

Acupressure Therapy and Liu-Zi-Jue Qigong for Pulmonary Function and Quality of Life in Patients with Severe Novel Coronavirus Pneumonia (COVID-19): Study Protocol for a Randomized Controlled Trial

Shuaipan Zhang

Shanghai University of Traditional Chinese Medicine

Qingguang Zhu

Yue yang Hospital of Integrated Medicine, Shanghai University of Traditional Chinese Medicine

Chao Zhan

Huangshi Hospital of Traditional Chinese medicine

Wei Cheng

Huangshi Hospital of Traditional Chinese Medicine

Xiaoming Fang

Huangshi Hospital of Traditional Chinese Medicine

Min Fang

Shanghai University of Traditional Chinese Medicine

Lei Fang (✉ fanglei586@126.com)

Rehabilitation Medicine College of Shanghai University of Traditional Chinese Medicine

Study protocol

Keywords: COVID-19, Acupressure therapy, Liuzijue Qigong, Traditional Chinese Medicine Rehabilitation, Randomized controlled trial, Study protocol

Posted Date: April 9th, 2020

DOI: <https://doi.org/10.21203/rs.3.rs-21844/v1>

License:   This work is licensed under a Creative Commons Attribution 4.0 International License.

[Read Full License](#)

Version of Record: A version of this preprint was published on August 27th, 2020. See the published version at <https://doi.org/10.1186/s13063-020-04693-5>.

Abstract

Background: In December, 2019, a pneumonia associated with the 2019 novel coronavirus (COVID-19) emerged in Wuhan, China. The number of cases has increased rapidly, severe patients have a poor prognosis and there are no effective therapies or vaccines for it. Only one rapid advice guideline for symptomatic supportive care has been used for it. A Traditional Chinese medicine Rehabilitation (TCMR) program consisting of acupuncture therapy and Liuzijue Qigong can be used as a complementary therapy for COVID-19. Hence, we designed a randomized trial to evaluate the efficacy and advantages of TCMR for treating severe patients with COVID-19.

Methods/design: This is a parallel-design, two-arm, analyst-assessor blinded, randomized controlled trial. A total of 120 patients with COVID-19 aged from 20 to 80 will be recruited and assigned randomly into a guideline therapy group and a guideline therapy plus TCMR group at a 1:1 ratio. Patients in both groups will receive guideline therapy. The patients in intervention group will perform acupuncture therapy and Liuzijue Qigong exercise on the basis of conventional treatments, twice a day, and have been persistent from admission to discharge. The primary outcomes are measured with Modified Dyspnea Scale (MDS) and Activities of Daily Living (ADL). The secondary outcomes include Patient Health Questionnaire-9 (PHQ-9), Length of Hospital Stay (LHS), Respiratory Symptoms (RS), Liver function test, Renal function test and lung CT. Clinical assessments will at three points (before treatment, 7th day during hospitalization and the discharge day). Adverse events will be noted and recorded for the safety evaluation.

Discussion: This trial will provide a high-quality evidence of the value of TCMR, which is consist of acupuncture therapy and Liuzijue Qigong exercise for treating severe patients with COVID-19.

Trial registration: Chinese Clinical Trial Registry, ChiCTR2000029994 Registered 18 February 2020, <http://www.chictr.org.cn/showproj.aspx?proj=49309>

Background

Since December 2019, a number of patients with pneumonitis infected by a new type of coronavirus called COVID-19 successively found in Wuhan, which raised intense attention worldwide¹. It is a novel type of coronavirus belonging to the beta coronavirus whose gene sequence are significantly different from the previous virus². It is mainly transmitted through respiratory droplets and contact with highly infectiousness. Though the authority gave the highest priority to its prevention and treatment promptly, such cases human-to-human transmission is gradually expanding in domestic and abroad. As of February 22, 2020, more than 54000 people have been infected, and more than 2300 deaths have occurred globally³. The COVID-19 had brought a heavy health and economic burden on the society⁴, which lead to a severe medical situation with more than 10,000 severe ill patients exit. Patients often develop dyspnea or hypoxemia one week after the onset of symptoms, and in severe cases, they progress rapidly to acute respiratory distress syndrome, septic shock, etc.⁵. An early study proved that due to a

