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Original Article

Comparing penetrating needles and non-penetrating needles with electrical stimulation combined with exercise training for relief of dyspnea and improving exercise tolerance in chronic obstructive pulmonary disease patients: A single-blind randomized controlled trial

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ABSTRACT

Background: Chronic obstructive pulmonary disease (COPD) is characterized by persistent airflow limitation. The purpose of this study was to evaluate the effectiveness of penetrating needles with electrical stimulation combined with exercise training on relieving dyspnea and improving exercise tolerance among COPD patients.
Method: A total of 85 patients were recruited and randomly assigned to receive either penetrating needles with electrical stimulation (PE) or non-penetrating needles with electrical stimulation (NPE), 3 times a week, for 8 weeks, totaling 24 treatments. Both groups underwent exercise training. The evaluations were conducted at the baseline, after 14 treatments, and after 24 treatments.
Results: The PE group showed significant improvement in 6-minute walk distance (6MWD) after the 14th treatment. For pulmonary function test, MVV%, MEF50%, MEF75% and MEF25% improved in the PE group, especially MVV% was significantly higher than the NPE group. For cardiopulmonary exercise testing, METs%, VO_2/kg%, V_E%, VO_2/HR%, V_{Emax}, V_E/VO_2 and V_E/VCO_2 in the PE group improved, especially VO_2/kg%, V_E%, V_{Emax}, V_E/VO_2 and V_E/VCO_2 were significantly higher than the NPE group. The scores of COPD assessment test in the PE group significantly improved. The scores of modified British Medical Research Council in the PE group was better than the NPE group after the treatment.
Conclusion: Penetrating needles with electrical stimulation combined with exercise training may be clinically useful for COPD patients in relieving dyspnea and improving exercise tolerance.
Trial Registration: Chinese Clinical Trial Registry, ChiCTR1900028627.

1. Introduction

Chronic obstructive pulmonary disease (COPD) is one of the most common respiratory diseases characterized by persistent airflow limitation, which is not completely reversible and develops progressively[1] and expected to be the third leading cause of death worldwide by 2030.[2] Dyspnea and decreased exercise tolerance are important features of COPD patients.[3] Standardized medication can reduce the above symptoms, but can not effectively slow down the progression of the disease, prevent the decline of lung function, or prevent recurrent acute aggravation.[1] Therefore, non-drug therapy in remission is getting more attention, especially pulmonary rehabilitation (PR) is the main means. As a

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comprehensive intervention recommended by international guidelines to slow down or even reverse the decline of lung function, to improve exercise endurance, to reduce recurrence, exacerbations and medication, PR includes supervised exercise training, self-management education, psychological and social support. Among them, exercise training is the core means, which can greatly benefit the improvement of exercise endurance, muscle oxygen intake, and quality of life, and it is complementary with drug therapy.[4-6]

Currently many PR programs are based on high intensity exercise training to promote motor function by improving the oxidation ability of skeletal muscle and enhancing muscle metabolism.[4-6] However, due to the fatigue of the peripheral skeletal muscle (mainly quadriceps) and diaphragm, increased end-expiratory lung volume and hyperventilation,[7] patients would easily experience dyspnea and chest tightness at the beginning of the training, so as to restrict the training progress and affect the confidence and compliance. Moreover, due to the limitation of cardiopulmonary function conditions, COPD patients can only reach 60 % −80 % of the target exercise intensity,[1] so they cannot adhere to sufficient and effective training. High-intensity exercise training also brings risks for the heart and lung of medium and advanced COPD patients. Therefore, improving the symptom limitations of high-intensity exercise training, and effectively and stably improving the exercise intensity of COPD patients are essential to establishment of effective PR programs.

