Treatment

Review

Acupuncture for attenuating dyspnea in patients with chronic obstructive pulmonary disease

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Abstract

Introduction

Chronic obstructive pulmonary disease (COPD) is an increasingly serious global health problem that is associated with significant morbidity and mortality. The main pathological feature of COPD is the persistent limitation of respiratory airflow, which leads to fatigue, dyspnea and decreased physical activity. Dyspnea is a cardinal symptom of COPD and increases in severity as the course of COPD progresses. Therefore, the Global Initiative for Chronic Obstructive Lung Disease (GOLD) recommended in 2011 that COPD assessment should be based on the combination of symptoms, lung function and the risk of exacerbations. Acupuncture has become a popular treatment for various medical conditions. Whether acupuncture can improve lung function and exercise capacity in COPD patients by attenuating the dyspnea and fatigue associated with COPD is unclear. In our review, we discuss the latest assessment criteria for COPD according to the revised GOLD guidelines and summarise the most common outcome measures used to assess COPD patients. We also discuss the results of clinical trials of acupuncture treatment for COPD. The concept of the minimal clinically important difference score of outcome measures in COPD is also addressed.

Conclusion

COPD is a heterogeneous, multi-component disease that is associated with significant clinical burden and increasing mortality. Dyspnea is a common symptom. Pulmonary rehabilitation and acupuncture are effective methods of treatment in COPD patients. We call for further studies into acupuncture as a treatment method to further our understanding.

Introduction

Chronic obstructive pulmonary disease (COPD) can be caused by cigarette smoking or exposure to noxious inhalants. COPD has become an increasingly serious worldwide health problem that is associated with significant morbidity and mortality[1]. It is estimated that COPD will be the third leading cause of death worldwide and the fifth leading contributor to global disease burden by 2020[1]. The main pathological feature of COPD is persistent restricted respiratory airflow caused by chronic airway inflammation, which leads to decreased physical activity, fatigue and dyspnea[2].

The previous guidelines for the assessment of COPD severity and treatment suggested lung function testing, especially the measurement of the one-second forced expiratory volume (FEV1). Dyspnea, the subjective sensation of difficulty during breathing, is a cardinal symptom of COPD, and its severity and magnitude increase as COPD progresses[3].

Therefore, the Global Initiative for Chronic Obstructive Lung Disease (GOLD) revised the assessment criteria for COPD in 2011, recommending that COPD patients should be assessed based on a combination of symptoms, lung function and the risk of exacerbation[4].

Pulmonary rehabilitation (PR) is suggested as a non-pharmacological treatment for COPD patients to improve their exercise tolerance and decrease the dyspnea and fatigue[4]. However, whether acupuncture may be an effective non-pharmacologic treatment in COPD to attenuate dyspnea and fatigue, improve lung function and increase exercise capacity, is uncertain. In this review, we have introduced the recently revised GOLD guidelines for the assessment of COPD and summarised the most common outcome measures used in COPD. We have also analysed the results of recent clinical trials of acupuncture treatment for COPD.

Discussion

Overview of the GOLD-2011 guidelines for COPD assessment

Since 2001, the GOLD has published its recommendations for the clinical diagnosis and management of COPD. The latest GOLD guidelines were announced in 2011, and emphasise that the assessment of COPD should include the evaluation of the combined symptoms that include the severity of respiratory airflow limitations, history of exacerbations and comorbidities[4,5]. In contrast to previous recommendations, the new GOLD guidelines place less emphasis on spirometry testing for the evaluation of disease severity than on the evaluation of symptoms. The absolute level of FEV1 is no longer considered

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to be the only tool for severity classification in COPD, based on its lack of reliability as a marker for the severity of dyspnea, exercise limitation and health status impairment[2,6].

For symptom assessment, several validated questionnaires have been used to distinguish patients with severe symptoms from those with less severe symptoms. The GOLD now recommends that the modified British Medical Research Council (mMRC) questionnaire or the COPD assessment test (CAT) be used to assess dyspnea in COPD[4]. In addition, the new GOLD guidelines recommend that all COPD patients should first be assessed using the mMRC or CAT scale, with an mMRC grade of >2 or a CAT score of ≥10 as the definition of severe symptoms. Subsequent assessment of exacerbation risk is suggested to include both spirometry testing and the analysis exacerbation history, with GOLD 3 or 4 spirometry classification and two or more exacerbations during the preceding year, each representing high risk[5]. Thus, according to the GOLD-2011 guidelines, the severity of COPD can be classified as category A, B, C or D (Figure 1).

