

ONLINE FIRST

A Randomized, Placebo-Controlled Trial of Acupuncture in Patients With Chronic Obstructive Pulmonary Disease (COPD)

The COPD-Acupuncture Trial (CAT)

Masao Suzuki, LAc, PhD; Shigeo Muro, MD, PhD; Yuki Ando, MSc; Takashi Omori, PhD; Tetsuhiro Shiota, MD, PhD; Kazuo Endo, MD; Susumu Sato, MD, PhD; Kensaku Aihara, MD; Masataka Matsumoto, MD; Shinko Suzuki, MD; Ryo Itotani, MD; Manabu Ishitoko, MD; Yoshikazu Hara, MD; Masaya Takemura, MD, PhD; Tetsuya Ueda, MD, PhD; Hitoshi Kagioka, MD, PhD; Masataka Hirabayashi, MD; Motonari Fukui, MD, PhD; Michiaki Mishima, MD, PhD

Background: Dyspnea on exertion (DOE) is a major symptom of chronic obstructive pulmonary disease (COPD) and is difficult to control. This study was performed to determine whether acupuncture is superior to placebo needling in improving DOE in patients with COPD who are receiving standard medication.

Methods: Sixty-eight of 111 patients from the Kansai region of Japan who were diagnosed as having COPD and were receiving standard medication participated in a randomized, parallel-group, placebo-controlled trial (July 1, 2006, through March 31, 2009) in which the patients, evaluators, and statistician were unaware of the random allocation. Participants were randomly assigned to traditional acupuncture (real acupuncture group, n=34) or placebo needling (placebo acupuncture group, n=34). Both groups received real or placebo needling at the same acupoints once a week for 12 weeks. The primary end point was the modified Borg scale score evaluated immediately after the 6-minute walk test. Measurements were obtained at baseline and after 12 weeks of treatment.

Result: After 12 weeks, the Borg scale score after the 6-minute walk test was significantly better in the real acupuncture group compared with the placebo acupuncture group (mean [SD] difference from baseline by analysis of covariance, -3.6 [1.9] vs 0.4 [1.2]; mean difference between groups by analysis of covariance, -3.58; 95% CI, -4.27 to -2.90). Patients with COPD who received real acupuncture also experienced improvement in the 6-minute walk distance during exercise, indicating better exercise tolerance and reduced DOE.

Conclusion: This study clearly demonstrates that acupuncture is a useful adjunctive therapy in reducing DOE in patients with COPD.

Trial Registration: umin.ac.jp/ctr Identifier: UMIN000001277

Arch Intern Med.

Published online May 14, 2012.

doi:10.1001/archinternmed.2012.1233

CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD), a common disease characterized by irreversible airflow limitation, is predicted to be the third leading cause of death worldwide by 2020.¹ Dyspnea, the most fundamental and debilitating symptom of COPD, is associated with considerable disease burden, affecting many aspects of everyday life. The severity of dyspnea generally progresses over time in patients with COPD,² and dyspnea has been found to be predictive of survival in COPD. Therefore, the management of dyspnea is one of the most important targets in the treatment of COPD.

Acupuncture has been shown to reduce breathlessness in patients with can-

cer.³ A review⁴ of 16 randomized controlled trials, involving 2937 participants, concluded that acupuncture is a safe and potentially effective intervention for patients with asthma and COPD.

See Invited Commentary at end of article

We previously demonstrated that dyspnea and exercise capacity evaluated by Borg scale scores and the 6-minute walk distance (6MWD) test could be markedly improved with acupuncture in a prospective, matched-pair trial in COPD patients who were receiving standard medication.⁵ However, the interpretation of our results is somewhat limited be-

Author Affiliations are listed at the end of this article.

