Study Protocol

Effects of combining acupuncture with exercise training on relieving dyspnea and improving exercise tolerance in chronic obstructive pulmonary disease patients: a protocol for a single-blind, randomized, sham-controlled trial

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Background: Exercise training is beneficial for patients with chronic obstructive pulmonary disease (COPD). However, the effect of exercise training is limited by patients' impaired exercise capacity, exertional dyspnea and other respiratory problems. Acupuncture, as a reliable and safe therapy, is effective in reducing dyspnea, relieving respiratory muscle fatigue, and improving exercise capacity of COPD patients. However, it is not known whether the combination of exercise training and acupuncture reduces dyspnea and improves quality of life of COPD patients or induces more pronounced effects in dyspnea and exercise tolerance. This trial aims to determine whether acupuncture enhances the effect of exercise training in COPD patients compared to sham acupuncture.

Methods: In this single-blind, randomized, sham-controlled trial, 70 COPD patients will be enrolled and randomly assigned (1:1) to the following 2 groups: (I) real acupuncture and exercise training group; and (II) sham acupuncture and exercise training group. For acupoint selection, CV 4, CV 12, CV 17, ST 40, ST 16 and ST 25 will be used for all patients. For sham acupuncture group, Streitberger placebo needles will be used. A single-blind method will be adopted in this trial. Data collectors and statisticians will be blinded in this trial, only the acupuncturists will know the group allocation. The intervention will be conducted 3 times a week for 8 weeks, totaling 24 treatments. Patients will be evaluated at the baseline, after 14 treatments during the 5th week, after 24 treatments during the 8th week, and at a 5-month follow-up period. The primary outcomes will be assessed by a modified British medical research council questionnaire (mMRC), COPD assessment test (CAT), and 6-minute walk test (6MWT). The secondary outcomes will be measured by changes in variables from the lung function test, cardiopulmonary exercise testing, and blood gas analysis. Two-independent sample *t*-tests will be used to compare differences in the changes in all outcome measures after the intervention between two groups. Safety evaluation will be performed at each treatment visit and assessment by recording adverse events (AE) in the AE Report Form.

Discussion: This study will help to determine whether acupuncture increases the benefits obtained from

exercise training in COPD patients.

Trial Registration: Chinese Clinical Trial Registry: ChiCTR1900028627. Registered on December 29, 2019.

Keywords: Chronic obstructive pulmonary disease (COPD); acupuncture; exercise training; sham acupuncture

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Introduction

It has been predicted that chronic obstructive pulmonary disease (COPD), which is characterized by airflow limitation and gradual lung function decline (1), will be the 3rd leading cause of death in the world by 2030 (2). Dyspnea and reduction in exercise capacity are the main complaints of COPD patients (3). These symptoms progress and reduce patients' ability to perform the activities of daily living (4), and contribute to the high rate of disability and mortality globally (5). Mild to very severe COPD patients benefit from reducing dyspnea (1,6,7) as a result of exercise training, which is an essential component of pulmonary rehabilitation and can improve COPD patients' exercise tolerance and quality of life (1,6,7). Thus, international guidelines recommend exercise training for the management of COPD (4,8). However, the exercise capacity of COPD patients is impaired and is often limited by exertional dyspnea resulting from dynamic hyperinflation, an increased respiratory load, or defective gas exchange, which places limitations on exercise training (9). Many adjuncts have been used to enhance the positive effects of exercise training for COPD patients, including pharmacotherapy, oxygen therapy, non-invasive mechanical ventilation, and breathing strategies (9); however, despite some promising results, each of these adjuncts still have limitations related to the costs, effectiveness, side effects, time consumption, and patients' adherence (10-20). Thus, the question of how exercise training can be delivered more effectively and safely to COPD patients to relieve dyspnea and maximize exercise performance requires both clinical and social considerations. As an integrated part of traditional Chinese medicine (TCM), acupuncture, has been widely used to treat bronchial asthma, chronic bronchitis, and chronic disabling breathlessness for the past 50 years in both China and western countries and has been proven to be reliable, convenient, and safe (21-25). From the perspective of TCM, pathological changes such as qi and blood stasis, phlegm and dampness stagnation have been frequently found in COPD patients and acupuncture on relevant points can promote the circulation of qi and blood, dispel phlegm and dampness. It has also been clearly proven to have beneficial effects on both subjective and objective indices of lung function for patients with the above-mentioned diseases (26). Further, a series of systematic reviews (27-31) and randomized controlled trials (RCTs) (32-36) have also reported that it is effective in reducing exertional dyspnea, relieving respiratory muscle fatigue, and improving the exercise capacity and quality of life of COPD patients because of the following possible mechanism: acupuncture regulates inflammatory factors and microstructure of skeletal muscle after exercise so as to maintain muscle mass and contractility and improve breathing and exercise ability. Additionally, there is evidence that acupuncture enables a significant reduction of medication, particularly corticosteroids, in the usual treatment of bronchial asthma (21,24,37-41). Given that acupuncture has been shown to have a positive role in relieving respiratory symptoms and facilitating reducing pharmacologic medication, it was hypothesized that acupuncture could be an ideal adjunctive therapy in the treatment of COPD if incorporated into exercise training. To date, no research appears to have been conducted to examine the effect of acupuncture as an adjunct to exercise training in COPD patients. Thus, we aim to investigate the potential benefits of acupuncture as an adjunctive therapy to exercise training by conducting a randomized sham-controlled trial. It is hypothesized that compared to sham acupuncture, acupuncture improves outcome measures in relation to dyspnea and exercise tolerance in COPD patients who perform exercise training. The study protocol was developed in accordance with the Consolidated Standards of Reporting Trials (CONSORT) guidelines (42). We present the following article in accordance with the SPIRIT reporting checklist (43) (available at https://apm.