As a core integrated part of traditional Chinese medicine (TCM), acupuncture, especially penetrating needle has been widely used in treating bronchial asthma, chronic bronchitis, chronic disability dyspnea and other respiratory diseases for the past 5 decades in both Asian and Western countries for its reliability, convenience and safety.[8-12] It has been also been reported to be effective in reducing exertional dyspnea, relieving respiratory muscle fatigue, and improving the exercise capacity and quality of life of COPD patients by a series of systematic reviews[13-17] and randomized controlled trials (RCTs).[18-22] There are a few clinical trials on penetrating needles combining with exercise training in the treatment of COPD. Therefore, this randomized controlled trial was conducted to investigate the potential benefits of penetrating needles with electrical stimulation as an adjunctive therapy to exercise training, in the aspect of relieving dyspnea and improving exercise tolerance during high intensity training in order to improve the compliance and achieve the training target.

2. Methods

2.1. Study design

A randomized, single-blind study was conduced in the outpatient clinic of TCM department of the First Affiliated Hospital of Guangzhou Medical University from August 2020 to August 2023. This study was registered on December 29, 2019, in the Chinese Clinical Trial Registry (ChiCTR1900028627). The study protocol[23] was developed in accordance with the SPIRIT reporting checklist,[24] and this trial was reported following the Consolidated Standards of Reporting Trials (CONSORT) guidelines.[25]

2.2. Patients

The Global Initiative for Chronic Obstructive Lung Disease (GOLD 2022)[1] defines the diagnostic criteria for COPD. Eligible patients aged between 40 and 75 years who were clinically stable and had not experienced any exacerbations or changes in medications within the last 3 months were recruited. Stable patients routinely used long-acting β-agonist (LABA) plus inhaled corticosteroids daily.

Patients with any of the following conditions were excluded: (I) 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.

2.3. Randomization and blinding

A total of 85 eligible participants were recruited and randomly assigned to receive either penetrating needles with electrical stimulation (PE) + exercise training (ET) or non-penetrating needles with electrical stimulation (NPE) + ET therapy in a 1:1 ratio. Randomization were 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 were sealed in opaque envelops before being provided to the acupuncturists, who were the only ones aware of the grouping allocation of the patients before the treatment.

A single-blind method was adopted in this trial. Data collectors and statisticians were blinded in this trial by using “A” and “B” to label the 2 groups, and allocation was unconcealed till the end of the study. Before that, only the acupuncturists knew the group allocation. The questionnaires regarding blinding were completed right after the 14th and 24th treatments. Additionally, the procedure was executed using Streitberger-like needles.[26] This kind of non-penetrating needle has been frequently used as a tool in single blind trials investigating for the effectiveness of needling techniques.[27-29]

2.4. Interventions

The intervention included acupuncture and exercise training, which was conducted 3 times a week[1,30] for 8 weeks, totaling 24 treatments. Each treatment session was separated by an interval of 2–3 days.[31] Treatment began with acupuncture for 30 min followed by exercise training for another 40 min with a break of 5 min between the two. To guarantee treatment adherence, acupuncture was performed by senior acupuncturists who had held a practitioner license for >10 years. Based on TCM theory[32] and previous acupuncture studies on COPD[13,14] with consideration given to the importance of needling points close to the respiratory muscles[17] and maintaining patients’ supine position during the acupuncture process to ensure greater comfort and compliance, a combination of 10 acupoints was used, including CV 4 (*Guanyuan*), CV 12 (*Zhongwan*), CV 17 (*Danzhong*), ST 40 (*Fenglong*, unilateral, on the left or right leg alternatively), ST 16 (*Yingchuang*, bilateral), ST 18 (*Rugen*, bilateral) and ST 25 (*Tianshu*, bilateral).

For the PE group, patients were treated with sharp-tip needles (0.30 × 25 mm, Wuxi Jiajian Medical Instrument Co., Ltd., China), an additional guide tube fixed above a silicone base (DongBang Acupuncture, Inc.) with an adhesive sheet at the bottom were used to provide better needle support and facilitate the use of the electric stimulator. After locating acupoints with the silicone base and disinfection of the skin with iodine, needles were inserted through the tube with an insertion depth of 3 mm, and connected with an electric stimulator (G6805–1A, Huayi Medical Co., Ltd., Shanghai, China).