shortage of medical resources, the mortality rate of patients with severe pneumonia was as high as 61.5%⁶. All medical measures have been taken to reduce mortality and reinfection. So a rapid advice guideline for the diagnosis and treatment of 2019 novel coronavirus (2019-nCoV) has been draught by a research Team in Wuhan⁷. However, more options should be explored to cope with this worldwide event due to the lack of targeted antiviral drugs and unpredictable side effect^{8,9}. Acupressure is a low risk physical therapy different from acupuncture as part of Traditional Chinese Medicine (TCM). Previous researches have shown that acupressure can improve the patient's symptoms of dyspnea in lung diseases and the quality of life^{10,11}. It is a non-invasive treatment acceptably by patients, which is characteristic by pressing on acupoints with hands to achieve the clinical efficacy. In addition, Liuzijue Qigong exercise has also been widely used in lung rehabilitation training, which can not only relieve breathlessness symptom, but also have benefit on mental illness¹²⁻¹⁴. It is applicable for the patients with COVID-19 that widely suffer panic and anxiety as its mortality and infectivity¹²⁻¹⁴. It adopts a combination of abdominal breathing and lip breathing to produce six different sounds (xu, he, hu, si, chui, and xi) and with the low intensity body movements¹⁶. This breathing pattern can change the rapid shallow breathing pattern of lung dysfunction, extend the opening time of the trachea, and maintain the airway pressure of the patient within a physiological range, thereby improving gas exchange^{17,18}. Now, we will combine the acupressure therapy with Liuzijue Qigong exercise as the clinical Traditional Chinese Medicine Rehabilitation (TCMR) method for patients with severe pneumonia. Therefore, a random control trail should be conducted to answer two questions. (1) Is TCMR method can improve the patient's pulmonary function and quality of life. (2) If effective, is it an official conventional therapy plus TCMR effect rather than the single guideline therapy.

Methods/design

Study design

This is a single-center, parallel-arms, clinical randomized controlled trial (RCT). The protocol was registered with the China Clinical Trial Registry (item number: ChiCTR2000029994) and the trial protocol was approved by the Ethics Committee of Huangshi Hospital of Traditional Chinese Medicine (item number: HSZYYJ-2020-003-01). A total of 120 patients will be recruited from the Huangshi hospital of Traditional Chinese Medicine in Hubei Provence. Written informed consent will be provided by all patients at the time of recruitment. Patients with severe pneumonia symptom will be recruit who have an equal chance of being allocated randomly to guideline therapy or guideline therapy plus TCMR. Due to the limitations of intervention methods, only the outcome assessors and statisticians are blinded. The assessor will perform evaluation and analysis of outcome at three points (before treatment, 7th day during hospitalization and the discharge day). Data management and statistics will be conducted in the Rehabilitation Medical College of Shanghai University of Traditional Chinese Medicine (SUTCM). The study design is illustrated in the flow chart in Figure.1 and the study schedule is presented in Figure.2 Additional file 1 shows the Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT) checklist.

Participants recruitment

Patients with severe COVID-19 will be recruited, which should meet the diagnostic criteria of "Diagnostic and treatment protocol for Novel Coronavirus Pneumonia (The Fifth Trial Version)" issued by the National Health Commission of China on February 8, 2020¹⁹. The participants are from Department of Infectious Diseases in Huangshi Hospital of Traditional Chinese Medicine. The recruitment advertisements will be placed on the inpatient, network, WeChat and Weibo official platforms to achieve the potential participants.

Inclusion criteria

Patients can only be recruited if they meet each of the following conditions (1) Meet the severity patient with COVID-19 critical diagnosis criteria²⁰; (2) The age of patients is between 20 and 80, and is not limited to male or female; (3) The patient's condition is basically stable, conscious and cooperative in examination; (4) Volunteer to join the trial and sign the "informed consent"; (5) Promise not to perform other exercise program.

Exclusion criteria

Those who meet one of the following conditions will be removed. (1) The patient is complicated by other serious underlying diseases, such as chronic obstructive pulmonary disease, obstructive pulmonary disease, coronary heart disease, and hypertension; (2) Serious mental illness; (3) Cognitive dysfunction, unable to understand the trial process and rehabilitation content; (4) Patients with severe bone and joint diseases (such as spinal arthritis, severe osteoporosis, peri-arthritis, etc.) affecting limb function and movement; (5) Patients have respiratory failure and require mechanical ventilation or shock or combined organ failure requiring Intensive Care Unit (ICU) monitoring and treatment. (6) Pregnant or lactating women; (7) Participate in other forms of exercise during the trial.

Drop out and suspension criteria

During the intervention period, patients have the right to withdraw whatever the reason and time under the protection of Declaration of Helsinki²¹. As long as any of the following conditions are met, it will withdraw. (1) Patients with poor compliance who did not follow treatment as required; (2) Those who had serious adverse reactions during the trial or the condition deteriorated further, with respiratory failure, multiple organ failure, shock, etc.; (3) Case data are incomplete and affect the judgement of curative effect; (4) Patients withdraws by himself; (5) Participants in other rehabilitation program during the trial; (6) Researchers do not consider the participants appropriate to continue participating in this researcher.

