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Effectiveness and safety of acupuncture as an adjunctive therapy for chronic obstructive pulmonary disease: a randomised controlled trial

Guixing Xu[1,2], Qin Luo[1], Mingsheng Sun[1], Liuyang Huang[1], Jiali Liu[3], Chunyan Yang[1], Qingsong Huang[2], Chan Xiong[4], Zuoqin Yang[5], Sha Yang[1], Fang Zeng[1,6*] and Fanrong Liang[1,6*]

Abstract

Background The effectiveness and safety of acupuncture therapy to delay lung function decline in chronic obstructive pulmonary disease (COPD) remain unclear. This study aimed to determine whether acupuncture, as an adjunctive therapy to COPD-guided medication, could prevent lung function decline.

Methods This randomised, two-centre study was conducted between February 2022 and July 2023. Men and women aged 40–80 years with COPD were recruited. Participants received active or sham acupuncture three times a week (36 sessions total). The primary outcome was the change in the percentage of forced expiratory volume for 1 s to the predicted value (FEV1%) between the baseline and after the intervention.

Results Overall, 238 participants were screened, and 74 (58 men [78.4%]; mean [standard deviation] age, 69.6 [7.2] years) were randomised into the acupuncture and sham acupuncture groups (37 per group). After the intervention, the change in FEV1% was 1.35 (95% confidence interval [CI]: -0.47 to 3.17) and -2.44 (95% CI: -4.56 to -0.33) in the acupuncture and sham acupuncture groups, respectively. The difference was -3.97 (95% CI: -6.2 to -1.74), and the adjusted difference was -3.46 (95% CI: -5.69 to -1.24, $P = 0.003$) between the groups. A significantly less decline was found in forced expiratory volume for 1 s in the acupuncture group. All treatment-related adverse events (acupuncture = 11, sham = 2) were mild.

Conclusions Compared with sham acupuncture, acupuncture plus medication may delay lung function decline. However, further studies with a larger sample size and longer-term follow-up are needed to clarify the effects.

Keywords Acupuncture therapy, Chronic obstructive, Forced expiratory volume, Lung, Pulmonary disease

*Correspondence:
Fang Zeng
zeng_fang@126.com
Fanrong Liang
acuresearch@126.com
Full list of author information is available at the end of the article

Background

Chronic obstructive pulmonary disease (COPD) is a growing global health problem [1–4], accounting for approximately 55% of all chronic respiratory diseases [5]. Between 1990 and 2017, COPD incidence showed a relative increase of 5.9% [6]. COPD affected over 300 million people and led to 3.3 million deaths [5, 6]. COPD is characterised by progressive lung function decline [7], which is associated with exacerbations [8]. Therefore, mitigating the decline in lung function stands as a crucial objective in COPD treatment.

According to the Global Strategy for the Diagnosis, Management, and Prevention of Chronic Obstructive Lung Disease, long-acting β2-receptor agonists, long-acting anticholinergics, and inhaled corticosteroids, or in combination, are recommended for COPD. These treatments have proven effective in preventing acute exacerbations in patients [9–17]. However, evidence supporting their ability to prevent a decline in forced expiratory volume in 1 s (FEV1) remains insufficient [18–21]; current evidence indicates that medications slightly reduce the FEV1 decline speed (4.9–7.3 mL/year) [22–24]. Therefore, a safe and effective treatment to delay FEV1 decline is urgently needed.

Acupuncture is one of the most popular non-pharmaceutical therapies [25], known to reduce pain, rhinitis, and other conditions [26–29]. Previous studies have demonstrated that acupuncture can improve COPD symptoms. However, evidence supporting the use of acupuncture as an adjuvant therapy to delay lung function decline in COPD is lacking [30–33]. Therefore, we aimed to conduct a randomised, two-centre, subject-blind, sham-controlled clinical trial to compare the efficacy and safety of guideline-recommended drugs plus acupuncture in Chinese patients with COPD with mild-to-severe airway obstruction.

Materials and methods

Study design

This randomised clinical trial was conducted in the Respiratory Departments of The Affiliated Hospital of Chengdu University of Traditional Chinese Medicine and Chengdu Pidu District Hospital of Traditional Chinese Medicine, Department of Respiratory Medicine, between February 2022 and July 2023. Written informed consent was obtained from all participants before randomisation. All procedures performed in studies involving human participants were conducted in accordance with the ethical standards of the Institutional Research Committees and with the 1964 Helsinki Declaration and its later amendments (all participants read and signed a dedicated consent form). The trial protocol and amendments were approved by the Ethics Committee of The Affiliated Hospital of Chengdu University of Traditional Chinese Medicine (2021KL-074) and registered in the Chinese Clinical Trial Registry (23/02/2022, https://www.chictr.org.cn/, ChiCTR2200056943). This study followed the Consolidated Standards of Reporting Trials reporting guidelines [34]. However, when this study was planned, China was experiencing the coronavirus disease 2019 (COVID-19) pandemic. Therefore, the sample size was increased to 37 participants in each group. Moreover, the revision of the protocol was reviewed and approved by the Clinical Data Testing Committee and the Ethics Committee.