Table 1 Study schedule

Period	Screening	Baseline	Intervention (W1–8)		Follow-up
Time point	W-1	W0	W5	W8	M5
Participants					
Eligibility	√				
Demographics	√				
Body mass index		√	√	√	√
Medical history	√				
Informed consent	√				
Intervention					
Real acupuncture + exercise training		√	√	√	
Sham acupuncture + exercise training		√	√	√	
Outcomes					
6MWT		√	√	√	√
mMRC		√	√	√	√
CAT		√	√	√	√
Lung function test	√	√	√	√	√
Cardiopulmonary exercise testing		√	√	√	√
Arterial blood gas analysis		√	√	√	√
Safety evaluation					
Adverse events			√	√	√

W, week; W5: after 14 treatments during the 5th week; W8: after 24 treatments during the 8th week; M5: 5 months after the baseline assessment. 6MWT, 6-minute walk test; mMRC, Modified British Medical Research Council; CAT, COPD assessment test; COPD, chronic obstructive pulmonary disease.

amegroups.com/article/view/10.21037/apm-22-949/rc).

Methods

Study design

A randomized sham-controlled trial will be conducted at The First Affiliated Hospital of Guangzhou Medical University in Guangzhou, China. A total of 70 eligible patients will be randomized at a 1:1 ratio to receive either real acupuncture and exercise training or sham acupuncture and exercise training. Patients in both treatment groups will be assessed based on outcome measures for dyspnea and exercise tolerance at the baseline and another 3 time points (see *Table 1*). *Figure 1* provides a flowchart of the design for the study, and *Table 1* sets out the study schedule. Participant recruitment started on August 2, 2020, and is expected to end on May 1, 2023.

Recruitment

Participants will be recruited from the National Clinical Research Center of Respiratory Disease at The First Affiliated Hospital of Guangzhou Medical University by telephone contact and the distribution of recruitment brochures. COPD patients meeting the study criteria will be asked to sign an informed consent form after being provided with an explanation of the study design (see the flowchart in *Figure 1*) and to undergo examinations. The screening process will last for 1 week.