During the needle retention of 30 min, no needling manipulation was carried out and no *de qi* sensation was required. CV 4 and CV 12 were connected with a pair of electrodes, the same approach was applied to connect CV 17 and ST 25 (unilateral), ST 40 and ST 25 (unilateral), ST 16 and ST 18 on the ipsilateral limb, continuous wave and frequency of 2 Hz was chosen, and the operating voltage was 6 V, the current was not specified on the device but later measurement found 18 mA output.

Care was taken to position the patient so as to block the patients' sight when withdrawing the needles, and put the discarded needles into the covered box as quickly as possible.

For the NPE group, patients were treated with blunt-tip needles (0.30 × 25 mm, Suzhou Hualun Medical Instrument Co., Ltd., China), needle tips could not be penetrated into the skin, the same guide tube with the attaching device was applied, and the needles were not electrically insulated from the skin. Acupoint selection, manipulation, retention duration and electrode connecting methods were the same as the PE group.

Both groups underwent exercise training after acupuncture. Patients were instructed to wear suitable clothes and sports shoes and not to participate in heavy physical activities on the day before the exercise training. After 5 min of acupuncture, exercise training was conducted on a cycle ergometer (model Monark Ergomedic 828E, Fitless & Health Trade Co.). Heart rate, blood pressure and oxygen saturation were measured before and after the training. The total duration of each training was 40 min. During the exercise, all the COPD patients were classified as very severe for airflow limitation severity, requiring oxygen therapy with the oxygen absorption flow rate of 2–4L/min. For those who were obviously unable to withstand high-intensity training (i.e., with shortness of breath, dizziness and lower limb fatigue), each duration were kept less than 10 min. The training intensity was set and adjusted according to the target heart rate, the resistance was controlled between 0.5–2.0kp. The training intensity was considered appropriate to reach 60 %–80 % of the maximal heart rate in PR for COPD patients.[1] The maximal heart rate (HR_{max}) and target heart rate (THR) during exercise was calculated according to Karvonen's formula[33]: HR_{max}=220-age, THR=(HR_{max}-HR_{rest})×(60 % −80 %)+$HR_{rest.}$ During the exercise, the electrodes of the electrocardiograph monitor (model PM-80,000 Express, Shenzhen Mindray Bio-Medical Electronics Co., Ltd.) were connected to observe the heart rate and skin oxygen saturation. The total mileage was recorded through the display screen of the ergometer. Fluctuation range of the heart rate and oxygen saturation during exercise were recorded in 5 sessions, including 0–5 min, 5–10 min, 10–20 min, 20–35 min and 35–40 min, to judge whether the actual heart rate matched the THR and to record the duration of the match. 0–5 min was the warm-up stage, where no training intensity was required, and 35–40 min was the cool-down stage. The patients were instructed to relax and adjust the breathing and training speed. Resistance was adjusted according to the heart rate changes from the second session (5–10 min). The patients were observed to prevent adverse events including chest tightness, chest pain, shortness of breath, dizziness and lower limb fatigue. The training terminated when the Borg dyspnea or fatigue scores[34] reached 7 or the rate of perceived exertion (RPE) scale[35] scores reached 14.

2.5. Outcome measures

The primary outcome was 6-minute walk distance (6MWD). The secondary outcomes included indicators of pulmonary function test (PFT), cardiopulmonary exercise testing (CPET), scores of COPD assessment test (CAT) and scores of modified British Medical Research Council (mMRC). The evaluation points were the same for both groups. Indicators of PFT and CPET were assessed at baseline, after the 24th treatment. The remaining outcome measures were assessed at baseline, after 14th treatment, and after the 24th treatment.

2.6. Ethical considerations

This trial protocol was approved by the Ethics Review Committee of the First Affiliated Hospital of Guangzhou Medical University (Approval Number: 2019–32) and was conducted in accordance with the Declaration of Helsinki. All the participants signed the informed consent before taking part in the trial.

2.7. Sample size calculation

We calculated the sample size based on the difference of 6-min walk test[36] between the PE group and NPE group, which was 16.2 ± 21.89 (mean difference ± standard deviation) according to the previous trial[37] and our pilot study. The ratio between the 2 groups was 1:1. A sample size[38] of 29 patients for each group (58 in total) was estimated to have at least 80 % power to detect a minimal difference between groups at a 2-sided significance level of 5 %, a drop-out rate of 20 % was estimated and the final sample size for the trial was 70. To increase the reliability of the trial, we expanded the sample size to 86 cases (43 cases per group).

