection and mentality has been severely affected, especially among patients and medical staff in Wuhan[8]. As far, there is still no specific drug for

coronavirus while only systematic symptomatic supportive treatment can be given.[9] Some measures like reducing travel aggregation and strengthening the aseptic concept has been performed to lower the risk of further disease transmission. In addition, isolation and supportive care are particularly important for the early diagnosis of affected patients[10]. Except for the basis of conventional treatment, attention should be paid to mental health and immune function. Exercise training is an important part of pulmonary rehabilitation and has been shown to improve dyspnea and health status and reduce medical expenses 11. Dao Yin, a low-risk traditional Chinese exercise, which is widely used to prevent heart and lung disease. It can be performed regardless of previous sports experience and age. At the same time, Dao Yin does not require expensive equipment, and can be practiced individually or in groups12, which is suitable for home practicing. It includes a series of physical and mental activities including Ba Duan Jin, Yi Jin Jing, Tai Chi, Wu Qin Xi, and Liu Zi Jue. Previous studies showed that traditional Chinese exercises have been widely used in clinical practice, which can promote mental and physical health, such as improving cardiopulmonary function, reducing high-risk factors for heart and cerebrovascular diseases, enhancing immune function to fight viruses[13-16]. Therefore, a randomized controlled clinical trial is being carried out to compare the clinical efficacy of the conventional therapy compared with conventional therapy plus Dao Yin. To explore the changes in respiratory function, immune function, and mental health of patients with 2019-nCoV after Dao Yin interventions and to analysis the potential correlation of these outcomes.

Methods/design

Study design

This is a multicenter randomized controlled trial with two parallel arms. Recruiting patients will be carried out in Hubei Hospital of Traditional Chinese Medicine and Huangshi Hospital of Traditional Chinese Medicine. Data management and statistics will be conducted in the Department of Yue yang Hospital of Integrated Traditional Chinese and Western Medicine, Shanghai University of Traditional Chinese Medicine. Due to the limitations of intervention methods, only the outcome assessors and statisticians are blinded. It is planned to recruit 186 patients and randomly assign them to the conventional treatment group and the conventional treatment plus Dao Yin group at a 1: 1 ratio. Dao Yin intervention is conducted once a day lasting from admission to cure discharge. The assessor, who was masked to the group assignment, will perform evaluation and analysis of outcome at five points (before treatment, 3rd, 6th, 9th day during hospitalization and the discharge day). All patients are provided with informed consent at the time of recruitment, and the trial protocol was approved by the Ethics Committee of Yue yang Hospital of Integrated Traditional Chinese and Western Medicine (item number:2020-002). The study was registered with the China Clinical Trial Registry (ChiCTR2000029978). The trial flow chart and research design are shown in Figure 1 and Figure 2 respectively.

Participants recruitment

The trial will recruit clinical patients with mild and general symptom. The participants will be diagnosed by the criteria of the "Novel Coronavirus–infected Pneumonia (2019-nCoV) Diagnosis and Treatment Scheme (Trial Fifth Version)" issued by the National Health Commission of China on February 4, 2020[17]. Participants are recruited from inpatients of the Department of Infectious Diseases of the two hospital in Hubei Province. All participants were between 18 and 60 years of age, with no difference in median age between the two groups.

Inclusion criteria

(1) The age of patients is between 18 and 60, and is not limited to male or female; (2) Patients diagnosed with mild pneumonia (slight clinical symptoms, no pneumonia manifestations on imaging), general pneumonia patients (with fever, respiratory tract symptoms, etc., imaging showed pneumonia but no multiple organ damage)[17] (3) Hospitalized patients; (4) Volunteer to join the trial and sign the "informed consent”. (5) Promise not to perform other exercise activities.

Exclusion criteria

One of the following conditions cannot be included in this test. (1) patients with severe diseases such as cardiovascular, cerebrovascular, hematopoietic, digestive system or mental illness; (2)pregnant and lactating women; (3) respiratory frequency> 30 times /min, showing respiratory failure; (4) complicated with other organ failure requires treatment by respiratory intensive care unit (ICU); (5) those who do not want to join the trial.