Interventions

All recruited patients in the two arms with severe syndrome should be treated routinely along with the official medical plan²². On the basis of the guideline therapy, the test group required a standardized TCMR program consisting of acupuncture therapy and Liuzijue Qigong exercise. Both of them are performed

twice a day at 10 am and 4 pm respectively. Each time, acupressure is performed first, and then Liuzijue Qigong exercises will continue. 20 minutes for each treatment, for a total of 40 minutes will be need. The TCMR program is ongoing during the patient's stay until the patient is discharged. They should reach a consensus in advance on the acupuncture points, pressure levels and duration. Liuzijue Qigong was demonstrated live by the therapists on the first day until the patient was able to operate it skillfully. Patients will be provided with paper and video versions of exercises to facilitate subsequent practice. Therapists performing rehabilitation therapy are required 10 years of clinical experience in acupressure and qigong therapy, which should undergo rigorous clinical trial training before conducting trials. Until pass the exam can they performed the intervention. Daily treatments are required to be recorded, and regular researchers will review completion.

Guideline therapy

The health authorities in China draft the conventional treatment plan for patients with severe condition which are described below.(1)Patients should ensure adequate rest time, and medical staff need to closely monitor vital signs, oxygen saturation, etc.;(2) Additionally, it is necessary to monitor blood routine, urine routine, C-reactive protein, biochemical indicators, blood coagulation function, arterial blood gas analysis, chest imaging, etc. according to the changes of the condition;(3)Timely effective oxygen therapy measures should be taken especially severe patients should receive nasal cannula or mask to inhale oxygen, and promptly evaluate whether respiratory distress and / or hypoxemia is relieved; (4)Doctors should use antiviral drugs and combined with antibiotics if necessary;(5)To maintain the stability of the internal environment, they should strengthen supportive treatment to ensure sufficient heat and pay attention to water and electrolyte balance; (6) Also, early Chinese medicine can be used to relieve the syndromes.

Guideline therapy plus TCMR

Conventional treatment as the authorities required is the same as the control group. At the same time, acupressure therapy and Liuzijue Qigong exercise will be carried out as the TCMR program.

(1) Acupressure therapy

The specific acupressure process is as follows. According to channel-collateral theory, the severe case dialectical is Lung qi deficiency pattern whose characterization is weak cough, dyspnea, low voice, and clear watery sputum with other symptoms of qi deficiency. Therefore, acupoints related to the lung viscera were selected including Feishu (T 3), Danzhong (CV 17), Zhongfu (Lu 1)²³. Pressing these points can improve lung symptoms²³. First the patient takes a sitting or lying position with the therapist on the patient's right side. Pressing and kneading constitute the manipulation of acupressure. The first step is called continuous shiatsu method. The therapist uses the thumb thread press on the selected acupuncture points with moderate force, which is about 10 Newtons²⁴ tested by a mechanical instrument²⁵. The direction of the pressure should be perpendicular to the skin surface, hold for 3-7 seconds and then relax, but not leave the skin surface. The second step is kneading the acupoint with the

thumb. The thumb acts on the skin surface of the acupoint with a slight force pressure (5N), and then performs a small circular sliding movement with the acupoint as the center. The operation is performed 50 times on each acupoint with pressing method and kneading method respectively.

(2) Liuziju Qigong exercise

The Liuzijue Qigong exercise operates as follows: (1) Preparation phase: the patient is standing with the body in a relaxed state, and abdominal breathing or nasal suction is used to relax the abdominal muscles, the diaphragm is contracted together with not breathing for 3 seconds. (2) Practice phase: Keep lips whistle to make the "Xu, he, hu, si, chui, xi" sound lasting 5seconds successively. After each of the 6 pronunciations, return to the ready posture, and then perform the next exercise. The "Xu, he, xi" sound is repeated 6 times, and the "hu, si, chi" sound is repeated 12 times.

Outcome measurements

All outcome will be managed by researchers masked to the group assignment, which include Modified Dyspnea Scale ²⁶(MDS), Activities of Daily Living (ADL)²⁷, Patient Health Questionnaire-9 (PHQ-9)²⁸ Length of Hospital Stay (LHS), Respiratory symptoms, Liver function test, Renal function test and lung CT. Evaluating outcomes will at three points (before treatment, 7th day during hospitalization and the discharge day). In addition, vital signs, clinical symptoms and related laboratory tests will be monitored daily.

Primary outcome measurements

We will use MDS, ADL as the primary outcome indicators to evaluate the dyspnea symptoms and physical health.

MDS

The scale is highly operable and is often used to measure the impact of activities on dyspnea. It is used to grade dyspnea and muscle fatigue on a scale of 0-10 to reflect the gradual increase in symptoms sensitively. Taking shortness of breath as an example, 0 points: None 10 points: the highest level is most serious of breathlessness. We will assess the MDS with a repeated longitudinal analysis.