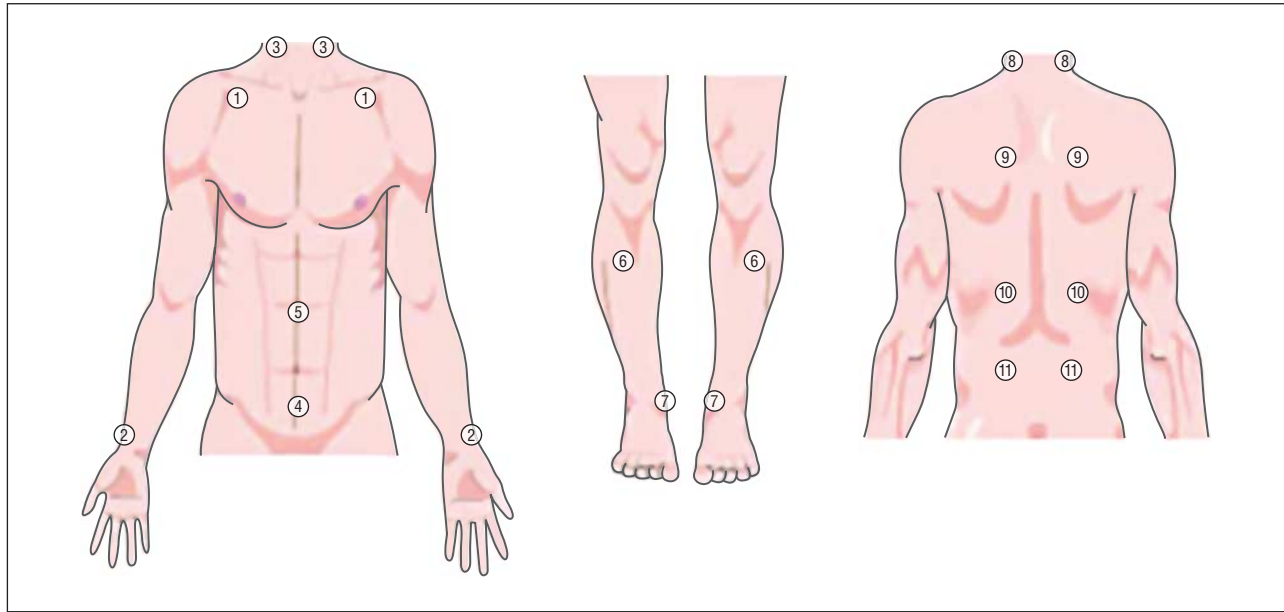


Figure 1. Acupuncture points used. The acupuncture points were selected according to traditional Chinese medicine theory: (1) LU1 (*Zhongfu*) and (2) LU9 (*Taiyuan*) in the lung meridian; (3) LI18 (*Futu*) in the large intestine meridian; (4) CV4 (*Guanyuan*) and (5) CV12 (*Zhongwan*) in the conception vessel; (6) ST36 (*Zusanli*) in the stomach meridian; (7) KI3 (*Taixi*) in the kidney meridian; (8) GB12 (*Wangu*) in the gallbladder meridian; and (9) BL13 (*Feishu*), (10) BL20 (*Pishu*), and (11) BL23 (*Shenshu*) in the bladder meridian.

cause the study was neither randomized nor masked in terms of patient allocation. In the present study, our objective was to evaluate the efficacy of acupuncture in patients with COPD, especially focusing on changes in dyspnea on exertion (DOE) evaluated with the 6-minute walk test (6MWT) and fully assessed respiratory functions, including respiratory muscular strength, in a randomized, single-blind trial.

METHODS

STUDY DESIGN

The present study was conducted as a prospective, single-blind randomized controlled trial. The study blinding procedure was achieved by using a device specially designed for placebo needle. The physician and the evaluators, including hospital staff and statisticians, were not involved in the treatment program. All outcome measures in the present study were assessed at baseline and after completion of 12 weeks of intervention.