Drop out and suspension criteria

During the intervention period, patients have the right to withdraw for any reason in accordance with the Patient Management and Protection Regulations. One of the following conditions is considered the withdrawal criteria: (1) the patient did not implement the treatment plan as planned; (2) participated in other exercise programs during the trial; (3) case data are incomplete and affect the judgement of curative effect; (4) unbearable adverse events; (5) patients voluntarily withdrew on their own. It is worth noting that the trial will be immediately terminated with poor clinical efficacy or severe adverse events such as respiratory failure, severe acid-base balance disorders, sepsis and even shock.

Randomization

Clinical researchers will get a random sequence number which is automatically generated by a random number generator (SPSS21.0, SPSS Inc., Chicago, Illinois, USA), and sequentially number them in an opaque envelope. Researchers will open random allocation envelopes and assign participants accordingly. Eligible patients will be randomly divided into a conventional treatment group and a conventional treatment plus exercise training group, with 93 patients in each group.

Blinding

Participants and Dao Yin trainers are unable to be blind about group assignments due to the specific intervention, but the trainers will not know the assessment of outcomes. To reduce the risk of bias, evaluators, data managers, and statisticians were unaware of group assignments in the outcome evaluation process and data analysis.

Interventions

Both groups of participants will receive routine treatment. Based on this, the experimental group will perform Dao Yin once a day until the discharge day. The daily routine treatment plan must be recorded in the electronic medical record by the doctor's system. In order to avoid cross-infection and ensure the identity of the training content, the training method will be presented to the subjects in text and video, including exercise action essentials, time, intensity, and precautions. It should be emphasized that during the test, other exercise rehabilitation methods, including aerobic exercise, stretching exercise, yoga and other sports therapy will be prohibited. If the subject receives any other exercise regimen, the changes should be recorded on the Clinical Report Form (CRF) each time.

Conventional treatment group

For patients with mild and common pneumonia, doctors strictly follow the general treatment plan "Novel Coronavirus-infected Pneumonia Diagnosis and Treatment Scheme (Trial Fifth Version)" for symptomatic supportive treatment. It mainly includes (1) rest in bed, strengthen supportive treatment to ensure sufficient heat; pay attention to water and electrolyte balance to maintain internal environment stability; closely monitor vital signs, oxygen saturation, etc. ; (2) monitor blood routine, urine routine, liver based on the condition function, renal function, myocardial enzymes, coagulation function, chest imaging, etc. ;(3) timely effective oxygen therapy measures, including nasal catheter, mask oxygen and trans nasal high-flow oxygen therapy. (4) antiviral therapy, although no effective antiviral therapy has been confirmed. α-interferon atomized inhalation is suggested to use (5 million U each time for adults, add 2ml of sterilized water for injection, 2 times a day) (5) antibiotic treatment will be given if a bacterial infection is confirmed diagnosis. (6) accurate Chinese medicine treatment.

Conventional treatment plus Dao Yin group

The selection of the movements is based on the methodology of the Delphi Expert Questionnaire, which focused on the syndrome differentiation of traditional Chinese medicine on 2019-nCoV and the benefits of Dao Yin on physical and mental health. Finally, seven chapters of exercise training was formed, in which participants may perform systematic self-learning of exercises for half of the day. Patients will be given written materials and video materials about Dao Yin movements including action details. Researchers will start a remote video conference to monitor and correct the exercises throughout the whole trail process. When officially begin, patients will perform Dao Yin every day at 9 am, which mainly includes 2 minutes of warm-up exercise, 8 minutes of traditional exercise combined with breathing and stretching, and 2 minutes of cool down. Exercise training will be performed until patients discharged. The 7 steps detailed movement is shown in Figure 3. The study showed that certain exercise intensity can

reach patient benefit goals[18]. Exercise intensity is adjusted gradually according to the patient's cardiopulmonary exercise function, from very low intensity (Heart Rate (HR)during exercise <57% or HR rise <30% Heart Rate rise (HRr) or Rating of Perceived Exertion (RPE)<9/20) → low intensity (HR during exercise 57-63% HR_{max} Or HRr 30-39% or RPE: 9-11/20) → moderate intensity (HR during exercise 64-76% HRmax or HRr 40-59% or RPE: 12-14/20).

Outcome measurements

All outcome will be managed by researchers masked to the group assignment, which include five points (before treatment, 3rd, 6th, 9th day during hospitalization and the discharge day) Outcomes included the patient's general vital signs, length of hospital stays, evaluation of dyspnea degree, mental health and immune cells.