ADL

The ADL is evaluated using BARTHEL index scale to judge the treatment value and prognosis. If its total score is greater than 40, the patient is considered more valuable. It mainly includes 10 daily life behaviors, such as: eating, bathing, dressing, and controlling bowel movements. Each item can be scored 10 points if it can be completed independently. 5 points are needed for partial help. A total score of 100 indicates that you have good daily activities and do not need to depend on others. A score of > 60 was considered good, indicating mild dysfunction and being able to take care of themselves in basic daily life. A score of

60-41 indicates moderate dysfunction, and it is obvious that daily life depends on others. A score <20 is completely disabled, and daily life is completely dependent on others.

Second outcome measurements

PHQ-9

PHQ-9 is used to detect and measure depression and severity in medical populations in clinical settings, which has been conducted in a variety of settings using medical populations. It is a questionnaire containing the frequency with 9 negative items happened to patients in the last 2 weeks. If the answer is not at all, get 0 points; once every few days, get 1 point; once more than half a day, get 2 points; every day, 3 points.

The PHQ-9 score was divided into the following categories of increasing severity: 0–4, 5–9, 10–14, 15–19, and 20 or greater.

LHS

The length of time patient is in the hospital will be used as an outcome indicator, which will be recorded on the CRFs by the evaluator and the reason for discharge.

RS

Respiratory symptoms include fatigue, cough, expectoration, chest tightness, dyspnea, sore throat, nasal congestion, runny nose, and some other none-specific symptoms. The severity of these symptoms is recorded sequentially as 0-10, with 0 being no and 10 being the most severe. Key factors such as vital signs and blood oxygen saturation should be monitored as well.

Lung CT

Lung CT is the main imaging method for diagnosis of COVID-19. which can directly visualize the lung inflammation of the patients. It can provide intuitive imaging evidence for the changes of condition. The degree of clinical rehabilitation can be assessed based on the absorption of inflammation in the lung CT of the patients.

Liver and renal function test

Relevant laboratory tests should also be monitored, especially liver and kidney function tests. The whole process of biological specimen inspection will be performed in the hospital, and the hospital laboratory will report the processing of biological specimens.

Sample size calculation

The trial takes the MDS as the primary efficacy outcome. Based on previous clinical studies on the effect of MDC after Liuzijue Qigong intervention, a superiority test was used to estimate the sample size ($\alpha =$

0.05 , $\beta = 0.10$).In this study, the target sample size will be 120 participants and anticipating on maximum loss to follow up of 20%.

Randomization

Department of Science and Technology of SUTCM will generate the randomization sequence using a random number generator (IBM, Chicago, IL, USA) and then sequentially number them in an opaque envelope. The researcher in Shanghai will randomize and inform the therapists in Hubei of the treatment assignments by phone. The allocation concealment procedure will not be exposed until the baseline data have been collected completely. Then eligible patients will be randomly divided into a guideline therapy group and a guideline therapy plus TCMR group, with an allocation proportion of 1:1.

Blinding

Participants and therapists are unable to be blind about group assignments due to the specific intervention, but the therapists will be masked to the evaluation of outcomes. To reduce the risk of bias, evaluators, data managers, and statisticians were unaware of group assignments during the outcome evaluation and data analysis process. And they will be required to do not share study information with each other. The blinding procedure will be operated until the data are locked.

Data collecting and monitoring

Screeners will complete the collection of demographic and baseline characteristics during the patient recruitment phase. The clinical assessor will use the case report forms (CRFs) to record detailed information on clinical symptoms, signs, auxiliary examinations, each scale outcome, and adverse events. A data manager will enter data into the electronic CRFs in real time carefully. All data managers have data analyze competence and receive unified training, who is independent of the research team and is unaware of the group assignment. Researchers should optimize the trial operation to reduce the risk of data loss, and exclude the data if very few data are lost. Electronic database will be closed after data entry is completed. The administer in Science and Technology Department of SUTCM will be responsible for monitoring the data management.

Statistical analysis

Statistical analysis will be performed by the research in Rehabilitation Medical College of SUTCM. The statistician will be blind to the allocation of groups. SPSS Windows version 24.0 software will be used for data analysis. The level of significance is established at $\alpha < 0.05$ with a two tailed test. Continuous variables will be expressed as mean \pm standard deviation, and categorical variables will be expressed as n (%). Demographic baseline information (age, gender, occupation, etc.) will be tested using a chi-square test and an independent t-test. Comparisons of differences within groups will use paired t-tests, and differences between groups will use independent t-tests. If the data does not have a normal distribution, a nonparametric test (Wilcoxon signed rank test or Wilcoxon rank sum test) will be used for the test. Information on adverse events will be collected through CRFs by researchers. In addition, we will perform

an intention-to-treat analysis of missing data in the primary and secondary analyses. As the main statistical analysis, the effectiveness of the TCMR program will be tested by calculating the difference in subject scales at each point (baseline, 7th day of hospitalization, discharge). Fisher's exact test will be used to compare the drop-out rate for compliance analysis. Adverse events will be listed and analyzed using a chi-square test or Fisher's exact test.