2.8. Statistical analysis

SPSS 22.0 software (SPSS, version 22.0, SPSS Inc., Chicago, IL, USA) was used for statistical analysis. Continuous data were expressed as the mean and standard deviation ($\bar{x} \pm s$) if normally distributed or had equal variance, or median (interquartile range, IQR) if abnormally distributed or had different variance. Categorical variables were expressed as numbers and percentages, and Chi-square test was performed for comparison between groups. Continuous data were compared using 2 sample *t*-test or Mann-Whitney U test if abnormally distributed for comparison between groups, and the data were compared using paired sample *t*-test or Wilcoxon signed-rank test if abnormally distributed for intra-group comparison. Comparison between groups of ordinal variables was performed using the Mann-Whitney U test. Comparison of the same variable at different time points was analyzed by general linear model for continuous numerical variables (non-parametric Scheirer-Ray-Hare test was used if abnormally distributed), and generalized estimating equation was used for ordered variables. *P-value*=0.05 (two-sided) was considered statistically significant.

3. Results

3.1. Participants and baseline characteristics

A total of 97 patients were recruited with 12 being excluded and 85 being eligible and randomized, 43 in the PE group and 42 in the NPE group. There were 71 patients completing 2 months' treatment and 14 cases dropped out. Among the drop-outs, 10 cases were classified as very severe and 4 cases were severe; 6 cases were in the PE group and 8 were in the NPE group. The drop-out reasons included fear of acupuncture pain, inability to tolerate training intensity and self-consciousness of poor treatment effect. The study was completed by 71 individuals (83.53 %), as presented in Fig.1.

Baseline characteristics were similar between the groups. No significant difference was found between the two groups in age, duration of the illness, body mass index (BMI), gender and classification of airflow limitation severity in COPD, as shown in Table 1.

Table 1
Baseline characteristics of the study participants.

Characteristic	PE+ET (*n* = 37)	NPE+ET (*n* = 34)	P
Age (year)	65.0 ± 6.9	65.3 ± 6.6	0.869
Gender: male (n,%)	35 (94.6 %)	28(82.4 %)	0.103
Duration of illness (year)	4.68±1.89	4.54±1.75	0.762
BMI	23.0 ± 3.9	22.6 ± 3.9	0.685
Airflow limitation severity			0.428
Mild	3 (0.08)	2 (0.06)	
Moderate	14 (0.38)	11 (0.32)	
Severe	9 (0.24)	8 (0.24)	
Sery severe	11 (0.30)	13 (0.38)	

Data are presented as mean±SD or n(%).
BMI, body mass index; ET, exercise training; NPE, non-penetrating needles; PE, penetrating needles.