Inclusion criteria

Participants will be eligible for inclusion in this study if they meet the following inclusion criteria: (I) are aged between 40–75 years; (II) have been diagnosed with COPD according to the Global Initiative for Chronic Obstructive

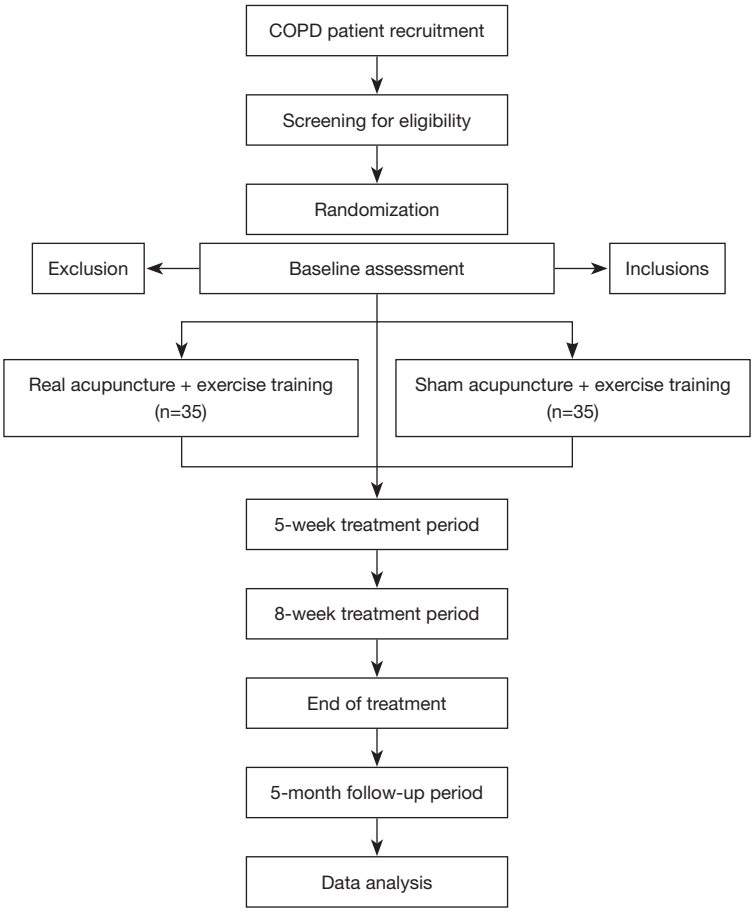

Figure 1 Flowchart of the study design. COPD, chronic obstructive pulmonary disease.

Lung Disease (GOLD) (1); (III) are clinically stable and have not experienced any exacerbations or changes in medications within the last 3 months; and (IV) are willing to participate in the trial and be randomly allocated to either study group.

Exclusion criteria

Participants will be excluded from the study if they meet any of the following criteria: have a neurological disease or mental illness affecting their cognition and communication; (II) have had a serious cardiovascular diseases within the past one year, including severe arrhythmia, severe cardiac insufficiency, unstable angina pectoris, and acute myocardial infarction; (III) have hypertension with unsatisfactory blood pressure control (systolic blood pressure >160 mmHg and/or diastolic blood pressure >100 mmHg) within the past 3 months; (IV) have a pathological condition affecting acupuncture and the performance of physical activity, including hemopathy, severe dermatopathy, serious diabetes, osteoarthropathy, and sequelae of cerebrovascular disease; (V) have undergone pulmonary rehabilitation in the last 6 months.

Randomization and allocation concealment

After completing the baseline evaluation, the eligible participants will be randomly allocated to either the real acupuncture and exercise training group (REG) or the sham acupuncture and exercise training group (SEG) by an independent investigator. All the participants will be informed that they will be allocated into 1 of the 2 groups with the same probability. Randomization will be performed according to the random sequence generated by SPSS software (SPSS, version 26.0, SPSS Inc., Chicago, IL, USA). The random sequence and group allocation information will be sealed in opaque envelops before being provided to the acupuncturists, who will be the only persons aware of the