Quality control

During the whole processing of the trial, quality control will be conducted under the surveillance of the steering committee. To ensure the consistency of methods, all the researchers should be trained with the trial methodology and monitoring technique before he participates in the trial. Supervision activities will be divided into online remote monitoring and offline personal inspection every day. As the research progresses, researchers can submit a request to modify the study scheme. But only the steering committee and ethics committee have the authority to modify or correct the protocol if necessary.

Safety evaluation

Safety evaluation will be conducted throughout the trial. Although TCMR programs are low-risk, the participants are illness with severe pneumonia. When adverse events occur, the researchers should record them in CRFs in detail and analyze whether they are directly related to the rehabilitation program. Regardless of the cause, if the condition suddenly worsens during the trial and accompanied by severe complications or serious adverse reactions, the trial should be terminated immediately. Researchers need to analyze whether the causes of adverse reactions are related to the intervention method, and take prompt medical measures, such as improving the level of monitoring, symptomatic supportive treatment such as: oxygen therapy support, improve ventilation and maintain vital signs normally.

Discussion

The city of Wuhan in China is the focus of global attention due to the outbreak of COVID-19²⁹, with an epidemiological link to the Huanan Seafood Wholesale Market. Although the whole mortality rate is relatively low compared to the other coronavirus epidemics³⁰, the infection has worsened due to encounter the mass migration³¹. Immediately medical measures and rescues has been taken to control the further deterioration of the epidemic by the Chinese government, which include intensive surveillance, epidemiological surveillance and symptomatic supportive treatment to reduce mortality. Though all costs of COVID-19 treatment are covered by medical insurance in China, there are still no effective therapies or vaccines expect for meticulous supportive care³². Therefore, it is necessary to find more measures to deal with this pneumonia. As a category of Complementary and Alternative Medicine, acupuncture therapy and Liuzijue Qigong exercise are performed widely in TCM^{33,34}. Some researchers have confirmed that they can improve the clinical symptoms and physical and mental health of patients with lung disease³⁵⁻³⁷. As for the health care system are overload, the TCMR program is highly operable and cost-effective³⁸. It is a low-risk therapy does not require large equipment, which is not restricted by location and time either³⁹.

Through TCM rehabilitation, the body's immune system can offset the damage of foreign microorganisms through the dynamic regulation of innate immunity⁴⁰. Previous studies have found that these points can significantly improve lung symptoms such as cough, chest tightness, sputum etc.⁴¹ In addition, the Liuzijue Qigong breathing exercise can help restore the physiology of lungs to diffuse and sink (Inhale and exhale). It is a pursed lip breathing and inspiratory muscle training which can increase muscle strength and respiratory muscles endurance to relieve dyspnea. During the operation of the low intensity exercise, patients are focus on themselves that can relieve some anxiety and tension attribute to the bad situation⁴². In accordance with TCM macro theory, The TCMR program can harmonize qi and blood coordination, regulate the balance of Yin and Yang. However, more strong evidence is necessary to further prove the effectiveness of TCMR programs on the symptoms and prognosis of patients with COVID-19. Therefore, this clinical trial was conducted to evaluate the effectiveness of the TCMR program which is composed of acupressure and Liuzijue Qigong exercise on the pneumonia function and quality of life of patients with COVID-19.

Trial Status

This trial is recruiting patients now. Participant recruitment started in 20 February 2020 and is expected to end in 30 June 2020. This trial was registered in Chinese Clinical

Trial Registry on 18 February 2020. The registration number is ChiCTR2000029994.

Protocol version 1, 18 February 2020.

Abbreviations

COVID-19: Novel Coronavirus Pneumonia; ADL: Activities of Daily Living; CRF: Case report form; CT: computed tomographic; MDS: Modified Dyspnea Scale; PHQ-9: Patient Health Questionnaire-9; SUTCM: Shanghai University of Traditional Chinese Medicine; RS: Respiratory Symptoms; TCMR: Traditional Chinese Medicine Rehabilitation;

Declarations

Acknowledgements

We sincerely thank the clinicians at the research center in Hubei for their medical work. This study is supported financially by the project of Emergency scientific research project for prevention and control of new coronavirus (COVID-19) 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), National Key Clinical Difficult Diseases Clinical Collaborative Pilot Construction Project - Osteoarticular Degenerative Disease (ZY(2018-2020)-FWTX-2005), High-level innovation team of "Peak and Plateau Discipline" in Traditional Chinese Medicine (30304114316). 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. All these funding is a wider group of projects and apply to this study.

