Acupuncture for attenuating dyspnea in patients with chronic obstructive pulmonary disease

PK Fu1, CL Hsieh2,3,4*

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.

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 comorbidities4,5. 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...
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. 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. 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.

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.
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\(^*\) and the CAT\(^2\) 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\textsuperscript{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 wellbeing, 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.\textsuperscript{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.\textsuperscript{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\textsuperscript{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\textsuperscript{17}, 2.0 points\textsuperscript{12} and 3.6 points\textsuperscript{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.

<table>
<thead>
<tr>
<th>Basic information</th>
<th>Intervention and control</th>
<th>Acupuncture points</th>
<th>COPD status (stable or AE)</th>
<th>Outcome measures</th>
<th>Major findings in acupuncture group</th>
</tr>
</thead>
<tbody>
<tr>
<td>#Jobst et al.\textsuperscript{20} (1986); UK</td>
<td>Acupuncture and placebo acupuncture 13 sessions in the period of three weeks</td>
<td>No mention about the acupuncture points</td>
<td>No mention about COPD stage Stable COPD</td>
<td>Primary: dyspnea (SOBQ score, general wellbeing score, modified Borg scale score), 6MWD</td>
<td>1. Significant improvement in dyspnea, general wellbeing and modified Borg scores 2. Significant increase in 6MWD: mean increase of 107.9 m</td>
</tr>
<tr>
<td>#Lau et al.\textsuperscript{18} (2008); Hong Kong</td>
<td>Acu-TENS (n = 23) and control (n = 23) Single 45-minute session</td>
<td>EX-B1 (Ding-chuan)</td>
<td>Stage I, II Stable COPD</td>
<td>Primary: lung function (FEV1 and FVC), dyspnea (100-mm VAS)</td>
<td>1. FEV1 significant improvement by 0.13 L 2. Dyspnea significant decrease by 11 mm</td>
</tr>
<tr>
<td>#Suzuki et al.\textsuperscript{17} (2008); Japan</td>
<td>Acupuncture (n = 15) and control (n = 15) Once a week Duration: 10 weeks</td>
<td>LU1 (Zhongfu), LU5 (Chize), LU9 (Taiyuan), CV4 (Guanyuan), CV12 (Zhongwan), KI3 (Taiixi), BL13 (Feishu) and BL23 (Shenshu)</td>
<td>Stage II, III, IV Stable COPD</td>
<td>Primary: score of modified Borg scale after 6MWT Secondary: 6MWD; the lowest SpO2 during 6MWT; FEV1, FVC and VC, MIP, MEP; FHJ score</td>
<td>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</td>
</tr>
</tbody>
</table>

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### Basic information | Intervention and control | Acupuncture points | COPD status (stable or AE) | Outcome measures | Major findings in acupuncture group
--- | --- | --- | --- | --- | ---
Ngai et al.\(^{15}\) (2010); Hong Kong RCT | Acu-TENS (n = 10), placebo-TENS (n = 8) and Sham-TENS (n = 10) | EX-B1 (Ding-chuan) | No mention about COPD stage | Stable COPD | 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) | LU1 (Zhongfu), LU9 (Taiyuan), LI18 (Futu), CV4 (Guanyuan), CV12 (Zhongwan), ST36 (Zusanli), KI3 (Taixi), GB12 (Wanggu), 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 6MW; 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 6MW 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) | LU1 (Zhongfu), LU9 (Taiyuan), LI18 (Futu), CV4 (Guanyuan), CV12 (Zhongwan), ST36 (Zusanli), KI3 (Taixi), GB12 (Wanggu), 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 6MW; pulmonary function test (FEV1, FVC, FEV1%); ventilator muscle strength and endurance (MIP, MEP); MRC dyspnea scale | 1. Borg scale score improved from 5.5 to 1.9 2. 6MWD, SpO2 during the 6MW and SGRQ improved 3. MRC score, nutritional status, respective function and respective muscle strength improved.
### 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 | REN20 (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 | 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 | Acupuncture with PR (A+PR, n = 16) and PR-only (n = 25) and control (n = 19) Once a week Duration: eight weeks | CO11 (Quichi), 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

### 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 SGRQ12,13,17. 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...