Primary outcome measurement

Length of Hospital Stay (LHS)

The key to treating pneumonia is to access if it can shorten the hospitalization time and reach the discharge standard. So, we treat length of hospital stays as the primary outcome.

Secondary outcome measurement

1. Vital signs[19]

Blood pressure, heart rate, respiration, and blood oxygen saturation will be monitored three times a day by the nurse and then an average data will be obtained.

2. Mental health

The Motivation Assessment Scale (MAS)[20] and Self Rating Depression Scale (SDS) [21]will be used to assess the psychological condition of patients during illness. MAS comprises 16 questions that are rated on a seven-point Likert scale ranging from 0 (never) to 6 (always). Items load onto one of four categories of reinforcement: sensory, escape, attention and tangible. SDS is based on factor analytic studies of depression symptoms, which involve psychological and physical symptoms and are scored by users on a 4-point scale based on their use over the past week, ranging from 1 (no time or very little time) to 4 (most or all time).

3. Respiratory symptoms questionnaire

By quantifying dyspnea, the doctor can assess its severity and its impact on a person’s functional health status. Patients with dyspnea a will be evaluated through some functional questionnaires. Perceived breathlessness on daily activities was measured by means of the Medical Research Council (MRC) breathlessness/dyspnea scale [22]and Modified Borg scale (MBS)[23] that had the potential to provide quick,

easy, and rapid information about a patient's subjective state of dyspnea. The original MRC dyspnea scale contains five grades (from 1 to 5) of dyspnea description that are more easily self-administered by the participants. A commonly used format of MBS is a 10-point scale with a non-linear scaling scheme using descriptive terms to anchor responses.

4. Main elements of the immune system

Under the effect of exercise stress, T lymphocytes will be redistributed in large quantities in lymphoid and non-lymphoid organs. These stress-induced immune profiles will increase immune surveillance and vigilances[24]. T-cell and Natural Killer cell will be detected in peripheral blood with the Flow cytometry[25]method to gain more insights into the underlying connection between exercise and immune respond.

Safety evaluation

The doctors should focus on the vital signs of patients with 2019-nCoV strictly to decrease the incidence of adverse events, which is refer to the unexpected responses that occur during or after treatment. Record and analyze them whether the adverse events are related to the treatment. If a serious adverse reaction occurs, the researchers should immediately take appropriate medical measures according to the situation. Liver function and renal function tests and lung CT imaging tests also need to be monitored.

Data collecting and monitoring

During the recruitment phase, screeners will collect demographics of the participants. The data assessor will record the baseline characteristics of the patient, the length of hospital stays, general vital signs, the questionnaire to evaluate respiratory function and psychological status, and the levels of immune cells through a CRF. Next, two third-party personnel who have received strict data management training will receive data in the form of an excel database, and then they will enter the real-time data into the China Clinical Trial Registration Center. This electronic data management system will be used in the Ministry of Science and Technology of Yue yang Hospital of Integrated Traditional Chinese and Western Medicine to collect and monitor test data in real time.

Statistical analyses

Statisticians will use SPSS Windows version 21.0 software to perform the data analysis within group and between groups. Data will be expressed as mean ± standard deviation. The data between groups will be compared by Student's t test when the continuous variables can meet a normal distribution or T distribution. Otherwise, Mann–Whitney test or Wilcoxon test will be used. For categorical data, the Fisher's exact or the Chi-square test will be adopted. We will conduct an intention-to-treat analysis if participants are lost to follow-up and perform a simple correlation analysis or simple regression analysis to determine the potential correlation between the outcome measurements. Adverse events in each group

will be documented as percentage (%) for safety assessments using the chi-square test or Fisher's exact test. All statistical analyses will be conducted in a two-sided manner, with a significance level of 5%.

Sample size calculation

The trial takes the LHS as the primary efficacy outcome. With reference to the latest literature[3], it is assumed that the average length of stay in the control group of this study is 10 days, the standard deviation is 3 days, and the average length of stay in the treatment group is 8.5 days, $\alpha = 0.05$, $\beta = 0.10$. Considering the 10% drooping rate, it was calculated that 93 subjects were needed in each group, and a total of 186 cases were required to be recruited.