Availability of data and material

Not applicable.

Authors' contributions

SZ planned the study protocol and drafted the manuscript. QZ planned the study protocol and participated in the critical revision of the manuscript. CZ carried out the physical therapy for patients. WC was the study coordinator. XF participated in designing the trial and helped to do the intervention. LF and MF were equal contributors responsible for study design, overseeing study implementation, providing methodological for this trail. All the authors have read and approved the final manuscript.

Ethics approval and consent to participate

Ethics approval was requested and granted by Ethics Committee of Huangshi Hospital of Traditional Chinese Medicine (item number: HSZYYJ-2020-003-01). All study participants will obtain informed consent before starting any data collection by the clinical trial communicator. All participants will provide their consent in writing. Only the investigators have access to the final data. This protocol was registered in the Chinese Clinical Trial Registry under identifier number ChiCTR2000029994 (18 February 2020).

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.

References

1. Wang C, Horby PW, Hayden FG, Gao GF. A novel coronavirus outbreak of global health concern. *Lancet (London, England)*. 2020;395(10223):470-473.
2. Zhu N, Zhang D, Wang W, et al. A Novel Coronavirus from Patients with Pneumonia in China, 2019. *New Engl J Med*. 2020;382(8):727-733.
3. National Health Commission of the People's Republic of China. <http://www.nhc.gov.cn>. Vol (Assess on February 22th 2020).
4. Ming W, Huang J, Zhang CJP. Breaking down of healthcare system: Mathematical modelling for controlling the novel coronavirus (2019-nCoV) outbreak in Wuhan, China. *bioRxiv*. 2020:2020-2021.
5. 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.

6. Yang X, Yu Y, Xu J, et al. Clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia in Wuhan, China: a single-centered, retrospective, observational study. *The Lancet Respiratory Medicine*. 2020.
7. 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.
8. C X, X L, S L, Y S, SJ G, F G. HIV-1 did not contribute to the 2019-nCoV genome. *Emerg Microbes Infectec*. 2020;9(1):378-381.
9. KJ G, FC Z, Y G, FL L, L Z, W Z. The influence of age, gender and treatment with steroids on the incidence of osteonecrosis of the femoral head during the management of severe acute respiratory syndrome: a retrospective study. *The bone & joint journal*. 2014(2):259-262.
10. Marciniuk DD, Goodridge D, Hernandez P, et al. Managing dyspnea in patients with advanced chronic obstructive pulmonary disease: a Canadian Thoracic Society clinical practice guideline. *Can Respir J*. 2011;18(2):69-78.
11. Improvement in respiratory function after self-administered acupressure. *Nursing older people*. 2007;19(4):39.
12. P L, J L, Y L, X L, Z W, W W. Effects of long-term home-based Liuzijue exercise combined with clinical guidance in elderly patients with chronic obstructive pulmonary disease. *Clin Interv Aging*. 2018;13:1391-1399.
13. W W, X L, P L, N L, Z W. Effect of Liuzijue Exercise Combined with Elastic Band Resistance Exercise on Patients with COPD: A Randomized Controlled Trial. *Evidence-based complementary and alternative medicine : eCAM*. 2018;2018:2361962.
14. CM X, YC Z. Efficacy of Liuzijue Qigong in Individuals with Chronic Obstructive Pulmonary Disease in Remission. *J Am Geriatr Soc*. 2015;63(7):1420-1425.
15. 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.
16. Xiao C, Zhuang Y. Efficacy of Liuzijue Qigong in Individuals with Chronic Obstructive Pulmonary Disease in Remission. *J Am Geriatr Soc*. 2015;63(7):1420-1425.
17. de Araujo CLP, Karloh M, Dos Reis CM, Palú M, Mayer AF. Pursed-lips breathing reduces dynamic hyperinflation induced by activities of daily living test in patients with chronic obstructive pulmonary disease: A randomized cross-over study. *J Rehabil Med*. 2015;47(10):957-962.
18. Spahija J, de Marchie M, Grassino A. Effects of imposed pursed-lips breathing on respiratory mechanics and dyspnea at rest and during exercise in COPD. *Chest*. 2005;128(2):640-650.
19. Diagnosis and treatment of COVID-19 with a new coronavirus infection (the fifth trail version 5). *China Journal of Integrated Traditional Chinese and Western Medicine*.:1-3.
20. 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.