Table 2 Details of the acupoints used in all groups

Acupoints (standard abbreviation/ Chinese nomenclature)	Location	Indication
ST 16/Yingchuang	4 cun* lateral to the anterior midline, in the 3rd intercostal space	Promotes the circulation of *qi*△
ST 18/Rugen	Directly below the nipple, on the root of breast, in the 5th intercostal space and 4 cun lateral to the anterior midline	Activates the circulation of *qi* to relieve symptoms, such as cough and asthma
ST 25/Tianshu	2 cun lateral to the center of the umbilicus	Regulates the function of the spleen and the stomach
ST 40/Fenglong	On the lateral side of the shank, 8 cun above the tip of external malleolus and 2 fingers' breadth from the anterior crest of the tibia	Strengthens the spleen to dispel water dampness and phlegm
CV4/Guanyuan	3 cun below the umbilicus at the anterior midline	Cultivates and replenishes the primordial *qi*
CV12/Zhongwan	4 cun above the umbilicus at the anterior midline	Cultivates the function of the stomach to benefit the generation of *qi* and blood
CV17/Danzhong	At the level of the 4th intercostal space and midway between the nipples	Improves the circulation of *qi* and relieves shortness of breath

*, cun is a measurement used to locate acupoints; 1 cun equals the distance between the 2 medial ends of the creases of the interphalangeal joints of the middle finger; under TCM theory; △*qi* is the most essential substance that makes up the body and maintains life activities. TCM, traditional Chinese medicine.

grouping allocation of the patients before the treatment.

Blinding

A single-blind method will be adopted in this trial. Data collectors and statisticians will be blinded in this trial by using "A" and "B" to label the 2 groups, and allocation will be unconcealed till the end of the study. Before that, only the acupuncturists will know the group allocation. The questionnaires regarding blinding will be completed right after the 14th and 24th treatments, as well as at the end of the follow-up. The success of these blinding strategies will be evaluated at the end of the study. Additionally, the procedure for the SEG group will be executed using Streitberger needles (44). This kind of non-penetrating placebo needle has been frequently used as a control treatment in single-blind trials for acupuncture effect investigations (45-47).

Intervention

The intervention will include acupuncture and exercise training, which will be conducted 3 times a week (1,48) for 8 weeks, totaling 24 treatments. Each treatment session will be separated by an interval of 2–3 days. Treatment will begin with acupuncture for 30 minutes followed by exercise training for another 40 minutes with a break of 5 min between the two. To guarantee treatment adherence, acupuncture will be performed by senior acupuncturists who have held a practitioner license for >10 years and who have received training on how to use Steinberger needles. For the acupoint selection, a combination of 10 points, which are CV 4 (the fourth acupoint of the Conception Vessel), CV 12 (the twelfth acupoint of the Conception Vessel), CV 17 (the seventeenth acupoint of the Conception Vessel), and ST 40 (the fortieth acupoint of the Stomach Meridian, unilateral, on the left or right leg alternatively), ST 16 (the sixteenth acupoint of the Stomach Meridian, bilateral), ST 18 (the eighteenth acupoint of the Stomach Meridian, bilateral) and ST 25 (the twenty-fifth acupoint of the Stomach Meridian, bilateral), are located on the anterior aspect of the body, will be used for all patients based on TCM theory (49) and previous acupuncture studies on COPD (27,28) with consideration given to the importance of acupuncture points close to the respiratory muscles (31) and maintaining patients' supine position during the acupuncture process to ensure greater comfort and compliance. Details of the acupoints are presented in *Table 2*.

Real acupuncture

For the REG, real acupuncture will be performed

using sterile stainless needles (length: 30 mm, diameter: 0.30 mm; Hualun, Suzhou Hualun Medical Instrument Co., Ltd., Suzhou, China). For patient blinding, acupoints will be marked with a plastic ring, which will be covered with a plastic sheet according to the Streitberger placebo needle device (44). An additional guide tube will be fixed exactly in the center of the plastic ring to provide better needle support and facilitate the use of the electric stimulator. After the skin is sterilized with disposable 75% alcohol swabs, the needles will first be inserted through the guide tube and the plastic sheet and then into the acupoints perpendicularly with an insertion depth of 3 mm. During the needle retention of 30 minutes, no needling manipulation will be carried out and no *de qi* sensation will be required. Needle handles with the respective guide tubes will be connected to an electric stimulator (G6805-1A, Huayi Medical Co., Ltd., Shanghai, China). ST 16 and ST 18 will be connected with a pair of electrodes on the ipsilateral limb, and the same approach will be used to connect CV 17 with CV 12, CV 4 with ST 25 (unilateral), and ST 40 with ST 25 (unilateral). Stimulation will be given at a low frequency of 2 Hz, continuous wave, with the intensity adjusted to produce minute vibrations of the needles without pain or discomfort. After 30 minutes, the stimulator will be turned off and the needles will be removed. After needle withdrawal, the acupuncturist will take an appropriate position to block the patient's sight and discard the needles in covered boxes to avoid unblinding.