Participants

The recruitment strategy included recruitment advertisements, online recruitment information on WeChat, free community clinics, and paper recruitment information distribution in the community. Eligible participants were men and women aged 40–80 years who received a diagnosis of COPD (post-bronchodilator ratio of FEV1 and forced vital capacity [FVC], [FEV1/FVC] < 0.7) according to the guidelines of the Global Initiative for Chronic Obstructive Lung Disease [9]; those without acute exacerbation in the past 4 weeks; those with an increase in FEV1 after inhalation of albuterol of < 200 ml, or an increase in the percentage of forced expiratory volume for 1 s to the predicted value (FEV1%) of < 12%; those with no history of infection, systemic oedema, or drug change within the last 3 months; those who could walk independently; individuals who did not receive pulmonary rehabilitation within the past 6 months; those willing to cooperate with the study; and individuals who provided written informed consent. The exclusion criteria were as follows: patients with severe cardiovascular, cerebrovascular, nervous system, blood system, immune system, digestive system, or thyroid dysfunction; chronic liver or kidney insufficiency; malignant tumours; pulmonary tuberculosis, bronchiectasis, pulmonary hypertension, pulmonary interstitial disease, or other active pulmonary diseases; those on long-term oxygen therapy (oxygen therapy time > 15 h/d) or mechanical ventilation; those with blood pressure or blood glucose levels outside the normal range; those with a history of mental illness or intellectual disability; pregnant or lactating women; or those who had participated in other clinical trials within the past 6 months.

Randomisation and blinding

Eligible participants who provided written informed consent were randomly assigned to receive acupuncture or sham acupuncture (1:1 ratio). An independent statistician used IBM SPSS Statistics for Windows, version 27·0 (IBM Corp., Armonk, NY, USA) to generate a 74-integer

randomisation sequence. Random sequences were placed in opaque envelopes held by research assistants not involved in participant recruitment, treatment, or evaluation. When eligible patients participated in the trial, the acupuncturist randomly received an envelope that specified the group. Only the research assistants and acupuncturists responsible for randomisation knew the patient group information, while the patients, other researchers, and statistical analysts did not know this information. All patients were in the prone position during acupuncture and could not see the acupuncture process. Additionally, each patient's acupuncture treatment was conducted in a separate room; thus, there was no opportunity for communication between the patients. The process of patient selection, randomisation, treatment, and evaluation is shown in Fig. 1, whereas the research flow chart is displayed in Fig. 2.

Interventions

Patients in all groups were required to adopt the COPD-guideline medication [9]. All patients received a total of 36 acupuncture or sham acupuncture treatment sessions (3 times/week) after baseline assessment. Each acupuncture session lasted for 30 min. Each centre had two acupuncturists who had a licenced medical certificate and > 3 years of clinical experience providing acupuncture or sham acupuncture. To improve the consistency of treatment, acupuncturists were trained using specific tests (standardised operating procedures) before treatment. Based on the revised STRICTA recommendation [35], detailed information on acupuncture and sham acupuncture are as follows:

Basic treatment

The basic treatment for all participants was based on the Global Strategy for the Diagnosis, Management, and Prevention of Chronic Obstructive Lung Disease: the GOLD Science Committee Report 2020 [9]; this included (1) Stable bronchodilators: β2 receptor agonists, anticholinergic drugs, methylxanthines, phosphodiesterase-4 inhibitors, and combination drugs; and (2) Stable anti-inflammatory drugs: glucocorticoids, antibiotics, phosphodiesterase-4 inhibitors, phlegm-reducing drugs, and other anti-inflammatory drugs.

We encourage all participants not to use drugs other than those recommended in the guidelines. However, considering that the use of traditional Chinese medicine in China during the COVID-19 pandemic was very common, the use of traditional Chinese medicine was allowed, but other TCM-related interventions were not allowed, and no participants received other treatments during the actual completion of the task.

Acupuncture group

The acupuncture points selected were based on the theory of traditional Chinese medicine and the statistical analysis of existing research regarding points suitable for patients with COPD [36]. These acupuncturists hold a Chinese medicine practice licence issued by the Ministry of Health of the People's Republic of China.

The location of acupoints is shown in Fig. 3. When the patient was relaxed and lying in the prone position, the acupuncturist disinfected the skin around the acupoints with a 75% alcohol pad and subsequently inserted the disposable Huatuo acupuncture needles (size 0.25 × 13, 0.25 × 25 and 0.25 × 40 mm) into the acupuncture points. For bilateral EX-B1 and BL20, the needle was inserted at a 90° angle and pierced down approximately 15 mm by 0.25 × 25 mm needle. For bilateral BL13, the needle was inserted at a 90° angle and pierced down approximately 10 mm by the 0.25 × 13 mm needle. Additionally, the needle of BL23 and ST36 was inserted vertically to a depth of 25–30 mm 0.25 × 40 mm needle. During acupuncture, the needle was advanced, and then the acupuncture

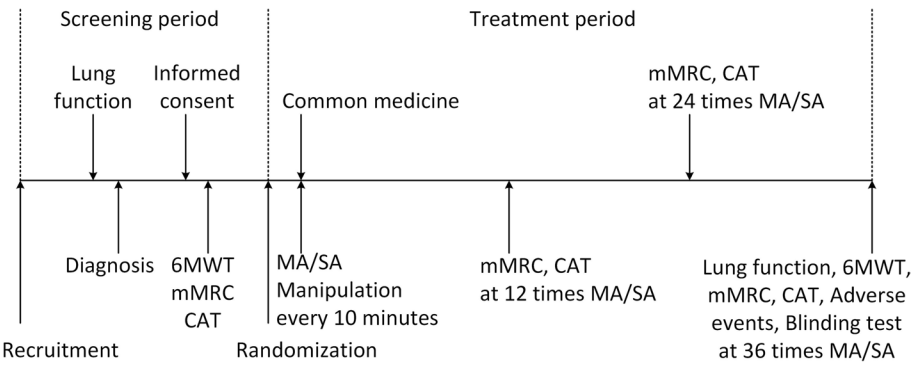

Fig. 1 Trial procedure; Note: 6MWT, six-minute walk test; mMRC, modified-medical research council; CAT, COPD assessment test; MA, Acupuncture; SA, Sham-acupuncture