Outcome measures and the minimal clinically important difference score
COPD requires a multifaceted approach to clinical assessment and treatment. The most common methods for assessing COPD progression rely on lung function testing, with an emphasis on FEV1. However, current trends in clinical practice focus on the evaluation of clinical outcomes and patient-reported measures, such as dyspnea, exercise capacity, exacerbations, level of physical activity and health status, as essential parts of the clinical assessment of COPD beyond FEV1 measurements[7-9]. The outcomes that have been most frequently applied to the assessment and treatment of COPD, including pulmonary rehabilitation, are summarised in Table 1.

The outcome measures are further classified into dyspnea scales, quality of life scales, exercise capacity scales, pulmonary function test score and a multidimensional score[7-9]. Because dyspnea is the most common COPD-related presentation, several different approaches have been used for measuring dyspnea in clinical trials, among which the Medical Research Council scale (MRCS), modified Borg scale (MBS), shortness of breath questionnaire, baseline dyspnea index and transition dyspnea index are most often used. For quality of life measures, the scales most commonly applied are the St. George respiratory questionnaire (SGRQ), chronic respiratory disease questionnaire, medical outcomes study short form-36 and frequency of exacerbations.

The methods most often used for assessing exercise capacity following treatment for COPD patients were the 6-minute walk test (6MWT), incremental shuttle walk test, endurance shuttle walk test and ergometry (usually bicycle-ergometer or treadmill). Pulmonary function tests, including measurements of the
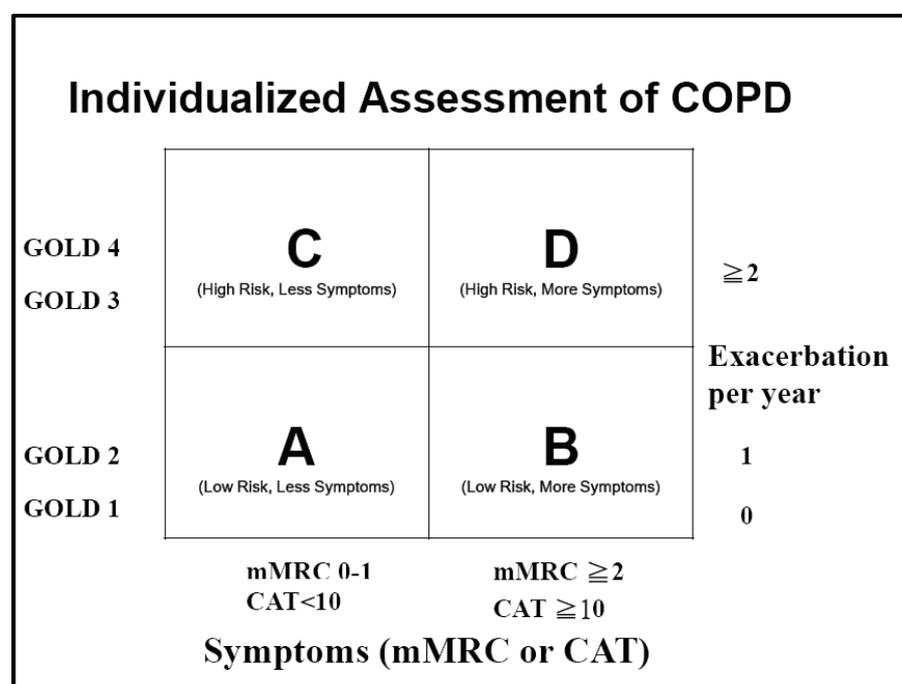
Figure 1: COPD assessment based on the severity of symptoms, spirometry and the risk of exacerbations. Based on the recommendations of the GOLD-2011 guidelines, patients with COPD should be evaluated using a two-step assessment. Patients should first be assessed using the mMRC or the CAT. Patients with less symptoms, such as mMRC grade 0–1 or CAT<10, are assigned to the left side of the box, whereas patients with more symptoms (mMRC>2 or CAT≥10) are assigned to the right side of the box. The exacerbation risk of patients should be subsequently classified as low-risk (lower area of the box) or high-risk (upper area of the box), based on spirometry results (GOLD 1–2 = low risk, GOLD 3–4 = high risk) and exacerbations history during the previous 12 months (0–1 = low risk, ≥2 = high risk). Thus, the severity of COPD can be classified as category A, B, C or D.
CAT, chronic obstructive pulmonary disease assessment test; COPD, chronic obstructive pulmonary disease; GOLD, Global Initiative for Chronic Obstructive Lung Disease; mMRC, modified British Medical Research Council questionnaire.