Sham acupuncture

For the SEG, Streitberger placebo needles (length: 30 mm, diameter: 0.30 mm; Asiamed Inc., Bridport, UK) with blunt tips (44) will be used in the same areas with the same device as those in the REG. However, while these placebo needles appear to penetrate the skin after puncturing, the need tip is actually telescoped back into the needle handle, so that the shortening of the needle appears the same as that in real acupuncture. The needle retention time, stimulation parameters, electrode connecting principle, and needle withdrawal method will be exactly the same as those in the REG.

Exercise training

Exercise training will be carried out on a cycle ergometer (Monark Ergomedic 828E, Fitness & Health Trade Co., Varberg, Sweden). The training session will consist of: (I) a warm-up: 5 minutes of cycling at 10% Watt (W) peak with an ergometer resistance of 0 kp (kp is a parameter of resistance in the context of Monark Ergomedic); (II) the exercise training: 30 minutes of cycling with a resistance between 0.5–2 kp, including 5 minutes at a high work rate, 70–80% W peak, and 10 minutes at 40–50% W peak; and (III) a cool-down: 5 minutes cycling at 10% W peak with a resistance of 0 kp. The progress of the work rate during the training will be decided on an individual basis to maximize the training effect using a Borg rated-dyspnea or fatigue score of 4–6 (somewhat severe to severe) or a Rating of Perceived Exertion (RPE) of 12–14 (somewhat hard) as a target training intensity (1,9) together with patients' target heart rate (HR) according to Karvonen's Formula (50), a method to determine the target HR in exercise training (51). The Saturation of Oxygen (SaO_2) and HR will be continuously monitored (PM-80000 Express, Shenzhen Mindray Biomedical Electronics Co., Ltd., Shenzhen, China) during the training sessions. Lower limb fatigue and dyspnea will be assessed using the Borg scale (52). The training will end when the Borg dyspnea or fatigue score reaches 7 or the RPE (53) score reaches 14. The modified Borg scale and the RPE scale is provided in the supplementary file (Appendix 1).

Outcome measures

The results of the lung function test and demographic information will be recorded during the screening period, including age, gender, and diagnosis. The outcome measures will be assessed at 4 time points as described in *Table 1*.

Primary outcomes

Modified British Medical Research Council (mMRC) questionnaire

The mMRC questionnaire will be used to assess dyspnea for the COPD patients (1), which is divided into 0–4 grades according to the degree of activity of the patient when the shortness of breath occurs; grade 4 indicates that the patient has difficulty breathing during the slightest activity. The mMRC questionnaire is provided in the supplementary file (Appendix 1).

COPD assessment test (CAT)

The CAT will be used to assess health status impairment in COPD (1). The questionnaire comprises a total of

8 items, including items related to cough, expectoration, chest tightness, sleep, energy, and mood, which can reflect the severity of COPD symptoms and the impact of the disease on daily life. Patients will be required to make a corresponding score for each item (using a scale of 0–5 points) according to their own conditions. The CAT score range is 0–40 points. Patients with a score of 0–10 points will be rated as being "slightly affected" by their COPD condition, those with a score of 11–20 points will be rated as "moderately affected", those with a score of 21–30 points will be rated as "severely affected", and those with a score of 31–40 points will be rated as "very severely affected". If the difference between the total scores of the tests before the treatment and after the treatment is ≥2 points, clinical significance is suggestive. The CAT is provided in the supplementary file (Appendix 1).

6-minute walk test (6MWT)

Exercise capacity will be measured by the increase in the distance of the 6MWT. The 6MWT will be performed according to the American Thoracic Society (ATS) Statement: Guidelines for the 6MWT (54). The results will be expressed as absolute values. During the walk test, fatigue and dyspnea will be measured using a modified Borg scale ranging from 0 (nothing at all) to 10 (very, very severe) (52). Oxygen saturation (SaO_2) and pulse rate will be measured by a finger pulse oximeter (YX303, Yuwell, Jiangsu Yuyue Medical Equipment Co., Ltd.) before and right after the test.