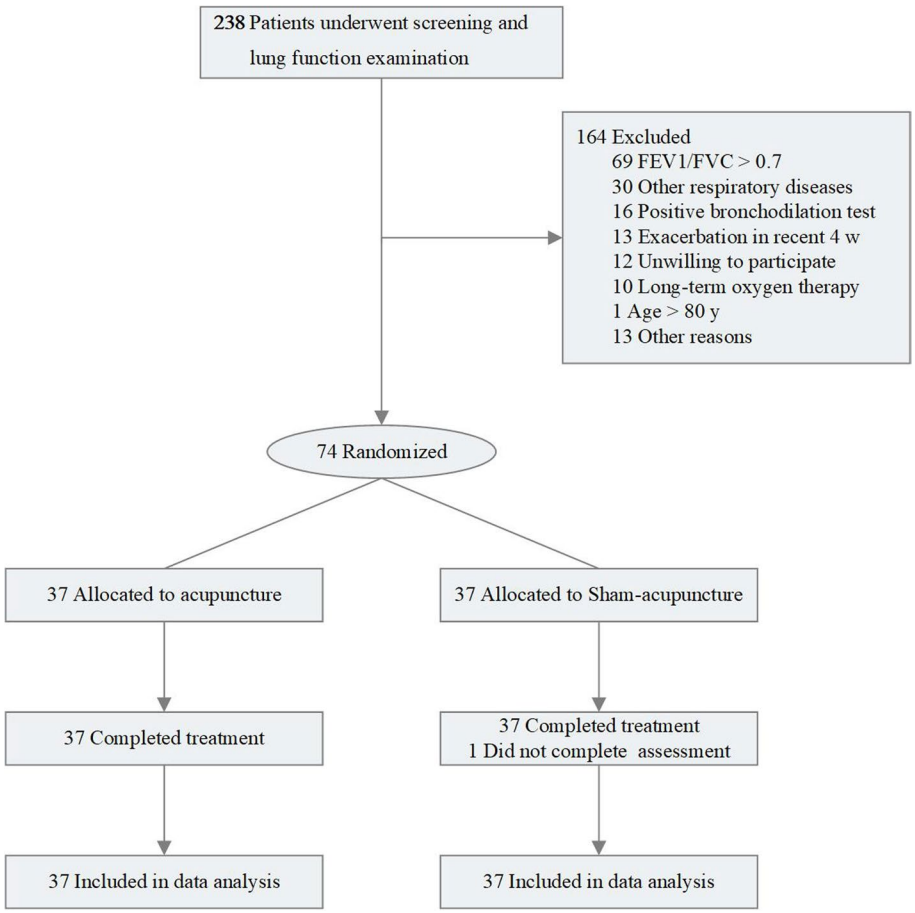

Fig. 2 Flow chart of the entire study

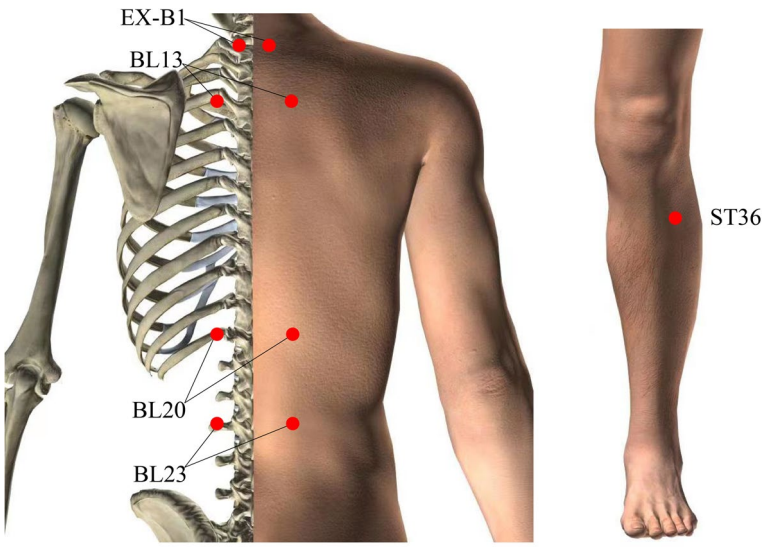

Fig. 3 Location of acupoints; Note: EX-B1, Ding chuan; BL13, Feishu; BL20, Pishu; BL23, Shenshu; ST36, Zusanli

technique of lifting and rotating was used to achieve deqi. Deqi refers to the acupuncture site's pain, soreness, swelling, heaviness, or numbness [37]. Gentle and even manipulations of deqi were conducted once every 10 min, 30 s each time. After the needle was removed, the acupuncturist immediately used a dry, sterile cotton ball to gently press the skin area punctured by the needle to avoid bleeding.

Sham acupuncture group.

In the sham acupuncture group, the bilateral dingchuai (EX-B1), feishu (BL13), pishu (BL20), shenshu (BL23), and zusanli (ST36) were performed similarly to that of Park sham acupuncture. The treatment plan of the sham acupuncture group was similar to that of the acupuncture group; however, the disposable Huatuo acupuncture needle (size 0.25 × 13 mm, no needle tip) was inserted into a silicone pad rather than the skin, and with a tingling sensation but no need deqi. The similarities and differences between acupuncture and sham acupuncture groups are summarised in Fig. 4.

In case the patient had moderate to severe acute exacerbation of COPD, we would advise the patient to suspend acupuncture treatment, undergo COPD acute attack standardised treatment and continue acupuncture after 1 week of stable condition. If a patient had COVID-19, we would suspend acupuncture treatment and continue acupuncture after 1 week of the nucleic acid test normal.