Quality control

Professional trial methodology should be trained before the researchers participate in the trial which can ensure the consistency of methods. Quality control will be conducted during the processing of the trail under the management of the steering committee. Supervisors will review the quality control of the trials via remote video surveillance, frequency is once every 2 weeks and recorded. Anything modification in the study protocol happen will inform the steering committee and ethics committee.

Discussion

The epidemic of 2019-nCoV has become a worldwide public health problem[26]. Although prompt emergency measures have been taken, the number of people with the disease has been increasing since the onset of the disease in China. Data from a clinical epidemic model showed that the reproduction number (R_0) has reached 2.68[27]. The current effective measures are to strictly control the spread of the disease throughout the country, mainly including limiting the occurrence of normal people, isolating suspected populations, and actively treating the diseased population. Only symptomatic supportive treatment can be used to reduce complications and prevent disease progression due to the shortage of antiviral drugs. The aged with a weak immune system show a worse prognosis and the sudden medical burden has caused a great psychological problem on patients and the medical workers[28]. Therefore, mental health and autoimmunity should be focused on, which may play an antiviral role at early stage. Dao Yin, as part of traditional Chinese medicine, has been proven in many ways to significantly improve lung function and physical and mental health, and is closely related to the human immune system [29-31]. The Yellow Emperor's Canon of Internal Medicine states that " a body full with healthy Qi energy will let the evil Qi energy go away ". Dao Yin can increase the body's ability to resist external evil through activities. Dao Yin breathing improve chest movement and lung ventilation as well as improve overall health by improving diaphragm muscle movement, which is the most important breathing muscles in the body. It is suitable for frail patients and seniors in the hospital status with the characterization of slow motion and respiration and relaxation. By training in body posture and movement, regulating breathing patterns and maintaining mental calmness, a variety of natural self-regulation and self-repair mechanisms in body can be activate to stimulate the balanced release of endogenous neurohormones[32].

However, further clinical evidence is needed for the specific clinical effectiveness of the newly edited Dao Yin. This protocol is suit to the research methodology of evidence-based medicine to ensure the reliability of clinical trials maximally. It is used to verify the clinical effectiveness of Dao Yin for the recovery of patients with 2019-nCoV. The role of immune cells, and the physical and mental health of the body. Patients' immune response, improvement of shortness of breath symptoms and mental health are also concerned.

Study Limitations

There is an inevitable limitation that it is difficult to control the methodology of blinding during the physical intervention. In this study, Dao Yin as a physical therapy is impossible to be blind for the participants and therapist. We have not conducted a comparison of efficacy between two different exercises.

Trial Status

This protocol is version 2.0 February 16, 2020. The participants will be recruited from February 24, 2020 to May 31, 2020. But no one will be enrolled until this paper is submitted. This trial was registered in Chinese Clinical Trial Registry on 18 February 2019. The registration number is ChiCTR2000029978.

Abbreviations

Clinical Report Form: CRF; Heart Rate: HR; Motivation Assessment Scale: MAS; Medical Research Council: MRC; Modified Borg scale: MBS; 2019 Novel Coronavirus: 2019-nCoV; Self-Rating Depression Scale: SDS; World Health Organization: WHO.

Declarations

Acknowledgements

We sincerely thank the clinicians at the two research centers in Hubei for their dedication to patients.

Funding

This study is supported financially by the project of Emergency scientific research project for prevention and control of new coronavirus (2019-nCoV) by Shanghai University of Traditional Chinese Medicine (first batch)（No fund number）, Shanghai Further accelerate the three-year action plan for the development of Chinese medicine (ZY (2018-2020)-CCCX-2004-02), Shanghai Health and Family Planning Commission Chinese Medicine Research Project (2018LP040), Shanghai Health and Family Planning System Outstanding Young Medical Talents (2018YQ004), China Association of Chinese Medicine Youth Enrollment Talent Project (QNRC2-A01). The funders had no role in the design of the study, analysis, collection, and interpretation of the data, or the writing and decision for publication of the manuscript.

Availability of data and material

The datasets analyzed during the current study are available from the corresponding author on reasonable request.