Secondary outcomes

Lung function test

Lung function will be assessed using a spirometer (Quark PFT, COSMED Co., Italy) according to ATS standards (55). Patients will complete the test for 3 times, and the best test result will be automatically selected. Absolute values (liters) and the predicted percentages (%) of the following variables will be used to assess the degree of airflow limitation: forced expiratory volume in the 1stsecond (FEV_1), forced vital capacity (FVC), FEV_1/FVC ratio, and maximum ventilatory volume (MVV) (1,56).

Cardiopulmonary exercise testing (CPET)

CPET will be carried out on a cycle ergometer (Quark CPET, COSMED Co., Italy) to evaluate patients' maximum exercise load and physical energy consumption, which can reflect exercise tolerance and assess factors that may be contributing to exercise limitations (57). During the test, the rotation speed of the cycle will be kept at 60–65 r/min, and the power will be kept at 15–25 W/min for men and 15–25 W/min for women until the patient has attained their maximum exercise tolerance. Exercise will be terminated once the patient reaches the maximum exercise load. Reasons for exercise termination and whether the patient has leg fatigue, breathlessness, chest tightness or palpitations will be recorded. A ramp-type incremental exercise program will be used to obtain the following data: pulmonary oxygen uptake (VO_2, mL min^{-1}), pulmonary carbon dioxide production (VCO_2, mL min^{-1}), metabolic volume (METs, mL $kg{\cdot}min^{-1}$), minute ventilation (V_E, L min^{-1}), oxygen pulse (VO_2/HR), maximum minute ventilation (V_{Emax}, L min^{-1}), ventilatory equivalent for oxygen (O_2), and carbon dioxide (CO_2) (V_E/VO_2 and V_E/VCO_2, respectively) (58).

Arterial blood gas analysis

Respiratory exchanges will be assessed by an arterial blood gas analysis. After routine disinfection, 2 mL of arterial blood will be extracted from each patient's femoral artery in accordance with the operating specifications. Values of potential of hydrogen (Ph), partial pressure of O_2 (Po_2, kPa), and partial pressure of CO_2 (Pco_2, kPa) will be recorded.

Patient safety

Patient safety will be assessed at each visit to avoid possible adverse events (AEs), including local pain, needle breakage, subcutaneous hematoma, bleeding, dizziness, chest pain, and fainting. All the AEs will be recorded in the AE Report Form in detail, including details of the occurrence time, end time, corresponding treatment, the relationship between the AEs and the interventions, whether or not the intervention was modified, and whether or not the relative participant was withdrawn from the trial. A primary investigation and follow-up monitoring will be performed if AEs are reported.

Data monitoring and quality control

All of the information for the interventions will be recorded at each visit on a Case Report Form (CRF), including the date of the visit, the patient's target HR for exercise training, resistance changes of the cycle ergometer, time for training and rest, training mileage, calories burned, fluctuations in HR and oxygen saturation during training, blood pressure values before and after training, and AEs. Demographics, the mMRC score, CAT score, 6MWT, results of lung function test, CPET and blood gas analysis results will also be recorded at each assessment time

point on the CRF. Drop-outs will be recorded truthfully, including the time and the reason. The drop-out rate will be included in the statistical analysis. Participant information will be confidential. All the data will be collected and reviewed by 2 data processors. To ensure the trial quality, every investigator will participate in professional training on research methods, implementation techniques, and data monitoring methods. The outcome assessments will be blinded to evaluate the recorded data. Any modification to the trial procedure will follow standard operating procedures, be recorded, and submitted to the Ethics Committee as soon as possible The data will be periodically reviewed by the director.

Sample size calculation

We propose a sample size based on the difference of 6MWT (58) between the 2 groups, which is 16.2±21.89 (mean difference ± standard deviation) according to previous trials (59) and our pilot study. The ratio between the 2 groups is 1:1. A sample size (60) of 29 patients for each group (totally 58) is estimated to have at least 80% power to detect a minimal difference between groups at a 2-sided significance level of 5% according to the following formula:

$$n1 = n2 = 2\left[\frac{\left(\mu_\alpha + \mu_\beta\right)}{\delta / \sigma}\right]^2 + \frac{1}{4}\mu_\alpha^2 \quad [1]$$

We estimate a drop-out rate of 20%. Thus, the final sample size for the trial is 70.