Outcomes

Primary outcome

The primary outcome was the change in FEV1% after 36 acupuncture treatments compared with the baseline.

Secondary outcomes

The secondary outcomes included the change in the modified British Medical Research Council (mMRC) Dyspnoea Scale; the COPD assessment test (CAT); 6-min walk distance (6MWD); Borg score before and after 6MWT; FEV1, FVC, and FEV1/FVC after 36 treatments compared with the baseline; the number of people whose FEV1 improvement was > 100 mL; and the number of people whose FEV1% improvement was > 5% after 36 treatments. Additionally, a blinded assessment was conducted.

Sample size determination and statistical analyses

Data from a previous study [33] showed that for the experimental population receiving acupuncture, FEV1% increased by 3.17, while the FEV1% for the population receiving sham acupuncture decreased by 1. After power

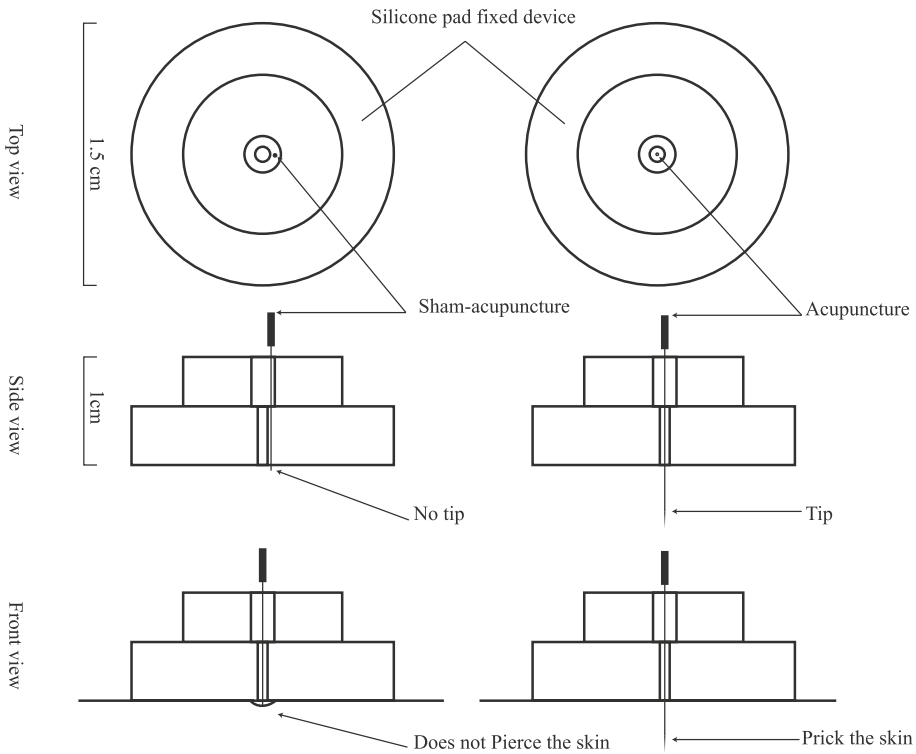

Fig. 4 Schematic diagram of acupuncture and sham acupuncture

and sample size analysis, it was estimated that 29 participants were required in each test group to detect a difference of 4.17 (4.8) in FEV1% between the acupuncture and sham acupuncture groups with 90% power at a 5% two-sided significance level. We considered a potential dropout rate of 20%; the number of participants in each group increased to 37, resulting in a total of 74.

All participants completed the treatment plan, with only one case of missing secondary outcome data; therefore, the last collected outcome was used as the subsequent evaluation result for intention-to-treat analysis. In presenting baseline characteristics, we used the mean (standard deviation [SD]) or median (interquartile range) values for continuous variables and frequencies and percentages for categorical variables. The main analysis results of this study were derived from all randomised patients based on the intention-to-treat principle. Sensitivity analysis excluded participants with FEV1% > 80% at baseline and those with moderate or severe deterioration during the study. For the change in value of FEV1, FEV1%, FVC, FEV1/FVC, 6MWD, Borg scores, mMRC, and CAT relative to baseline, we used a linear mixed-effects model with a restricted maximum likelihood for statistical analysis, setting the participant as the centre. Fixed effects included the group, sex, age, body mass index, COPD subtype, moderate-to-severe acute exacerbations during the study period, long-acting beta-agonist, long-acting anticholinergic, and smoking pack years. Random effects included the centre, baseline value of the outcome, number of moderate-to-severe acute exacerbations in the past year, acupuncture expectation, acupuncture sensation, the use of traditional Chinese medicine, antibiotic use, and the intercept.

Estimates of treatment effects are presented as adjusted differences. For the number of people whose FEV1 improvement was > 100 mL and the number of people whose FEV1% improvement was > 5%, we used the generalised offline mixed model for analysis, and its fixed and random effect settings were consistent with the main outcome analysis. Due to the possibility of type I error in multiple comparisons, the secondary outcome should be interpreted as exploratory. Statistical analyses were performed using SPSS statistical software with a 5% two-sided significance level.

Results

Study details

Between February 2022 and July 2022, 238 participants were screened, and 74 (31.9%) (58 [78.4%] men; mean [SD] age, 69.6 [7.2] years) were randomly assigned to receive the acupuncture ($n = 37$) or sham acupuncture ($n = 37$). All patients completed the trial (Fig. 2). The demographic characteristics at baseline are presented in Table 1. All results presented in Table 2 are consistent with sensitivity analysis findings presented in eTables 2 and 3 in Additional file 1.