Table 1. Outcome measures applied in COPD.	
Dyspnea measure scales	
Parameters	**Recommended MCID**
Medical Research Council scale	1-point
Modified Borg scale (category ratio-10)	1-unit
UCSD Shortness of breath questionnaire	5-units
Visual analogue scale	10%
Baseline dyspnea index/transition dyspnea index	1-unit
Quality of life scales	
Parameters	**Recommended MCID**
St. George`s respiratory questionnaire	4-points
Chronic respiratory disease questionnaire	0.5-point
Medical outcomes study short form-36	No MCID has been established yet
Frequency of exacerbations	≤1 year or ≥2 year
Exercise capacity	
Parameters	**Recommended MCID**
6-minute walk test	54–80 m
Incremental shuttle walk test	47.5 m
Endurance shuttle walk test	No MCID has been established yet
Ergometry (bicycle-ergometer or treadmill)	No MCID has been established yet
Pulmonary function test	
Parameters	**Recommended MCID**
Forced expiratory volume in one second	Suggested 100-140 ml
Functional residual capacity, inspiratory capacity, residual volume and total lung capacity	Neither a standardised classification for the severity of hyperinflation nor a MCID has been established yet
Multidimensional scoring systems	
Parameters	**Recommended MCID**
BODE index*	No MCID has been established yet
CAT	3.76

CAT, chronic obstructive pulmonary disease assessment test; MCID, minimal clinically important difference score; UCSD, University of California San Diego.

* BODE index comprises of four components: nutritional state (body mass index), airflow limitation (obstruction, one-second forced expiratory volume), breathlessness (Medical Research Council dyspnea scale) and exercise capacity (6-minute walk test).

FEV1, functional residual capacity, inspiratory capacity, residual volume and total lung capacity have been frequently applied. Currently, multidimensional scoring, such as that based on the BODE (body mass index, degree of airflow obstruction, dyspnea and exercise capacity) index[10] and the CAT[7] are thought to be important prognosticators for COPD patients.

We suggest that acupuncture clinical trials that evaluate the treatment effect as the endpoint should use a standard set of outcome measures (Table 1). In addition, we suggest that the outcome measures should be quantified based on the minimal clinically important difference score (MCID). The MCID was developed by Jaeschke et al. in 1989 to improve assessments in which instrument-based measurements of outcomes that show statistically significant changes after intervention are not accompanied by significant changes in clinical parameters[11]. A summary of the MCIDs of standard outcome measures is shown in Table 1.

The clinical trials of acupuncture in COPD
In our survey of the literature for studies of acupuncture treatments for COPD, we used the keywords 'acupuncture and COPD' to search for clinical trials in the PubMed database. All potentially relevant full-text articles in English that used dyspnea or breathlessness as an endpoint were included in our critical review. We reviewed nine clinical trials (Table 2), including one descriptive study trial and eight randomised controlled trials (RCTs)[12-20]. Two of the RCTs used transcutaneous electrical nerve stimulation over acupoints (Acu-TENS) and the remaining seven trials used standard acupuncture for COPD patients. The outcome measures that were used included the reduction of dyspnea or the improvement of lung function. In six of the nine trials, positive results were observed following the acupuncture treatments[12,13,17,20], with the two studies of Acu-TENS treatment reporting improvements in both dyspnea and lung function in stable COPD patients[15,18].

Detailed information regarding the study design, patient selection and outcome measures of the clinical trials of acupuncture treatments for COPD are listed in Table 2. Jobst et al. used a three-week randomised controlled study to investigate whether acupuncture provided benefits based on subjective scores

of dyspnea following the 6MWT[20]. Twenty-six COPD patients were enrolled in the acupuncture and control groups. The four subjective scores derived from the outcome measures were the general well-being, shortness-of-breath, oxygen cost and modified Borg scores. The 6MWT and lung function testing, including the peak expiratory flow rate, FEV1 and forced vital capacity measurements, were conducted.

The Jobst et al.[20] study showed that the acupuncture group had significantly greater improvement in the 6MWT results and all of the subjective scores, compared with the control group. After three weeks of treatment, the mean distance of the 6MWT for the acupuncture group was 49.6 m greater than that of the control group. However, the results of lung function tests conducted before and after treatment showed no change in both groups. Jobst et al.[20] proposed that their results demonstrated significantly greater improvement in dyspnea in the COPD patients who received the acupuncture treatment.