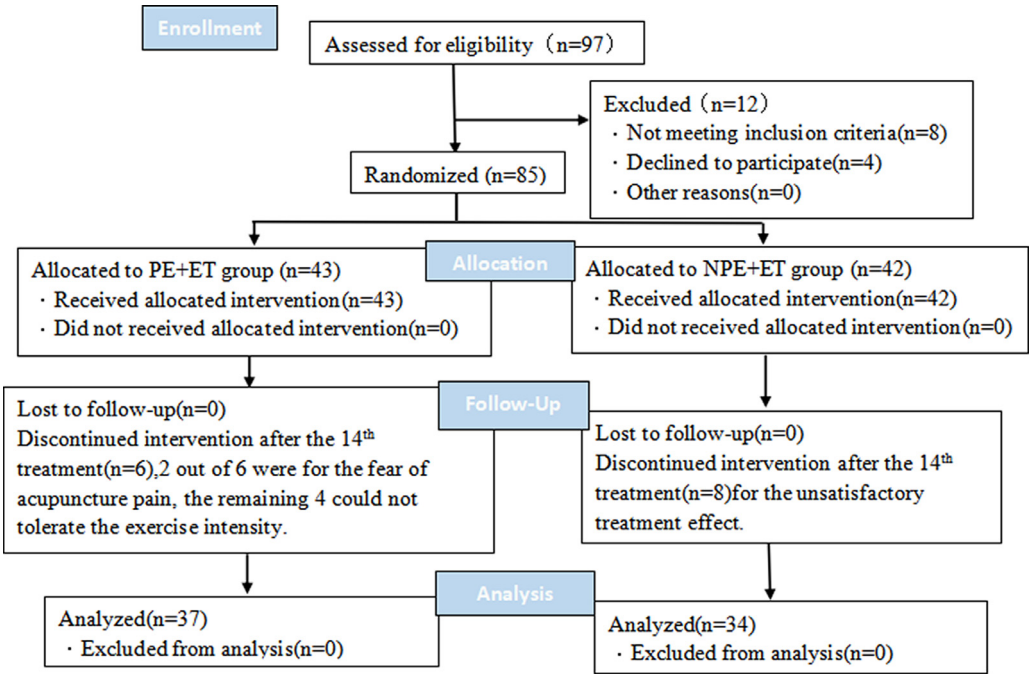

Fig.1. CONSORT flow chart of the study.

Table 2
Comparison of 6MWD and CAT scores at 3 time points between the two groups[($\bar{x} \pm s$),Median(Q25,Q75)].

	PE+ET (n = 37)	NPE+ET (n = 34)	P
6MWD			
Baseline	424.98±134.85	422.78±102.44	0.939
After the 14th treatment	462.79±140.15	425.49±105.87	0.213
After the 24th treatment	479.94±148.28	427.97±108.29	0.099
CAT scores			
Baseline	7 (4-14.5)	7.5 (5.75-15.25)	0.5
After the 14th treatment	4 (3-9.5)	7 (4-11.5)	0.071
After the 24th treatment	4 (2-7)	6 (3-12.25)	0.055

6MWD, 6-minute walk distance; CAT, COPD assessment test.

3.2. 6WMD and CAT scores

6MWD and CAT scores showed no statistical difference between the groups at each time point (Table 2).

Comparison of 6MWD at 3 time points within groups suggested a statistical difference between baseline and the 2nd as well as the 3rd time point for PE group on 6MWD ($P < 0.001$), while there was no significant different between two groups. CAT scores showed no statistical difference between the groups at each time point, but pairwise comparison of three time points of the PE group showed a statistical difference between the 1st and 3rd time point (Supplement 1, 2).

3.3. Indicators of PFT and CPET

During the trial, for pulmonary function test (PFT) indicators, FVC%,FEV_1 % and FEV_1/FVC did not improve after the treatment in both groups for comparison between groups and within groups. There were significant difference on MVV%, VO_2/kg%, V_E%, V_{Emax}, V_E/VO_2 and V_E/VCO_2 in the PE group improved after the treatment, among which VO2/kg%, VE%, VEmax, VE/VO2 and VE/VCO2 were significantly higher than the NPE group (Table 3).

FVC, forced vital capacity; FEV_1, forced expiratory volume in the first second; MEF75, forced expiratory flow after 75 % of the FVC; MEF50, forced expiratory flow after 50 % of the FVC; MEF25, forced expiratory flow after 25 % of the FVC; MET, metabolic equivalent; MVV, maximal voluntary ventilation; VO_2/HR, oxygen pulse; V_{Emax}, maximal ventilation volume per minute; VO_2/kg, oxygen consumption per kg body weight; V_E, ventilation volume per minute; V_E/VCO_2, ventilatory equivalent for carbon dioxide; V_E/VO_2, ventilatory equivalent for oxygen.

3.4. mMRC scores

There was statistical difference between groups after the treatment ($P = 0.035$), while there was no statistical difference between groups at baseline and after the 14th treatment.

Comparison of mMRC scores at 3 time points within groups showed statistical difference between the 3rd time point (after the final treatment) and 1st time point (baseline), suggesting that the dyspnea was improved in both groups at the end of treatment (Supplement 3) (Table 4).