Primary outcome

For the primary outcome, the acupuncture group showed a smaller decline in FEV1% after 36 treatments than the sham acupuncture group (1.35 [95% confidence interval [CI]: -0.47 to 3.17] vs. -2.44 [95% CI: -4.56 to -0.33]; adjusted difference, -3.46 [95% CI: -5.69 to -1.24]; $P = 0.003$) in Fig. 5. However, no significant difference was observed in the number of participants whose FEV1% improvement was > 5% (21.6% [8 of the 37 patients] vs. 13.5% [5 of the 37 patients]; adjusted difference, -4.72 [95% CI: -16.02 to 6.59]; $P = 0.407$).

Secondary outcomes

FEV1 declined significantly less in the acupuncture group after 36 treatments than in the sham acupuncture group (0.03 [95% CI: -0.02 to 0.07] vs. -0.06 [95% CI: -0.09 to -0.02], $P = 0.023$), and the number of patients whose FEV1 increased > 100 mL was (56.8% [21 of the 37 patients] vs. 35.1% [13 of the 37 patients], $P = 0.001$) in the acupuncture and sham acupuncture groups in Fig. 5. However, the FVC change was not significantly different between the groups in Fig. 5. The FEV1/FVC change was significantly different (1.44 [95% CI: 0.22–2.66] in the acupuncture group vs. -1.42 [95% CI: -3.45 to 0.62] in the sham acupuncture group, $P = 0.006$) in Fig. 5.

For the 6MWT, a slight increase was observed in the 6MWD in the acupuncture group compared with that in the sham acupuncture group (4.13 [95% CI: -8.56 to 16.82] vs. -5.29 [95% CI: -18.64 to 8.05], $P = 0.032$). The Borg after test revealed a slight decrease in the acupuncture group (-0.62 [95% CI: -1.07 to -0.17]) and a slight increase in the sham acupuncture group (0.27 [95% CI: -0.25 to 0.79]), $P = 0.035$).

The acupuncture group showed a decrease in the mMRC score (-0.65 [95% CI: -0.83 to -0.47]) vs. (-0.24 [95% CI: -0.48 to 0]) in the sham acupuncture group, $P = 0.025$. No significant difference was observed in CAT scores between the two groups. All results were consistent after sensitivity analyses (eTables 2 and 3, Additional file 1).

Notably, no serious adverse events (AEs) were observed in the two groups. AEs occurred in 13 patients (acupuncture = 11 and sham = 2) during the study period. Three patients in the acupuncture group complained of a tingling sensation after inserting the acupoint, seven experienced subcutaneous bruising after acupuncture, and three described local pain at the acupoint lasting 1–2 days after acupuncture of ST36. Two patients in the sham acupuncture group described skin itching

Table 1 Participant demographic and baseline characteristics

Variable	Participants, No. (%)		*P* value
	Acupuncture (*N* = 37)	Sham-acupuncture (*N* = 37)	
Age, mean (SD), years	68.35 (7.66)	70.78 (6.55)	0.15
Sex			
Female, No. (%)	7 (19%)	9 (24%)	0.57
Male, No. (%)	30 (81%)	28 (76%)	
Body mass index, mean (SD), kg/m^2	23.17 (4.55)	23.42 (3.45)	0.79
Height, mean (SD), cm	159.46 (7.91)	159.58 (8.39)	0.95
Weight, mean (SD), kg	59 (12.5)	59.54 (9.03)	0.83
Education, mean (SD), year	7.59 (3.9)	7.19 (3.98)	0.66
Smoking, No.(%)	25 (68%)	26 (70%)	0.80
Smoking package year, mean (SD)	28.92 (25.45)	24.87 (23.56)	0.48
Quitting smoking, mean (SD), year	7.81 (6.22)	7.15 (6.70)	0.76
Course, mean (SD), year	6.43 (4.78)	7.86 (7.28)	0.32
Subtype of COPD			
Emphysema, No. (%)	25 (68%)	22 (59%)	0.76
Chronic bronchitis, No. (%)	11 (30%)	14 (38%)	
Combine, No. (%)	1 (3%)	1 (3%)	
Complication	1 (3%)	5 (14%)	0.20
Chronic expiratory failure, No. (%)	0 (0%)	2 (5%)	
Spontaneous pneumothorax, No. (%)	0 (0%)	0 (0%)	
Pulmonary arterial hypertension, No. (%)	0 (0%)	0 (0%)	
Chronic pulmonary heart disease, No. (%)	1 (3%)	3 (8%)	
Exacerbation[a]			
In the past 1 year, mean (SD), times/year	3.22 (1.89)	2.95 (2.47)	0.60
During the study period, mean (SD), times/year	0.08 (0.28)	0.11 (0.31)	0.70
Infected with COVID-19, No. (%)			
Lung function			
FVC, mean (SD), L	2.17 (0.75)	2.10 (0.72)	0.66
FEV1, mean (SD), L	1.16 (0.51)	1.17 (0.58)	0.95
FEV1%, mean (SD)	49.12 (18.7)	51.77 (22.7)	0.59
> 80%, No. (%)	3 (8%)	2 (5%)	0.64
< 30%, No. (%)	1 (3%)	0 (0%)	0.31
FEV1/FVC, mean (SD)	48.39 (11.12)	49.22 (9.43)	0.73
6MWT			
6MWD, mean (SD), m	390.58 (68.96)	382.37 (92.71)	0.67
Borg before test	0.86 (0.97)	0.86 (1.06)	> 0.99
Borg after test	5.07 (1.92)	4.66 (2.31)	0.41
mMRC, mean (SD)	1.78 (0.89)	1.65 (0.82)	0.50
CAT, mean (SD)	13.24 (6.73)	14.3 (7.15)	0.52
Medicine, No. (%)	26 (70%)	28 (76%)	0.43
SABA, No. (%)	4 (11%)	1 (3)	0.17
SAMA, No. (%)	0 (0%)	0 (0%)	> 0.99
LABA, No. (%)	21 (57%)	25 (68%)	0.34
LAMA, No. (%)	18 (49%)	17 (46%)	0.82
ICS, No. (%)	16 (43%)	22 (59%)	0.16
Theophylline, No. (%)	8 (22%)	9 (24%)	0.78
Antibiotic, No. (%)	8 (22%)	5 (14%)	0.36
Herb, No. (%)	9 (24%)	8 (22%)	0.78
Other, No. (%)	9 (24%)	14 (38%)	0.21