During the past five years, the Suzuki group has conducted three RCTs of acupuncture treatment for COPD[12,13,17]. The major acupuncture points treated in the Suzuki group's studies were the LU1 (Zhongfu), LU9 (Taiyuan), LI18 (Futu), CV4 (Guanyuan), CV12 (Zhongwan), ST36 (Zusanli), KI3 (Taixi), GB12 (Wangu), BL13 (Feishu), BL20 (Pishu) and BL23 (Shenshu; Table 2). They determined the efficacy of acupuncture treatment in stable COPD patients for improving dyspnea following exercise, using the Borg scale following the 6MWT; the lung function tests and the SGRQ were also conducted. The Borg scale results showed mean improvements of 2.2 points[17], 2.0 points[12] and 3.6 points[13] in the acupuncture treatment groups. They also reported improvements in the FEV1 measurements, SGRQ scores and 6MWT distances. The results of the Suzuki group's RCTs are summarised in Table 2.

Table 2. Experimental design of clinical trials using acupuncture for dyspnea for COPD.					
Basic information	**Intervention and control**	**Acupuncture points**	**COPD status (stable or AE)**	**Outcome measures**	**Major findings in acupuncture group**
Trials with positive results					
#Jobst et al.[20] (1986); UK RCT	Acupuncture and placebo acupuncture 13 sessions in the period of three weeks	No mention about the acupuncture points	No mention about COPD stage Stable COPD	Primary: dyspnea (SOBQ score, general wellbeing score, modified Borg scale score), 6MWD	1. Significant improvement in dyspnea, general wellbeing and modified Borg scores 2. Significant increase in 6MWD: mean increase of 107.9 m
#Lau et al.[18] (2008); Hong Kong RCT	Acu-TENS (*n* = 23) and control (*n* = 23) Single 45-minute session	EX-B1 (*Ding-chuan*)	Stage I, II Stable COPD	Primary: lung function (FEV1 and FVC), dyspnea (100-mm VAS)	1. FEV1 significant increase by 0.13 L 2. Dyspnea significant decrease by 11 mm
#Suzuki et al.[17] (2008); Japan RCT	Acupuncture (*n* = 15) and control (*n* = 15) Once a week Duration: 10 weeks	LU1 (*Zhongfu*), LU5 (*Chize*), LU9 (*Taiyuan*), CV4 (*Guanyuan*), CV12 (*Zhongwan*), KI3 (*Taixi*), BL13 (*Feishu*) and BL23 (*Shenshu*)	Stage II, III, IV Stable COPD	Primary: score of modified Borg scale after 6MWT Secondary: 6MWD; the lowest SpO2 during 6MWT; FEV1, FVC and VC; MIP, MEP; FHJ score	1. Borg scale score improved from 4.4 to 2.2 2. Significant increase in 6MWD: from 380.2 to 425.6 m (+45.4 m) 2. Post-6MWT, SpO2 decline significantly improved 3. Significant increase in FEV1: from 1.25 L to 1.34 L 4. Significant improvement in MIP, MEP 5. Significant improvement in FHJ score