3.5. Adverse event analysis

There was one case of subcutaneous hemorrhage after acupuncture of ST40 in both groups, and no subcutaneous hematoma was found in the subsequent treatment after pressing the acupoints with cotton swabs. 4 cases in the PE group and 5 cases in the NPE group had lower limb fatigue and shortness of breath so as to interrupt training due to the up-regulation of cycle ergometer resistance during the exercise training, which could be improved after resting, down-regulating the resistance and having low flow oxygen inhalation. The above adverse reactions turned positive after the treatment, with no serious adverse reactions and not affecting the research progress, indicating that acupuncture and exercise training were safe.

4. Discussion

There was no statistical difference between groups on 6MWD at each time point, indicating that the PE group was not better than the NPE group in improving functional exercise ability. However, the PE group improved significantly after the 14th treatment compared with the baseline, and the mean difference was 78.985 m (Supplement 3), which was

Table 3
Mean change from baseline in indicators of PFT and CPET domains by treatment group.

	PE+ET (n = 37)		NPE+ET (n = 34)		Between-group difference	
	Mean change (95 % CI)	P	Mean change (95 % CI)	P	Mean change (95 % CI)	P
FVC%	−2.9 (−6.1 to 0.1)	0.059	−0.1 (−2.6 to 2.4)	0.926	6.5 (−2.8 to 15.8)	0.170
FEV_1 %	−1.3 (−2.8 to 0.2)	0.087	1.0 (−0.7 to 2.7)	0.233	6.7 (−2.8 to 16.3)	0.165
FEV_1/FVC	−2.7 (−5.8 to 0.3)	0.084	2.3 (0.3 to 4.3)	0.024	6.6 (−2.6 to 15.9)	0.156
MVV%	−3.8 (−5.7 to −1.9)	<0.001	−0.1 (−1.6 to 1.4)	0.871	9.9 (−0.1 to 19.7)	0.046
MEF75 %	−1.6 (−2.6 to −0.7)	0.001	0.4 (−0.5 to 1.4)	0.358	4.7 (−3.6 to 12.9)	0.261
MEF50 %	−2.3 (−3.1 to −1.5)	<0.001	0.6 (0.1 to 1.1)	0.016	5.4 (−0.2 to 11.1)	0.060
MEF25 %	−2.4 (−3.3 to −1.5)	<0.001	2.1 (0.7 to 3.5)	0.003	2.9 (−2.4 to 8.2)	0.280
METs%	−3.6 (−5.6 to −1.6)	0.001	2.4 (−1 to 5.9)	0.166	7.6 (−3.6 to 18.8)	0.179
VO_2/kg%	−4.7 (−6.6 to −2.8)	<0.001	3.5 (1.8 to 5.3)	<0.001	11.1 (1.0 to 21.2)	0.031
V_E%	−13.3 (−18.5 to −8.1)	<0.001	11.0 (5.4 to 16.7)	<0.001	14.6 (4.1 to 25)	0.007
VO_2/HR%	−4.8 (−6.4 to 3.1)	<0.001	5.7 (3.4 to 8.1)	<0.001	3.7 (−6.0 to 13.5)	0.446
V_{Emax}/L·min $^{-1}$	−5.4 (−6.9 to −4)	<0.001	3.8 (2 to 5.6)	<0.001	13.8 (6.4 to 21.1)	<0.001
V_E/VO_2	4.7 (3.5 to 6.0)	<0.001	−3 (−4.7 to −1.2)	0.001	−6.0 (−10.4 to −1.7)	0.007
V_E/VCO_2	3.8 (2.7 to 4.9)	<0.001	−5 (−6.4 to −3.6)	<0.001	−6.8 (−10.9 to −2.7)	0.002

Table 4
Comparison of mMRC Dyspnea Scale scores at 3 time points between the two groups (N, %).