Table 1 (continued)

Variable	Participants, No. (%)		*P* value
	Acupuncture (*N* = 37)	Sham-acupuncture (*N* = 37)	
Acupuncture expectation value, mean (SD)	12.89 (4.75)	11.97 (2.73)	0.31
MASS index, mean (SD)	4.79 (1.63)	1.05 (0.79)	< 0.001

MWD 6-min walk distance, *MWT* 6-min walk test, *CAT* COPD assessment test, *COPD* Chronic obstructive pulmonary disease, *COVID-19* Coronavirus disease 2019, *FEV1* Forced expiratory volume in 1 s, *FEV1%* Proportion of FEV1 to the expected value, *FVC* Forced vital capacity, *ICS* Inhaled corticosteroid, *LABA* Long-acting beta agonist, *LAMA* Long-acting anticholinergic, *mMRC* modified-medical research council, *SABA* Short-acting beta-agonist, *SAMA* Short-acting anticholinergic drug, *SD* Standard deviation

[a] Moderate to severe acute exacerbation, defined as requiring SABAs in combination with antibiotics and/or oral hormone therapy or requiring hospitalisation or emergency department visits, combined with acute respiratory failure

approximately 30 min after acupuncture. All AEs were reported as mild or moderate, and no special medical intervention was required. All patients fully recovered from the AEs, and none withdrew from the trial. 36 participants in the sham acupuncture group believed they had received acupuncture, and 37 participants in acupuncture group believed that they had received acupuncture, and chi-square test $P = 0.157$.

Discussion

This trial showed the value of acupuncture as an adjunctive treatment to delay the decrease in lung function among patients with COPD. The change in FEV1% after 36 acupuncture treatments significantly differed between the two groups. Secondary outcome analysis results indicated the potential benefit of acupuncture in improving FEV1, FEV1/FVC, motor function, dyspnoea symptoms, and the number of patients whose FEV1 increased to 100 mL.

Although the study duration lasted slightly over 3 months, the results may have implications for long-term treatment of COPD. The acupuncture points selected were based on the theory of traditional Chinese medicine and the statistical analysis of existing research regarding points suitable for patients with COPD [36]. Therefore, the acupuncture protocol for this study can be used as an adjuvant treatment option to delay the decline of COPD lung function.

A previous study showed that acupuncture had benefits regarding breathlessness and the 6MWD [32], and a recent study by Suzuki et al. showed similar results [33], which are consistent with our study. However, a previous study reported no discernable benefit of acupuncture on lung function [32], contrary to other results [33]. We believe the 3-week interval in the previous study was insufficient to observe a significant decrease in COPD lung function [32]. In our study and that of Suzuki et al., a more pronounced decline in lung function was evident when measured at intervals of more than 3 months. The FEV1 at baseline in our study (1.16 [0.51]) and that in Suzuki et al.'s study (1.2 [0.4]) [33] was better than that in the study by Jobst et al. (0.83 [0.42]) [32], which account for the difference. The study found no difference in the number of patients whose FEV1% increased by > 5% between the two groups; this may be related to the irreversibility of COPD airway damage.

Another study comparing shallow acupuncture with sham TENS revealed no significant difference in dyspnoea improvement between the two groups; however, both treatments benefited patients with COPD [31]. This may be because acupuncture has a strong placebo effect. Although shallow acupuncture is considered to have a certain acupuncture effect, it is usually regarded as placebo acupuncture in existing acupuncture research [38]. However, considering its simple method of use and benefits to patients, it also may be used as an adjuvant treatment for COPD.

In COPD, delaying the decline of lung function is crucial to patients. Excessive FEV1 decline is related to the exacerbation of COPD [8]. Previous studies have found that acupuncture is beneficial in improving COPD symptoms; however, its effect on lung function is controversial. Hence, we examined the change in FEV1% as the primary outcome and explored the effect of acupuncture as an adjuvant therapy for COPD. Additionally, to evaluate the real effect of acupuncture, we used a sham acupuncture device similar to Park for the control group to reduce the psychological comfort effect.

It is worth noting that the compliance of the subjects in this study was very good. We believe that there may be several reasons: first, this study was mainly conducted in two traditional Chinese medicine hospitals, and there was a certain trust and reliance on traditional Chinese medicine treatment; second, COPD patients have been troubled by their condition for a long time and hope that more intervention measures can relieve symptoms such as dyspnea; third, the researchers and acupuncturists in this study have a high level of skills and are recognized by the subjects; fourth, most of the subjects in this study are elderly people who do not have fixed jobs and have a lot