Authors' contributions

SZ planned the study protocol and drafted the manuscript. ZL planned the study protocol and participated in the critical revision of the manuscript. QZ, carried out the Dao Yin movements for patients. MF managed the study. WS was the study coordinator, responsible for generating and distributing the random numbers. FY participated in designing the outcome measurements and assessing the outcomes. LF participated in designing the trial and helped to prepare the manuscript. LK participated in designing the trial and helped to prepare the manuscript. YC participated in writing the manuscript. ZW participated in the remote intervention supervision. All the authors have read and approved the final manuscript.

Ethics approval and consent to participate

Ethics approval was requested and granted by the ethics committee of Yue yang Hospital of Integrated Traditional Chinese and Western Medicine (item number :2020-002). Informed consent will be obtained from all study participants before starting any data collection by the clinical trial communicator. All participants will provide their consent in writing. Nobody except the investigators have access to the final data.

Consent for publication

It is "not applicable" in this section as no personal information is provided in this manuscript.

Competing interests

The authors declare that they have no competing interests.

Author details

1 Tuina Department, Yueyang Hospital of Integrated Traditional Chinese and Western Medicine, Shanghai University of Traditional Chinese Medicine, Shanghai 200437, China.2 Institute of Tuina, Shanghai Institute of Traditional Chinese Medicine, Shanghai 200437, China. 3. Shanghai University of Traditional Chinese Medicine, Shanghai 200437, China.

References

1. Huang C, Wang Y, Li X, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *Lancet (London, England).* 2020:S140-S6736.
2. Lu R, Zhao X, Li J, et al. Genomic characterisation and epidemiology of 2019 novel coronavirus: implications for virus origins and receptor binding. *Lancet (London, England).* 2020:S140-S6736.

3. Guan WZNN. Clinical characteristics of 2019 novel coronavirus infection in China. *medRxiv.* 2020.
4. Phan LT, Nguyen TV, Luong QC, et al. Importation and Human-to-Human Transmission of a Novel Coronavirus in Vietnam. *The New England journal of medicine.* 2020:10-1056.
5. Jin Y, Cai L, Cheng Z, et al. A rapid advice guideline for the diagnosis and treatment of 2019 novel coronavirus (2019-nCoV) infected pneumonia (standard version). *Military Medical Research.* 2020;7(1):4.
6. Minodier L, Charrel RN, Ceccaldi P, et al. Prevalence of gastrointestinal symptoms in patients with influenza, clinical significance, and pathophysiology of human influenza viruses in faecal samples: what do we know? *Virol J.* 2015;12:215.
7. National Health Commission of the People's Republic of China. http://www.nhc.gov.cn. Vol (Assess on February 14th 2020).
8. Xiang Y, Yang Y, Li W, et al. Timely mental health care for the 2019 novel coronavirus outbreak is urgently needed. *The Lancet Psychiatry.* 2020.
9. de Wit E, van Doremalen N, Falzarano D, Munster VJ. SARS and MERS: recent insights into emerging coronaviruses. *Nature reviews. Microbiology.* 2016;14(8):523-534.
10. Hui DS, I Azhar E, Madani TA, et al. The continuing 2019-nCoV epidemic threat of novel coronaviruses to global health — The latest 2019 novel coronavirus outbreak in Wuhan, China. *Int J Infect Dis.* 2020;91:264-266.
11. Divo M, Pinto-Plata V. Role of exercise in testing and in therapy of COPD. *The Medical clinics of North America.* 2012;96(4):753-766.
12. Yeh GY, Wang C, Wayne PM, Phillips R. Tai chi exercise for patients with cardiovascular conditions and risk factors: A SYSTEMATIC REVIEW. *J Cardiopulm Rehabil Prev.* 2009;29(3):152-160.
13. Zou L, Pan Z, Yeung A, et al. A Review Study on the Beneficial Effects of Baduanjin. *Journal of alternative and complementary medicine (New York, N.Y.).* 2018;24(4):324-335.
14. Wang C, Ng S, Ho RTH, Ziea ETC, Wong VCW, Chan CLW. The effect of qigong exercise on immunity and infections: a systematic review of controlled trials. *The American journal of Chinese medicine.* 2012;40(6):1143-1156.
15. Wu W, Liu X, Liu J, Li P, Wang Z. Effectiveness of water-based Liuzijue exercise on respiratory muscle strength and peripheral skeletal muscle function in patients with COPD. *Int J Chronic Obstr.* 2018;13:1713-1726.
16. Xiong X, Wang P, Li S, Zhang Y, Li X. Effect of Baduanjin exercise for hypertension: a systematic review and meta-analysis of randomized controlled trials. *Maturitas.* 2015;80(4):370-378.
17. Diagnosis and treatment of pneumonitis with a novel coronavirus infection (trial version 5). China Journal of Integrated Traditional Chinese and Western Medicine.
18. Galloza J, Castillo B, Micheo W. Benefits of Exercise in the Older Population. *Phys Med Reh Clin N.* 2017;28(4):659-669.