Statistical analysis

The statistical analysis will be performed using the Statistical Package for Social Sciences (SPSS, version 26.0, SPSS Inc., Chicago, IL, USA) software. All the statistical analysis will be carried out according to the study protocol. For the measurement data, the distribution of the continuous variables will be verified by the Shapiro-Wilk test. All the normally distributed data will be presented as the mean (standard deviation) or mean (95% confidence interval). All the non-normally distributed data will be presented as the median and interquartile range. Two-independent sample *t*-tests will be used to compare differences in the changes in all outcome measures after the intervention between the REG and control SEG. Paired sample *t*-tests will be used in the same group before and after the intervention. For the count data, binary and categorical outcomes will be described using frequencies and percentages for each group. The rank-sum test will be used to compare two independent samples which are not normally distributed. For repeated measurement analysis of continuous numerical variables, general linear models will be used, for repeated measurement analysis of ordinal variables, generalized estimating equations will be used. In addition, both intention-to-treat (ITT) analysis and per-protocol set (PPS) analysis will be used to analyze the trial relevant factors and final results. Missing data will be incorporated in the full analysis set (FAS) for the FAS analysis. The results of FAS and PPS analyses will be compared to ensure that the results are consistent. A P value <0.05 will be considered to be statistically Significant (two-sided).

Ethics and publication

The study will be conducted in accordance with the Declaration of Helsinki (as revised in 2013). This trial protocol has been approved by the Ethics Review Committee of The First Affiliated Hospital of Guangzhou Medical University (reference No. 2019-32) and registered at the Chinese Clinical Trial Registry at http://www.chictr.org.cn/ on December 29, 2019 (No. ChiCTR1900028627). All the participants will sign the informed consent before taking part in the trial. Before signing the informed consent form, the participants will be fully informed of the purpose, method, and process of this trial, be aware of the possible therapeutic benefits and medical risks of participating in this study, and be aware that they can withdraw from this study at any time without discrimination and without their medical rights being affected. The personal information and data of the participants will be kept strictly confidential, and their personal identities and information will not be disclosed in the published research results. During the implementation of the trial, details of any modification to the trial protocol, the informed consent form, and other relevant documents will be submitted to the Ethics Committee as soon as possible, and updated documents will be supplemented. Serious AEs and any events that may affect the risks and benefits of the subjects will be reported to the Ethics Committee in a timely manner. Findings of this trial will be published in peer-reviewed journals, and none of the authors has any conflicts of interest to declare.

Discussion

COPD is a leading cause of morbidity and mortality

globally, which has an economic and social burden that is both substantial and increasing (1). This trial will help to identify whether the addition of acupuncture to exercise training promotes the positive effects in relieving dyspnea and improving exercise tolerance for COPD patients compared to sham acupuncture. From the perspective of TCM, COPD is caused by a deficiency of the lung, spleen, and kidney, resulting in phlegm, blood stasis, an obstructed airway, and the stagnation of qi. Acupuncture on relevant points can promote the circulation of qi and blood, dispel phlegm and dampness, and adjust and coordinate the function of the zang-fu organs (according to TCM, zang-fu organs not only refer to the anatomical structures of the organs, but also to their physiological functions, pathological changes, and their relationship with the body and orifices). In this study, CV17, ST 16, and ST 18 have been selected to regulate qi in the chest to relieve breathlessness, while CV12, CV4, ST25, and ST40 have been selected to nourish the spleen and kidney to resolve phlegm. Acupuncture is regarded as an effective therapy for many clinical problems. It dynamically harmonizes the imbalance of qi through the meridians and acupoints. The efficacy of acupuncture in relieving respiratory symptoms for COPD patients has been shown (21-36).

By applying this safe, convenient and extensively used therapy, we expect that more positive results will be obtained to enable COPD patients to carry out exercise training more efficiently and to enrich the strategies of pulmonary rehabilitation.