Table 2 Primary and secondary outcomes during the study

Outcomes	Acupuncture (*N* = 37)	Sham-acupuncture (N = 37)	Difference	Adjusted difference	Adjusted *P* value
Lung function					
FEV1, mean (SD), L					
Before acupuncture	1.16 (0.99–1.33)	1.17 (0.97–1.36)	NA	NA	NA
After 36 times acupuncture	1.19 (1–1.37)	1.11 (0.92–1.3)	NA	NA	NA
Changes after 36 times acupuncture	0.03 (-0.02 to 0.07)	-0.06 (-0.09 to -0.02)	-0.09 (-0.14 to -0.04)	-0.11 (-0.2 to -0.02)	0.023
FEV1 change > 100 ml, No.(%)[a]	21 (56.8%)	13 (35.1%)	1.55 (0.22–2.89)	7.75 (3.2–12.3)	0.001
FEV1%, mean (SD), %[b]					
Before acupuncture	49.12 (42.89–55.36)	51.77 (44.2–59.34)	NA	NA	NA
After 36 times acupuncture	50.47 (43.83–57.11)	49.33 (41.68–56.97)	NA	NA	NA
Changes after 36 times acupuncture	1.35 (-0.47 to 3.17)	-2.44 (-4.56 to -0.33)	-3.97 (-6.2 to -1.74)	-3.46 (-5.69 to -1.24)	0.003
FEV1% change > 5%, No. (%)[a]	8 (21.6%)	5 (13.5%)	0.57 (-0.68 to 1.81)	-4.72 (-16.02 to 6.59)	0.407
FVC, mean (SD), L					
Before acupuncture	2.17 (1.92–2.42)	2.1 (1.85–2.34)	NA	NA	NA
After 36 times acupuncture	2.15 (1.91–2.39)	2.05 (1.81–2.3)	NA	NA	NA
Changes after 36 times acupuncture	-0.47 (-1.13 to 0.19)	-1.55 (-3.21 to 0.11)	-1.08 (-2.84 to 0.68)	-0.37 (-2.13 to 1.39)	0.577
FEV1/FVC, mean (SD)					
Before acupuncture	48.39 (44.68–52.1)	49.22 (46.07–52.36)	NA	NA	NA
After 36 times acupuncture	49.83 (46.04–53.62)	47.8 (44.31–51.29)	NA	NA	NA
Changes after 36 times acupuncture	1.44 (0.22–2.66)	-1.42 (-3.45 to 0.62)	-2.96 (-5.12 to -0.8)	-3.78 (-6.41 to -1.14)	0.006
6MWT					
6MWD, mean (SD), m					
Before acupuncture	390.58 (367.59–413.58)	382.37 (351.46–413.28)	NA	NA	NA
After 36 times acupuncture	394.71 (370.01–419.42)	377.08 (348.98–405.17)	NA	NA	NA
Changes after 36 times acupuncture	4.13 (-8.56 to 16.82)	-5.29 (-18.64 to 8.05)	-9.68 (-27.58 to 8.23)	-36.68 (-69.78 to -3.59)	0.032
Borg before test, mean (SD)					
Before acupuncture	0.86 (0.54–1.19)	0.86 (0.51–1.22)	NA	NA	NA
After 36 times acupuncture	0.68 (0.35–1)	1.03 (0.6–1.45)	NA	NA	NA
Changes after 36 times acupuncture	-0.19 (-0.55 to 0.17)	0.16 (-0.31 to 0.64)	0.34 (-0.24 to 0.92)	0.21 (-0.32 to 0.73)	0.430
Borg after test, mean (SD)					
Before acupuncture	5.07 (4.43–5.71)	4.66 (3.89–5.43)	NA	NA	NA
After 36 times acupuncture	4.45 (3.89–5)	4.93 (4.27–5.59)	NA	NA	NA
Changes after 36 times acupuncture	-0.62 (-1.07 to -0.17)	0.27 (-0.25 to 0.79)	0.89 (0.22–1.57)	0.76 (0.06–1.47)	0.035
mMRC[c]					
Before acupuncture	1.78 (1.49–2.08)	1.65 (1.37–1.92)	NA	NA	NA
After 12 times acupuncture	1.51 (1.22–1.8)	1.57 (1.27–1.87)	0.06 (-0.34 to 0.46)	0.22 (-0.04 to 0.48)	0.092

Table 2 (continued)

Outcomes	Acupuncture (*N* = 37)	Sham-acupuncture (N = 37)	Difference	Adjusted difference	Adjusted *P* value
After 24 times acupuncture	1.3 (0.98–1.61)	1.49 (1.18–1.8)	0.2 (-0.22 to 0.62)	0.3 (-0.59 to 1.18)	0.259
After 36 times acupuncture	1.14 (0.85–1.42)	1.41 (1.11–1.7)	0.27 (-0.14 to 0.68)	0.31 (0.04–0.58)	0.025
Changes after 36 times acupuncture	-0.65 (-0.83 to -0.47)	-0.24 (-0.48 to 0)	0.42 (0.13–0.7)	0.31 (0.04–0.58)	0.025
CAT, mean (SD)					
Before acupuncture	13.24 (11–15.49)	14.3 (11.91–16.68)	NA	NA	NA
After 12 times acupuncture	11.62 (9.44–13.81)	11.92 (9.92–13.92)	0.3 (-2.61 to 3.21)	1.34 (-2.86 to 5.54)	0.505
After 24 times acupuncture	9.86 (7.95–11.78)	10.57 (8.6–12.54)	0.7 (-2 to 3.4)	2 (-0.65 to 4.65)	0.133
After 36 times acupuncture	8.57 (6.57–10.57)	10.38 (8.39–12.37)	1.81 (-0.97 to 4.59)	1.19 (-0.54 to 2.92)	0.173
Changes after 36 times acupuncture	-4.68 (-5.82 to -3.53)	-3.92 (-5.55 to -2.28)	0.77 (-1.18 to 2.72)	1.19 (-0.54 to 2.92)	0.173

MWD 6-min walk distance, *MWT*, 6-min walk test, CAT, COPD assessment test, *FEV1* Forced expiratory volume in 1 s, *FEV1%* Proportion of FEV1 to the expected value, *FVC* Forced vital capacity, *mMRC* modified-medical research council, *NA* Not applicable, *SD* Standard deviation