19. Mok WQ, Wang W, Liaw SY. Vital signs monitoring to detect patient deterioration: An integrative literature review. *Int J Nurs Pract.* 2015;21 Suppl 2:91-98.
20. Koritsas S, Iacono T. Psychometric comparison of the Motivation Assessment Scale (MAS) and the Questions About Behavioral Function (QABF). *Journal of intellectual disability research : JIDR.* 2013;57(8):747-757.
21. ZUNG WW. A SELF-RATING DEPRESSION SCALE. *Archives of general psychiatry.* 1965;12:63-70.
22. Williams N. The MRC breathlessness scale. *Occupational medicine (Oxford, England).* 2017;67(6):496-497.
23. O'Donnell DE. Breathlessness in patients with chronic airflow limitation. Mechanisms and management. *Chest.* 1994;106(3):904-912.
24. Krüger K, Mooren FC. T cell homing and exercise. *Exerc Immunol Rev.* 2007;13:37-54.
25. McKinnon KM. Flow Cytometry: An Overview. *Current protocols in immunology.* 2018;120:1-5.
26. Huang C, Wang Y, Li X, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *Lancet (London, England).* 2020:S140-S6736.
27. Kang L, Li Y, Hu S, et al. The mental health of medical workers in Wuhan, China dealing with the 2019 novel coronavirus. *The lancet. Psychiatry.* 2020:S2215-S2366.
28. Wu J, Zhang Y, Du W, et al. Effect of Qigong on self-rating depression and anxiety scale scores of COPD patients: A meta-analysis. *Medicine.* 2019;98(22):e15776.
29. Vera FM, Manzaneque JM, Rodríguez FM, Bendayan R, Fernández N, Alonso A. Acute Effects on the Counts of Innate and Adaptive Immune Response Cells After 1 Month of Taoist Qigong Practice. *Int J Behav Med.* 2016;23(2):198-203.
30. Carlson LE, Zelinski E, Toivonen K, et al. Mind-Body Therapies in Cancer: What Is the Latest Evidence? *Curr Oncol Rep.* 2017;19(10):67.
31. Jahnke R, Larkey L, Rogers C, Etnier J, Lin F. A comprehensive review of health benefits of qigong and tai chi. *American journal of health promotion : AJHP.* 2010;24(6):e1-e25.