21. World MA. World Medical Association Declaration of Helsinki: ethical principles for medical research involving human subjects. *JAMA*. 2013;310(20):2191-2194.
22. Diagnosis and treatment of COVID-19 with a new coronavirus infection (the fifth trail version 5). *China Journal of Integrated Traditional Chinese and Western Medicine*.:1-3..
23. Yang B, Lu Y, Qin Y, et al. Influence of moxibustion apparatus as adjuvant treatment for pulmonary tuberculosis and patient's immune function. *Zhongguo zhen jiu = Chinese acupuncture & moxibustion*. 2013;33(4):299-302.
24. Bi-ling W. Analysis on acupoint prescription for acupoint sticking therapy of treating winter diseases in summer for preventing and curing chronic cough and asthma. Paper presented at: 2016 International Conference of the World Federation of Acupuncture Societies, 2016; Tsukuba, Japan.
25. Li Wu, Jiang Quanrui, Ai Kun, et al. Theoretical discussion and mechanical analysis of finger-operated parameter. *Chinese Journal of Traditional Chinese Medicine*. 2019; 34 (12): 5700-5702.
26. Beaumont M, Couturaud F, Jego F, et al. Validation of the French version of the London Chest Activity of Daily Living scale and the Dyspnea-12 questionnaire. *Int J Chronic Obstr*. 2018;13:1399-1405.
27. QX L, XJ Z, HY F, et al. Application Values of Six Scoring Systems in the Prognosis of Stroke Patients. *Front Neurol*. 2019;10:1416.
28. C H, B L, KE R, et al. The Accuracy of the Patient Health Questionnaire-9 Algorithm for Screening to Detect Major Depression: An Individual Participant Data Meta-Analysis. *Psychother Psychosom*. 2020;89(1):25-37.
29. Chen N, Zhou M, Dong X, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. *The Lancet*. 2020;395(10223):507-513.
30. Zhang R, Liu H, Li F, et al. Transmission and epidemiological characteristics of Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) infected Pneumonia (COVID-19): preliminary evidence obtained in comparison with 2003-SARS. *medRxiv*. 2020:2020-2021.
31. Donnelly CA, Ghani AC, Leung GM, et al. Epidemiological determinants of spread of causal agent of severe acute respiratory syndrome in Hong Kong. *The Lancet*. 2003;361(9371):1761-1766.
32. de Wit E, van Doremalen N, D F, VJ M. SARS and MERS: recent insights into emerging coronaviruses. *Nature reviews. Microbiology*. 2016;14(8):523-534.
33. Tang J, Huang W, Chen X, et al. Liuzijue Qigong: A Voice Training Method For Unilateral Vocal Fold Paralysis Patients. *The Annals of otology, rhinology, and laryngology*. 2019;128(7):654-661.
34. Tan J, Suen LKP, Wang T, Molassiotis A. Sham Acupressure Controls Used in Randomized Controlled Trials: A Systematic Review and Critique. *Plos One*. 2015;10(7):e132989.
35. Yorke J, Lloyd-Williams M, Smith J, et al. Management of the respiratory distress symptom cluster in lung cancer: a randomised controlled feasibility trial. *Supportive care in cancer : official journal of the Multinational Association of Supportive Care in Cancer*. 2015;23(11):3373-3384.
36. Li P, Liu J, Lu Y, Liu X, Wang Z, Wu W. Effects of long-term home-based Liuzijue exercise combined with clinical guidance in elderly patients with chronic obstructive pulmonary disease. *Clin Interv*

Aging. 2018;13:1391-1399.

37. 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.
38. FK C. Effects of Baduanjin on mental health: a comprehensive review. *Journal of bodywork and movement therapies*. 2015;19(1):138-149.
39. Dalusung-Angosta A. The impact of Tai Chi exercise on coronary heart disease: a systematic review. *J Am Acad Nurse Pract*. 2011;23(7):376-381.
40. J Z, H Z, AP G, et al. Yin Yang 1 Dynamically Regulates Antiviral Innate Immune Responses During Viral Infection. *Cellular physiology and biochemistry : international journal of experimental cellular physiology, biochemistry, and pharmacology*. 2017;44(2):607-617.
41. Rui Jinglin, Cen Yanhui, Shang Zhihao, et al. Analysis of clinical acupuncture points based on data mining technology for chronic bronchitis. *Chinese Journal of Traditional Chinese Medicine*. 2019; 37 (08): 2004-2008.
42. Z L, S L, L W, L S. Mind-Body Exercise for Anxiety and Depression in COPD Patients: A Systematic Review and Meta-Analysis. *Int J Env Res Pub He*. 2019;17(1).