mMRC scores	Grade 0	Grade 1	Grade 2	Grade 3	Grade 4	P (between groups)
Baseline						
PE+ET (n = 37)	16 (43.2)	5 (13.5)	8 (21.6)	8 (21.6)	0 (0)	0.281
NPE+ET (n = 34)	7 (20.6)	11 (32.4)	9 (26.5)	6 (17.6)	1 (2.9)	
After the 14th treatment						
PE+ET (n = 37)	16 (43.2)	9 (24.3)	7 (18.9)	4 (10.8)	1 (2.7)	0.507
NPE+ET (n = 34)	12 (35.3)	9 (26.5)	7 (20.6)	6 (17.6)	0 (0)	
After the 24th treatment						
PE+ET (n = 37)	22 (59.5)	6 (16.2)	5 (13.5)	4 (10.8)	0 (0)	0.035
NPE+ET (n = 34)	11 (32.4)	8 (23.5)	10 (29.4)	5 (15.7)	0 (0)	

mMRC, modified British Medical Research Council.

much greater than the minimal clinically important difference (MCID) of 50 m.[39] It showed that the exercise endurance of the PE group had improved significantly after the 14th treatment, and it was increased even more significantly after the 24th treatment. Although there was no difference in 6MWD between groups, it was significantly improved after the treatment for the PE group, indicating that penetrating needles had a benign adjustment effect on exercise restriction caused by pulmonary symptoms in COPD patients, so as to carry out target intensity of the exercise training more effectively.

MVV%, MEF75 %, MEF50 % and MEF25 % of the PE group were significantly improved, among which MVV% and MEF50 % were significantly better than the NPE group. MVV evaluated the maximum amount of ventilation achieved by spontaneous inhalation and exhalation over a certain period of time, and reflected the ventilatory reserve. Previous study[40] showed that MVV had equal or better correlation with clinical study data for dyspnea, exercise capacity, inspiratory muscle strength and functional status in COPD patients, which was a better predictive indicator than FEV_1. For FVC%, FEV_1 % and FEV_1/FVC, there were no significant differences between the PE and NPE groups.

The VO_2/kg%, VO_2, V_E, V_E/VO_2 in the PE group were better than the NPE group after the treatment, reflecting PE group had better improvement in oxygen utilization capacity, respiratory exchange rate, maximum exercise capacity and gas exchange efficiency in unit time than the NPE group. In addition, METs%, VO_2/kg%, V_E%, VO_2/HR%, V_{Emax}, V_E/VO_2, and V_E/VCO_2 in PE group improved after the treatment, indicating the overall situation in energy metabolism and cardiopulmonary reserve had improved for PE group. mMRC dyspnea scale scores in the PE group was better than the NPE group after the final 24th treatment. However, there were no significant differences between the two groups at the other two time points, and both groups could improve the scores after the full treatment, indicating that both groups could improve dyspnea, and the PE group had better results.

Overall, the PE group showed higher improvement than the NPE group in small airway ventilation, ventilation reserve, oxygen utilization, gas exchange efficiency, exercise capacity, and dyspnea. This study used CV17, CV12 and CV4 which were the main acupoints of the upper, middle and lower energizers respectively to regulate the transforming functions of the triple energizer and make the qi activity normal.[41] The main acupoints when combined with ST16 and ST18 (acupoints locating in the chest), it would improve the dispersing and descending functions of the lung; when combined with ST25 (acupoint locating in the abdomen), it would improve the transportation and transformation functions of the spleen; and when combined with ST 40, it would expel phlegm and replenish the kidney to improve the function of discharging water so that shortness of breath could be relieved.[42] Moreover, as the main manifestation of COPD patients is respiratory muscle fatigue,[1] needle penetration has the role of relieving muscle tension and fatigue.[43] The core acupoints used in this study included ST16 and ST18, located in the 3rd and 4th intercostal area, corresponding to the inspiratory muscle, and CV12, CV4 and ST25, located in the rectus abdominis, corresponding to the accessory expiratory muscle. Therefore acupuncture had the effect of relaxing muscle tension and improving the respiratory muscle force.[44]