Figures

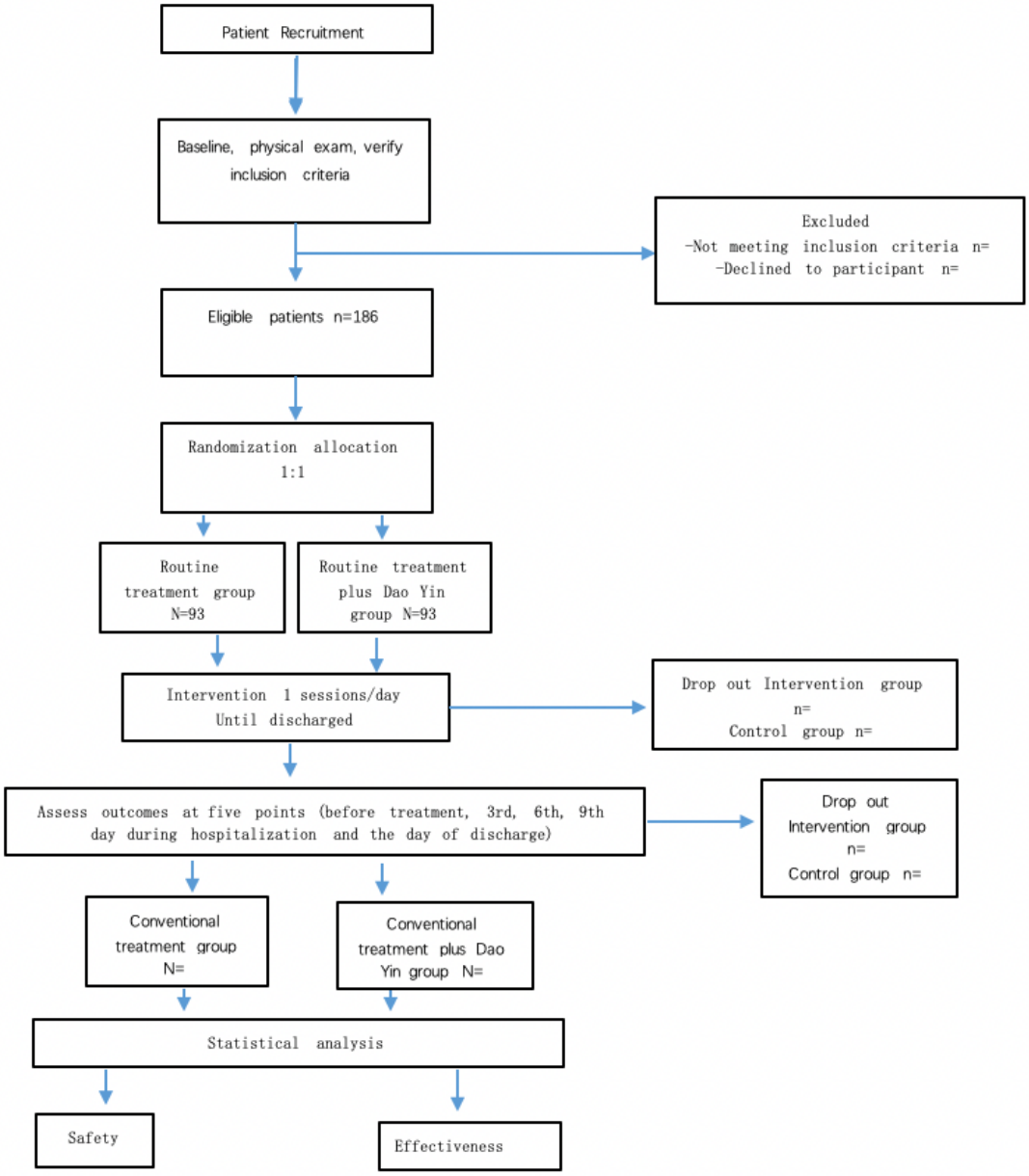

Fig.1 Flow chart of the study.

Figure 1

Time	M-1	M0	D3	D6	D9	Dsarged	
Period	Screening	Baseline	Intervention				
Patients							
Eligibility	x						
Demography	x						
Informed consent	x						
Sign the informed consent		x					
Medical history	x		x	x	x	x	x
Physical examination	x		x	x	x	x	x
Randomization		x					
intervention							
Conventional treatment group (n = 80)			Intervention 1 sessions/day Until discharged				
Conventional treatment plus Dao Yin group (n = 80)			Intervention 1 sessions/day Until discharged				
Outcomes							
Length of hospital stays	x						
Vital signs		x	x	x	x	x	x
MAS		x	x	x	x	x	x
SDS		x	x	x	x	x	x
MRC		x	x	x	x	x	x
MBS		x	x	x	x	x	x
Trail evaluation							
Patient' s compliance			x	x	x	x	x
Safety evaluation			x	x	x	x	x
Credibility test			x	x	x	x	x
Adverse events			x	x	x	x	x
Analysis	x	x	x	x	x	x	x

Fig. 2 Study schedule showing time points for enrollment and assessment.
MAS Motivation Assessment Scale, SDS Self Rating Depression Scale, MRC Medical Research Council, MBS Modified Borg scale D-1 screening before enrollment, D0 baseline assessment,D1 assessment after the 3th treatment, which is in the 3th day be hospitalized, D2 assessment after the 6th treatment, which is in the 6th day be hospitalized, D3 assessment after the 9th treatment, which is in the 9th day be hospitalized,, Last assessment when the patients are about to be discharged.