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Basic information	Intervention and control	Acupuncture points	COPD status (stable or AE)	Outcome measures	Major findings in acupuncture group
Trials with positive results					
#Ngai et al.[15] (2010); Hong Kong RCT	Acu-TENS (*n* = 10), placebo-TENS (*n* = 8) and Sham-TENS (*n* = 10) Five sessions per week Duration: Four weeks	EX-B1 (*Ding-chuan*)	No mention about COPD stage Stable COPD	Primary: physical (lung function, 6MWD) and psychosocial (SGRQ) function Secondary: β-endorphin, immunologic marker (IL-8, TNF-α, C-RP) levels	1. Significant increase in FEV1: from 0.79 L to 0.86 L 2. Significant increase in 6MWD: from 305.8 to 329.5 m (+23.7 m) 3. Post-6MWT, SpO2 decline significantly improved 4. SGRQ score improved (total: −5.2, activity:−9.0) 5. β-endorphin increased, 6. No changes in IL-8, TNF-α and C-RP
#Suzuki et al.[12] (2012); Japan Prospective case series	Acupuncture (*n* = 26) Once a week Duration: 10 weeks	LU1 (*Zhongfu*), LU9 (*Taiyuan*), LI18 (*Futu*), CV4 (*Guanyuan*), CV12 (*Zhongwan*), ST36 (*Zusanli*), KI3 (*Taixi*), GB12 (*Wangu*), BL13 (*Feishu*), BL20 (*Pishu*) and BL23 (*Shenshu*)	Stage I, II, III, IV Stable COPD	Primary: score of modified Borg scale after 6MWT Secondary: BODE index (BMI, degree of airflow obstruction, functional dyspnea and exercise capacity) Other: 6MWD; the lowest SpO2 during 6MWT; pulmonary function test (FEV1, FVC, FEV1%); ventilator muscle strength and endurance (MIP, MEP); MRC dyspnea scale	1. Borg scale score improved from 4.0 to 2.0 2. BODE index improved from 4.0 to 2.1 3. 6MWD increased from 371.2 m to 420.0 m (+48.8 m) 4. SpO2 during the 6MWT 5. MRC score, nutritional status, respective function and respective muscle strength improved
#Suzuki et al.[13] (2012); Japan RCT	Acupuncture (*n* = 34) and placebo needling (*n* = 34) Once a week Duration: 12 weeks	LU1 (*Zhongfu*), LU9 (*Taiyuan*), LI18 (*Futu*), CV4 (*Guanyuan*), CV12 (*Zhongwan*), ST36 (*Zusanli*), KI3 (*Taixi*), GB12 (*Wangu*), BL13 (*Feishu*), BL20 (*Pishu*) and BL23 (*Shenshu*)	Stage II, III, IV Stable COPD	Primary: score of modified Borg scale after 6MWT Secondary: 6MWD; the lowest SpO2 during 6MWT; FEV1; SGRQ Other: (DLCO, RV, TLC); (MIP, MEP, Rib cage ROM); (BMI, prealbumin); MRC dyspnea scale	1. Borg scale score improved from 5.5 to 1.9 2. 6MWD, SpO2 during the 6MWT and SGRQ improved 3. MRC score, nutritional status, respective function and respective muscle strength improved.

Review

Basic information	Intervention and control	Acupuncture points	COPD status (stable or AE)	Outcome measures	Major findings in acupuncture group
Trials with negative results					
Lewith et al.[19] (2004); UK	Acupuncture and mock TENS (n = 24) six sessions Duration: three weeks	RNE20 (*Huagai*), REN21(*Xuanji*) and LI4 (*HeGu*)	No mention about COPD stage Stable COPD	Primary: dyspnea (VAS), SGRQ	No significant treatment difference between acupuncture and mock TENS in VAS and SGRQ scores
Whale et al.[16] (2009); UK RCT	Acupuncture (n = 4) and sham (n = 5) group Daily treatment for three days	Real acupuncture-LI4 (*Hegu*) Sham acupuncture-ST25 (*Tianshu*)	No mention about COPD stage AECOPD	Primary: symptoms of dyspnea (10 cm VAS) and anxiety (10 cm VAS)	No static difference between the groups
Deering et al.[14] (2011); Ireland RCT	Acupuncture with PR (A+PR, n = 16) and PR-only (n = 25) and control (n = 19) Once a week Duration: eight weeks	CO11 (*Quchi*), CO10 (*Shousanli*), TH10 (*Tianjing*), TH6 (*Zhigou*), LU5 (*Chize*) and LU7 (*Lieque*)	Stage I, II, III, IV Stable COPD Modified MRC≥3	Primary: systemic inflammatory cytokines, such as IL-6, IL-8, TNF-α and C-RP levels Secondary: change in QoL (SGRQ and EQ-5D), MRC dyspnea scale , Borg score, Lung function (FEV1%, FVC%, MIP), ISWT and free living activities	1. No significant difference in the inflammatory markers 2. No change on spirometry 3. No significant change on the MIP and the SGRQ 4. Only small but significant benefit in the Borg score comparing A+PR with PR-only

6MWD, 6-minute walk distance; 6MWT, 6-minute walk test; Acu-TENS, acupuncture points; AE, acute exacerbations; AECOPD, acute exacerbations of COPD; BMI, body mass index; COPD, chronic obstructive pulmonary disease; CRP, C-reactive protein; DLCO, diffusing capacity of the lung for carbon monoxide; EQ-5D, EuroQoL; FEV1, forced expiratory volume in one second; FHJ score, the Fletcher Hugh-Jones category; FVC; IL, interleukin; ISWT, incremental shuttle walk test; MEP, maximum expiratory mouth pressure; MIP, maximum inspiratory mouth pressure; MRC, Medical Research Council; PR, pulmonary rehabilitation; QoL, quality of life; RCT, randomised controlled trial; ROM, range of motion; RV, residual volume; SGRQ, St George respiratory questionnaire; SOBQ, shortness of breath questionnaire; SpO2, oxygen saturation by pulse oximetry; TLC, total lung capacity; TNF, tumor necrosis factor; VAS, visual analogue scale; VC, vital capacity.
#Significant change compared with the control group by the definition of minimal clinically important difference score