[a] According to the literature, it is considered that an increase in FEV1 of at least 100 ml and an increase in FEV1% of at least 5% will have minimal clinically important differences in lung function improvement

[b] FEV1% change after 36 times acupuncture was the primary outcome; other outcomes were secondary outcomes

[c] Dyspnoea was scored on a five-point Likert scale; the higher the score, the more severe the symptoms of dyspnoea, 0 means no symptoms of dyspnoea, and 4 means extremely severe dyspnoea

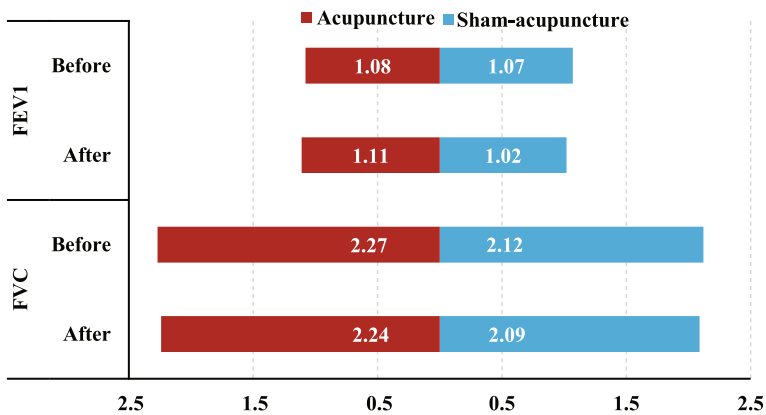

Fig. 5 The main outcome of lung function; Note: FVC, forced vital capacity (L); FEV1, forced expiratory volume in 1 s (L); Before, baseline period measurement (before acupuncture); After, post-treatment measurement (after acupuncture); Red represents the acupuncture group, and blue represents the sham acupuncture group

of time to participate in the management of diseases and interpersonal relationships; fifth, the entire treatment process in this study is completely free, and the transportation expenses they incur during the treatment process can be reimbursed, which reduces their financial burden.

This trial had some limitations. First, the trial was conducted in two centres, and potential participant bias could affect generalisation; however, conducting a study at fewer centres helps to control the quality of research. Second, during the COVID-19 pandemic, considering the potential benefit of traditional Chinese medicine for infected patients [39, 40], we could not insist that they discontinue its use; however, in the mixed model, traditional Chinese medicine did not show a significant effect in our study. Third, considering that this is a preliminary study and there is no follow-up, the long-term curative effect of acupuncture and the impact of

acupuncture on acute deterioration, death, and other patient endpoints is unclear.

Conclusions

The results of this randomised clinical trial revealed that in patients with stable COPD, compared with sham acupuncture, acupuncture, and medications may delay the decline of FEV1. Acupuncture, which is acceptable and safe for COPD, may be used as a selective adjuvant therapy to delay the decline of lung function. Further studies are needed to explore the long-term effects and mechanisms of action of this intervention.

Abbreviations

COPD	Chronic obstructive pulmonary disease
FEV1	Forced expiratory volume for 1 s
FEV1%	Percentage of forced expiratory volume for 1 s to the predicted value
FVC	Forced vital capacity
SD	Standard deviation
CI	Confidence interval
mMRC	Modified British Medical Research Council
CAT	COPD assessment test; 6MWT: 6-min walk test
6MWD	6-Minute walk distance
LABA	Long-acting beta agonist
LAMA	Long-acting anticholinergic
AEs	Adverse events

Supplementary Information

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Supplementary Material 1.

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Authors' contributions

Drs. ZF and LFR had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. Dr XGX, LQ, and SMS contributed equally to this work. Concept and design: ZF and LFR. Acquisition, analysis, or interpretation of data: XGX, LQ, YCY, HLY, and LFR. Drafting of the manuscript: XGX, LQ, and SMS. Critical revision of the manuscript for important intellectual content: HLY, YS, ZF, and LFR. Statistical analysis: LJL. Obtained funding: YZQ and LFR. Administrative, technical, or material support: HQS, XC, YZQ, YS, and LFR. Supervision: LFR.

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Availability of data and materials

The data supporting the results of this study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

All procedures performed in studies involving human participants were conducted in accordance with the ethical standards of the Institutional Research Committees and with the 1964 Helsinki Declaration and its later amendments (all participants read and signed a dedicated consent form). The trial protocol and amendments were approved by the Ethics Committee of The Affiliated Hospital of Chengdu University of Traditional Chinese Medicine (2021KL-074) and registered in the Chinese Clinical Trial Registry (https://www.chictr.org.cn/, ChiCTR2200056943).

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

Author details

[1]Acupuncture and Tuina School, Chengdu University of Traditional Chinese Medicine Chinese Medicine, Chengdu, Sichuan, China. [2]Affiliated Hospital of Chengdu University of Traditional Chinese Medicine, (Sichuan Hospital of Traditional Chinese Medicine), Chengdu, Sichuan, China. [3]Chinese Evidence-Based Medicine Center and Cochrane China Center, West China Hospital, Sichuan University, Chengdu, Sichuan, China. [4]Chengdu Pidu District Hospital of Traditional Chinese Medicine, Department of Respiratory Medicine, Chengdu, Sichuan, China. [5]Chengdu Pidu District Hospital of Traditional Chinese Medicine, Department of Acupuncture and Moxibustion, Chengdu, Sichuan, China. [6]Acupuncture and Moxibustion Prevention and Treatment of Senile Diseases Key Laboratory of Ministry of Education, Chengdu University of Traditional Chinese Medicine, Chengdu, Sichuan, China.

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