Figures

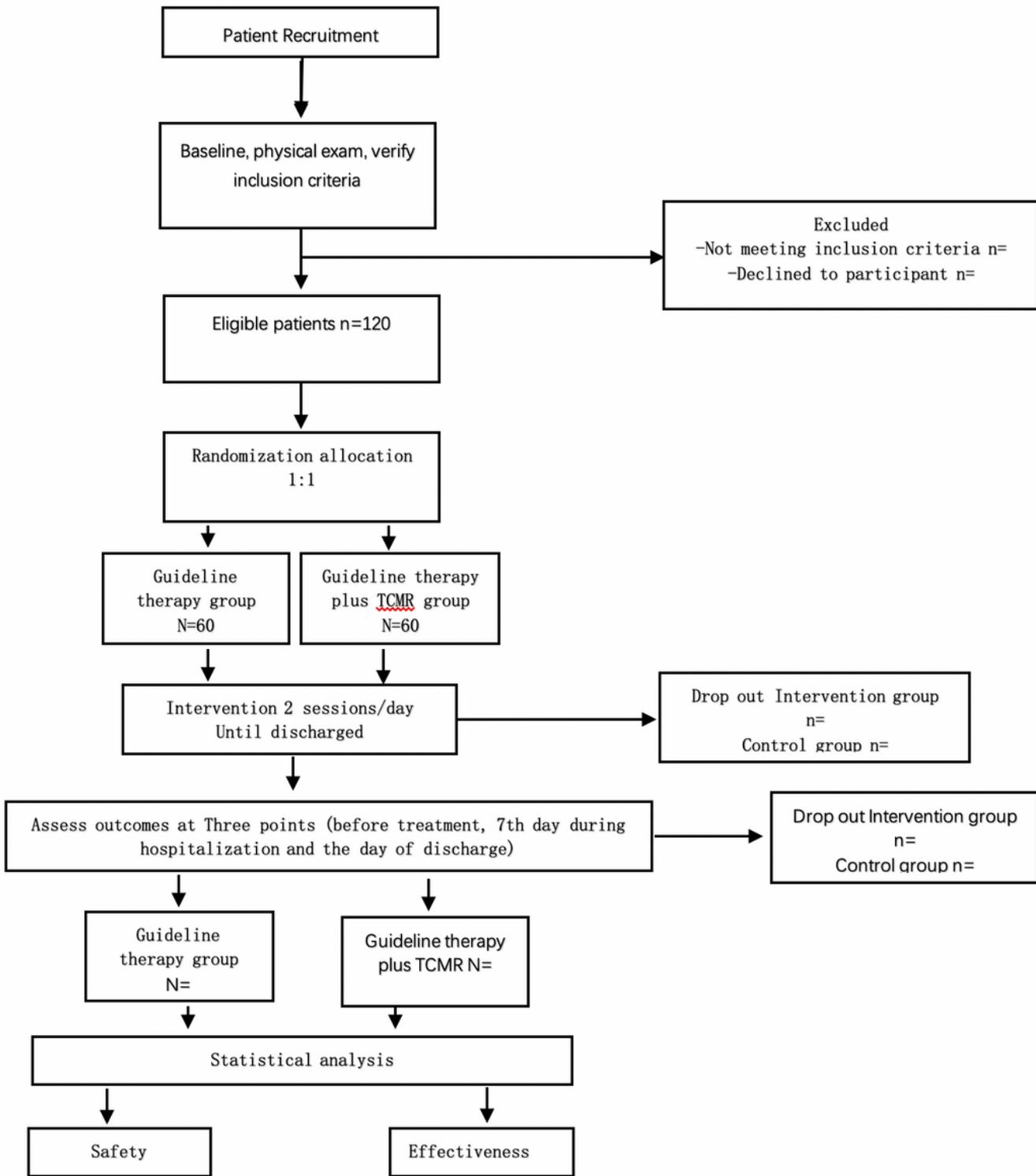


Figure 1

Flow chart of the trial.

Time	M-1	M0	D7	Discharged
Period	Screening	Baseline	Intervention	
Patients				
Eligibility	x			x
Demography	x			x
Informed consent	x			x
Medical history	x		x	x
Physical examination	x		x	x
Randomization		x		
intervention				
Guideline therapy group (n = 60)			Intervention 2 sessions/day Until discharged	
Guideline therapy plus TCMR group (n = 60)			Intervention 2 sessions/day Until discharged	
Outcomes				
MDS		x	x	x
ADL		x	x	x
PHQ-9		x	x	x
LHS		x	x	x
RS		x	x	x
Lung CT		x	x	x
Liver and renal function test		x	x	x
Vital signs		x	x	x
Trail evaluation				
Patient' s compliance		x	x	x
Safety evaluation			x	x
Credibility test			x	x
Adverse events		x	x	x
Analysis	x	x	x	x

Figure 2

Study schedule showing time points for enrollment and assessment. ADL: Activities of Daily living; CRF: case report form; CT: computed tomographic; MDS: modified dyspnea scale; PHQ-9: patient health questionnaire-9; RSL respiratory symptoms; TCMR: traditional Chinese medicine rehabilitation