Critical appraisal of the validity of acupuncture in COPD based on the MCID

The results of studies that assessed outcomes based on the MCID are summarised in Table 3. The two RCTs in which acupuncture treatment did not improve dyspnea used the visual analogue scale to quantify the outcome[16,19], whereas the Suzuki group's studies used more objective methods to measure the outcome beyond the FEV1, including the MBS, MRCS, SGRQ and 6MWT[12,13,17]. The parameters that exhibited the greatest significant differences following treatment were the MBS, SGRQ and 6MWT, all of which contributed to the significant changes observed in the MCID scores. However, the changes in the MRCS and the FEV1 following treatment were of borderline significance based on the MCID score. Thus, investigators should evaluate the data from clinical trials based on both the p value and the MCID score.

Conclusion
COPD is a heterogeneous, multi-component disease associated with significant clinical burden and increasing mortality. Dyspnea is a very common symptom in COPD because of the persistent airflow limitations caused by the chronic airway inflammation. In addition to PR, a growing body of evidence suggests that acupuncture may be an effective non-pharmacologic treatment for attenuating dyspnea in COPD patients. We suggest that studies of

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Table 3. Analysis of the clinical significance of acupuncture in COPD trials by the definition of MCID.				
Parameters	Baseline	After treatment	Change	Trial results
Modified Borg scale	5.5	1.9	−3.6	*#Suzuki et at.[13]
	4.0	2.0	−2.0	*#Suzuki et at.[12]
	4.4	2.2	−2.2	*#Suzuki et at.[17]
MRCS	3.2	2.3	−0.9	*Suzuki et at.[13]
	2.4	1.6	−0.85	*Suzuki et at.[12]
SOBQ	3.9	3.0	−0.9	*Jobst et al.[20]
SGRQ (total score)	46.2	30.2	−16.0 −5.2	*#Suzuki et at.[13] *#Ngai et al.[15]
SGRQ (symptom)	54.7	26.9	−27.8 −0.3	*#Suzuki et at.[13] Ngai et al.[15]
SGRQ (activity)	58.6	44.6	−12.0 −9.0	*#Suzuki et at.[13] *#Ngai et al.[15]
SGRQ (impact)	33.5	20.5	−13.0 −8.5	*#Suzuki et at.[13] #Ngai et al.[15]
6-MWD	373.2 335.5 305.8 380.2 227.3	436.7 389.0 329.5 425.6 304.1	+63.5 +53.5 +23.7 +45.4 +76.8	*#Suzuki et at.[13] *#Suzuki et at.[12] *Ngai et al.[15] *Suzuki et at.[17] *#Jobst et al.[20]
FEV1	1.0 1.19 0.79 1.25 1.24 0.81	1.1 1.31 0.86 1.34 1.37 0.83	+0.07 +0.12 +0.07 +0.09 +0.13 +0.02	Suzuki et at.[13] *#Suzuki et at.[12] *Ngai et al.[15] Suzuki et at.[17] *#Lau et al.[18] Jobst et al.[20]

6MWD, 6-minute walk distance; COPD, chronic obstructive pulmonary disease; FEV1, one-second forced expiratory volume; MCID, minimal clinically important difference score; MRCS, Medical Research Council scale; SGRQ, St. George respiratory questionnaire; SOBQ, shortness of breath questionnaire.

*Significant change compared with the control group by the definition of the study

#Significant change compared with the control group by the definition of MCID

the efficacy of acupuncture in COPD should use a standard set of subjective scales to obtain comparable evaluations of the clinical significance of their data, such as that provided by the MCID score.

Abbreviations list

6MWT, 6-minute walk test; Acu-TENS, acupuncture points; CAT, chronic obstructive pulmonary disease assessment test; COPD, chronic obstructive pulmonary disease; FEV1, one-second forced expiratory volume; GOLD, Global Initiative for Chronic Obstructive Lung Disease; MBS, modified Borg scale; MCID, minimal clinically important difference score; mMRC, modified British Medical Research Council questionnaire; MRCS, Medical Research Council scale; PR, pulmonary rehabilitation; RCT, randomised controlled trial; SGRQ, St. George respiratory questionnaire.

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