Table 3. Analysis of the clinical significance of acupuncture in COPD trials by the definition of MCID.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Baseline</th>
<th>After treatment</th>
<th>Change</th>
<th>Trial results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Modified Borg scale</td>
<td>5.5</td>
<td>1.9</td>
<td>-3.6</td>
<td>*Suzuki et al.13</td>
</tr>
<tr>
<td></td>
<td>4.0</td>
<td>2.0</td>
<td>-2.0</td>
<td>*Suzuki et al.12</td>
</tr>
<tr>
<td></td>
<td>4.4</td>
<td>2.2</td>
<td>-2.2</td>
<td>*Suzuki et al.17</td>
</tr>
<tr>
<td>MRCS</td>
<td>3.2</td>
<td>2.3</td>
<td>-0.9</td>
<td>*Suzuki et al.13</td>
</tr>
<tr>
<td></td>
<td>2.4</td>
<td>1.6</td>
<td>-0.8</td>
<td>*Suzuki et al.12</td>
</tr>
<tr>
<td>SOBQ</td>
<td>3.9</td>
<td>3.0</td>
<td>-0.9</td>
<td>*Jobst et al.20</td>
</tr>
<tr>
<td>SGRQ (total score)</td>
<td>46.2</td>
<td>30.2</td>
<td>-16.0</td>
<td>*Suzuki et al.13</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>-5.2</td>
<td>*NGai et al.15</td>
</tr>
<tr>
<td>SGRQ (symptom)</td>
<td>54.7</td>
<td>26.9</td>
<td>-27.8</td>
<td>*NGai et al.13</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>-0.3</td>
<td>*NGai et al.15</td>
</tr>
<tr>
<td>SGRQ (activity)</td>
<td>58.6</td>
<td>44.6</td>
<td>-12.0</td>
<td>*Suzuki et al.13</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>-9.0</td>
<td>*NGai et al.15</td>
</tr>
<tr>
<td>SGRQ (impact)</td>
<td>33.5</td>
<td>20.5</td>
<td>-13.0</td>
<td>*Suzuki et al.13</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>-8.5</td>
<td>*NGai et al.15</td>
</tr>
<tr>
<td>6-MWD</td>
<td>373.2</td>
<td>436.7</td>
<td>+63.5</td>
<td>*Suzuki et al.13</td>
</tr>
<tr>
<td></td>
<td>335.5</td>
<td>389.0</td>
<td>+53.5</td>
<td>*Suzuki et al.12</td>
</tr>
<tr>
<td></td>
<td>305.8</td>
<td>329.5</td>
<td>+23.7</td>
<td>*NGai et al.15</td>
</tr>
<tr>
<td></td>
<td>380.2</td>
<td>425.6</td>
<td>+45.4</td>
<td>*Suzuki et al.17</td>
</tr>
<tr>
<td></td>
<td>227.3</td>
<td>304.1</td>
<td>+76.8</td>
<td>*Jobst et al.20</td>
</tr>
<tr>
<td>FEV1</td>
<td>1.0</td>
<td>1.1</td>
<td>+0.07</td>
<td>Suzuki et al.13</td>
</tr>
<tr>
<td></td>
<td>1.19</td>
<td>1.31</td>
<td>+0.12</td>
<td>*Suzuki et al.12</td>
</tr>
<tr>
<td></td>
<td>0.79</td>
<td>0.86</td>
<td>+0.07</td>
<td>*NGai et al.15</td>
</tr>
<tr>
<td></td>
<td>1.25</td>
<td>1.34</td>
<td>+0.09</td>
<td>Suzuki et al.17</td>
</tr>
<tr>
<td></td>
<td>1.24</td>
<td>1.37</td>
<td>+0.13</td>
<td>*Lau et al.18</td>
</tr>
<tr>
<td></td>
<td>0.81</td>
<td>0.83</td>
<td>+0.02</td>
<td>*Jobst et al.20</td>
</tr>
</tbody>
</table>

6-MWD, 6-minute walk distance; 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, 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

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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.

References


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Review

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