Figure 2

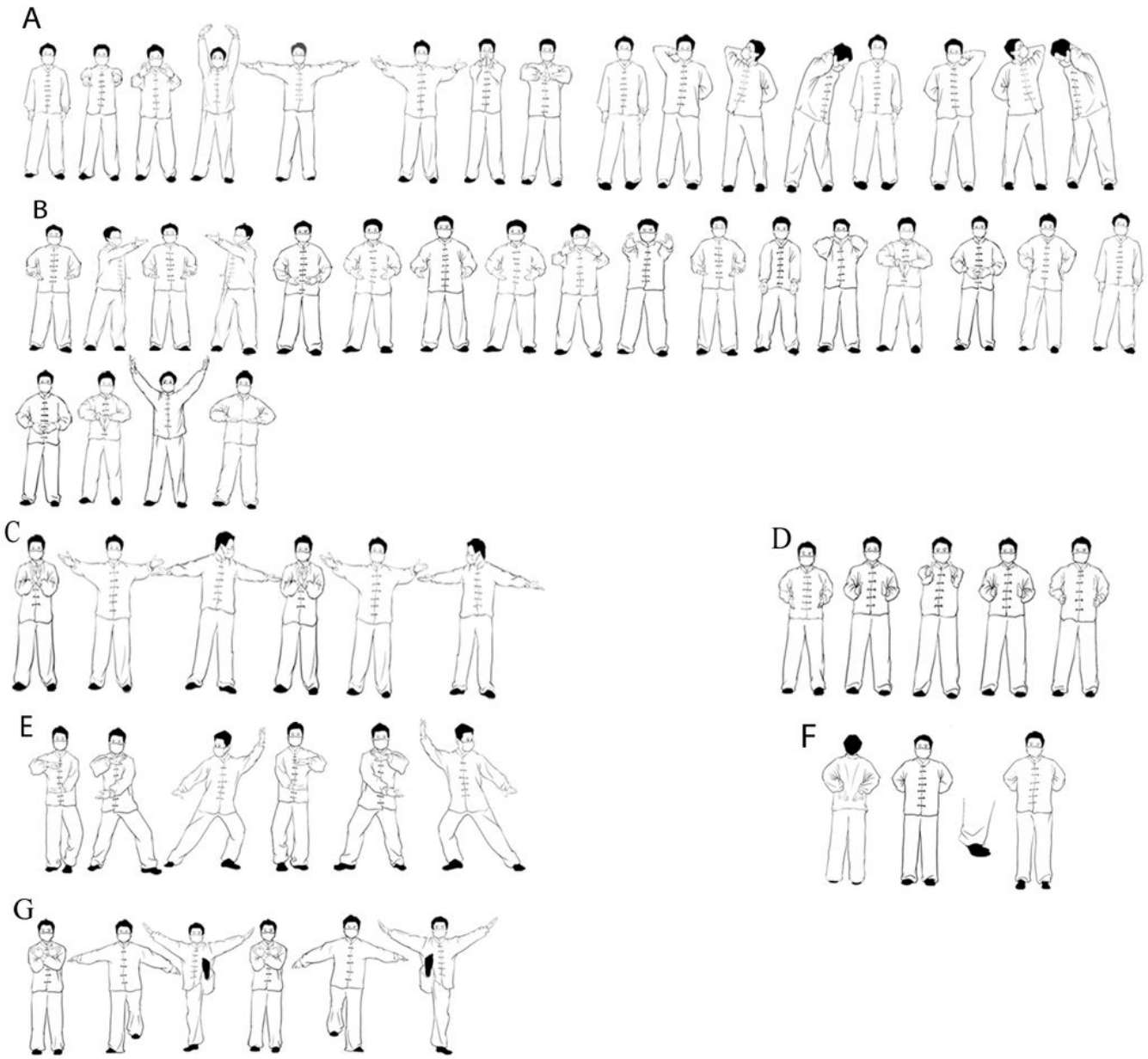

Figure 3 Illustration of seven steps Dao Yin movements.
(A)The warming part: Standing between heaven and earth; Boy worships Buddha; Looking up at the moon;(B) Six-character breathing exercise to spread Lung Qi(C): Chest expansion exercise to harmonious qi and blood;(D): Push and pull hardly to increase strength(E): Tai Chi oblique regulate yin and yang;(F): Raising the heel to eliminate all diseases(G): Retractable :Guide the gas downwards to adjust the bones and tendons.

Figure 3

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- SPIRIT2019cNoV.doc