This study has a number of limitations. First, the practitioners who perform the acupuncture will not be blinded to group allocation; however, efforts will be made to reduce the effect of this on the trial; for example, only the acupuncturists will know the grouping of the patients before the treatment. Second, this trial will be performed at only 1 center. Thus, it will not determine whether the results of the study are applicable to patients at other medical institutions. We hope the results of the trial provide more convincing evidence on acupuncture as an adjunctive therapy for COPD.

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Footnote

Reporting Checklist: The authors have completed the SPIRIT reporting checklist. Available at https://apm.amegroups.com/article/view/10.21037/apm-22-949/rc

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://apm.amegroups.com/article/view/10.21037/apm-22-949/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study will be conducted in accordance with the Declaration of Helsinki (as revised in 2013). This trial protocol has been approved by the Ethics Review Committee of The First Affiliated Hospital of Guangzhou Medical University (reference No. 2019-32). All the participants will sign the informed consent before taking part in the trial.

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Supplementary

Appendix 1

MODIFIED MRC DYSPNEA SCALE[a]

PLEASE TICK IN THE BOX THAT APPLIES TO YOU | ONE BOX ONLY | Grades 0 - 4

mMRC Grade 0.	I only get breathless with strenuous exercise.	☐
mMRC Grade 1.	I get short of breath when hurrying on the level or walking up a slight hill.	☐
mMRC Grade 2.	I walk slower than people of the same age on the level because of breathlessness, or I have to stop for breath when walking on my own pace on the level.	☐
mMRC Grade 3.	I stop for breath after walking about 100 meters or after a few minutes on the level.	☐
mMRC Grade 4.	I am too breathless to leave the house or I am breathless when dressing or undressing.	☐

[a] Fletcher CM. BMJ 1960; 2: 1662.

TABLE 2.5

CAT™ ASSESSMENT

For each item below, place a mark (x) in the box that best describes you currently. Be sure to only select one response for each question.

			SCORE
EXAMPLE: I am very happy	0 (X) 2 3 4 5	**I am very sad**	
I never cough	0 1 2 3 4 5	I cough all the time	
I have no phlegm (mucus) in my chest at all	0 1 2 3 4 5	My chest is completely full of phlegm (mucus)	
My chest does not feel tight at all	0 1 2 3 4 5	My chest feels very tight	
When I walk up a hill or one flight of stairs I am not breathless	0 1 2 3 4 5	When I walk up a hill or one flight of stairs I am very breathless	
I am not limited doing any activities at home	0 1 2 3 4 5	I am very limited doing activities at home	
I am confident leaving my home despite my lung condition	0 1 2 3 4 5	I am not at all confident leaving my home because of my lung condition	
I sleep soundly	0 1 2 3 4 5	I don't sleep soundly because of my lung condition	
I have lots of energy	0 1 2 3 4 5	I have no energy at all	

Reference: Jones et al. ERJ 2009; 34 (3); 648-54.

TOTAL SCORE: ◯

FIGURE 2.3

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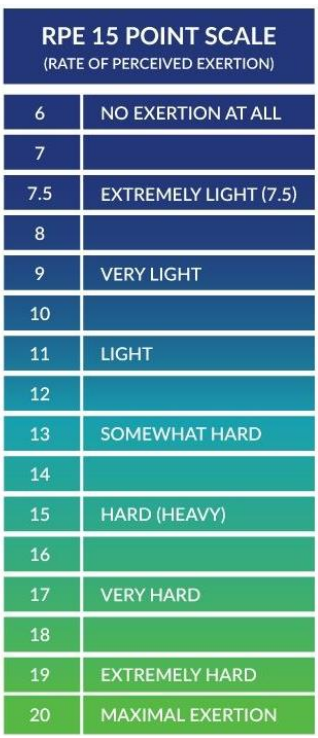
Table 1. Modified 10-Point Borg Scale[a]

Score	Severity
0	Nothing at all
0.5	Very, very slight, just noticeable
1	Very slight
2	Slight, light
3	Moderate
4	Somewhat severe
5	Severe
6	
7	Very severe
8	
9	
10	Very, very severe, maximal



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