There are three reasons for applying this technique in this study. First, almost half of the acupoints were located in the intercostal muscles, deep needling would possibly cause pneumothorax for COPD patients with pulmonary bullae, and superficial needling was chosen to maintain the consistency of the stimulation of all the acupoints. Second, pathogenesis of COPD in the perspective of TCM mostly involves deficiency of lung, spleen and kidney. Considering the majority of the subjects were asthenia syndrome and repeated needling, superficial needling is suitable and can improve their compliance. Third, to compare the efficacy of penetrating needles and non-penetrating needles, it is necessary to use retractable needles with blunt tips and a guide tube mounted on a base adherent to the skin,[45] with the needling direction

could only be perpendicular rather than oblique or horizontal. Combined with the above-mentioned characteristics of the disease and the patients' constitution, superficial needling could only be chosen. Studies have found that superficial needling can stimulate the skin and lead to activity of afferent nerves, affecting the corresponding functional areas of the brain and producing the "limbic touch response" and acupuncture effect.[46-47]

For NPE group, the guide tube was known to create a stretching and pressure on the tissue at the insertion site and the tapping insertion method accelerated the speed of a needle insertion.[48] Therefore, although the needle with the blunt tip did not penetrate the skin with only a slight pinprick sensation, the stimulation of the acupoints included pressure and electricity, both could still be partially transmitted through the skin to the acupoints, and needle selection for NPE group was according to the theory of meridians and acupoints, which was the same as PE group, it could still produce some acupuncture effect on the body,[49] therefore, some of the results changed.[50-51]

This study included some limitations. First, effectiveness of adjunctive acupuncture in COPD patients was supposed to be tested at the beginning of the trial design. However, we mistakenly used Streitberger-like needles as a placebo needle without varying the sites of needling for the sham treatment comparator group. Retractable needles with blunt tips like Streitberger needles had been widely used in various clinical trials as a placebo since its report, but the actual effect was questioned.[52-55] Klaus Linde's systematic review[56] showed a large effect of placebo needles, including retractable blunt needles, compared with other physical comfort treatments and placebo drugs. The reasonable placebo needle setting should take the needling technique and puncturing site into account so as to clarify the specificity and the true effect of acupuncture more scientifically and correctly. Therefore, sham needles should have been placed at other locations like non-acupoints outside of the same dermatomes.[57] Second, it is important to provide all the trial details for replicability of the results, but unfortunately the electric stimulator we used did not specify current output,which appears to be a problem with EA devices,[58] so we made subsequent measurements to obtain some information on current output, and in the future studies we will need to address this problem with EA devices to secure reproducibility of results. Third, the practitioners who conducted the acupuncture treatment were not be blinded to group allocation, however, efforts were made to reduce the effect of this on the trial. Fourth, this study was only conducted in a single center which resulted in the relatively small sample size. Last, there was a lack of follow-up period.The intervention period of this study was 2 months, including 24 treatments,some subjects' compliance was poor,therefore,no follow-up period was set.For further study, a follow-up period of 3 months should be set to evaluate the long-term efficacy of acupuncture as a supplementary means of pulmonary rehabilitation.

This study showed that penetrating needles with electrical stimulation combined with exercise training might improve dyspnea and exercise tolerance, reduce symptom limitation,delay other respiratory symptoms such as chest tightness in aerobic training by improving small airway ventilation, so as to improve the compliance and tolerance of aerobic training,thus more likely to achieve the target exercise intensity.

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CRediT authorship contribution statement

Ying He: Data curation, Writing – original draft. **Gui-yuan Li:** Investigation. **Chun-zhi Tang:** Investigation. **Li-ming Lu:** Data curation. **Guang-yi Xiong:** Formal analysis, Writing – original draft. **Yi Gao:** Investigation. **Juan Tong:** Conceptualization, Methodology, Writing – review & editing. **Guang-en Zhong:** Conceptualization, Methodology, Writing – review & editing.

Declaration of competing interest

The authors have no competing interests to declare.

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Ethical statement

This trial has been approved by the Ethics Review Committee of The First Affiliated Hospital of Guangzhou Medical University (Approval number: 2019–32).All participants have signed written indormed consent.

Data availability

The obtained data in the current study are available upon reasonable request from the corresponding authors.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.imr.2024.101117.

Supplement 1. Comparison of 6MWD at 3 time points within groups

Supplement 2. Comparison of CAT scores at 3 time points within groups

Supplement 3. Comparison of mMRC scores at 3 time points within groups

Supplement 4. Flow chart with outcome measures

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