PATIENTS AND RECRUITMENT

The study was conducted from July 1, 2006, through March 31, 2009, at the Graduate School of Medicine Kyoto University Hospital, Ako City Hospital, Division of Respiratory Medicine, Respiratory Disease Center, Kitano Hospital, and Hyogo Prefectural Amagasaki Hospital, all of which are located in the Kansai region of Japan. Physicians in the Department of Respiratory Medicine recruited the participants at their outpatient sites. All participants met the following criteria: (1) diagnosed as having stage II, III, or IV COPD, in accordance with the Global Initiative for Chronic Obstructive Lung Disease (GOLD) guidelines¹; (2) clinically stable with no history of infections or exacerbation of respiratory symptoms, no changes in medication within the 3 months preceding the study onset, and no signs of edema; (3) stage II or higher dyspnea ac-

ording to the Medical Research Council (MRC) criteria⁶; (4) able to walk unassisted; (5) no pulmonary rehabilitation in the previous 6 months; and (6) outpatients only. Patients presenting with evidence of cardiovascular disease, collagen disease, renal failure, thyroid dysfunction, hepatic function disorder, cancer, and severe mental disorders were excluded. This study was performed in accordance with the Declaration of Helsinki and its amendments and the Guidelines for Good Clinical Practice for Epidemiological Studies and Clinical Research issued by the Japanese Ministry of Health. The institutional review board of Kyoto University Graduate School and Faculty of Medicine approved the study, and each patient provided written informed consent. The protocol of this study has been registered as a clinical trial at the University Hospital Medical Information Network in Japan (C000001217).

INTERVENTION

Patients in the real acupuncture group (RAG) received acupuncture treatment once a week for 12 weeks, in addition to daily medication. Selection of standardized acupuncture points was done in accordance with past research on acupuncture for pulmonary dysfunction^{4,5} and literature describing traditional prescription of acupuncture points for bronchial asthma and chronic bronchitis, of which the effect on COPD was verified through our clinical experiences during the past 10 years. Also, the importance of acupuncture points close to the respiratory accessory muscles was emphasized in the process of determination of the standardized treatment. The standardized acupuncture points used in the present study were as follows: (1) LU1 (*Zhongfu*) and (2) LU9 (*Taiyuan*) in the lung meridian; (3) LI18 (*Futu*) in the large intestine meridian; (4) CV4 (*Guanyuan*) and (5) CV12 (*Zhongwan*) in the conception vessel; (6) ST36 (*Zusanli*) in the stomach meridian; (7) KI3 (*Taixi*) in the kidney meridian; (8) GB12 (*Wangu*) in the gallbladder meridian; and (9) BL13 (*Feishu*), (10) BL20 (*Pishu*), and (11) BL23 (*Shenshu*) in the bladder meridian (**Figure 1**).

A Park sham device, which comprises a needle (real or placebo), was used with a guide tube mounted on a base adher-

Table 1. Modified 10-Point Borg Scale^a

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

^aAt the beginning of the 6-minute walk test (6MWT), show the scale to the patient and ask the patient the following: "Please grade your level of shortness of breath using this scale." At the end of the 6MWT, remind the patient of the breathing number that he or she chose before the 6MWT and ask the patient to grade his or her breathing level again.

ent to the skin.⁷ The tips of the placebo needles used for the placebo acupuncture group (PAG) were blunt and appeared to be penetrating the skin but actually telescoped back into place. The real and placebo needles appear similar and were the same size (0.35 × 70 mm, stainless steel; Dong Bang Acupuncture, Inc). To achieve proper handling of the Park sham device, the acupuncturists had been trained for at least 2 weeks before the commencement of the study. For the RAG patients, needles were inserted to a depth ranging from 5 to 25 mm and were manually rotated clockwise and counterclockwise for 3 to 4 minutes at each point during a 50-minute treatment period. No electrical stimulation was performed. Perception of *de qi* (tingling, numbness, heaviness, and other feelings that occur after acupuncture needle insertion) during insertion and/or manipulation was confirmed at every point in the RAG.

The PAG underwent treatment at the same acupuncture points as the RAG. Perception of sensation during treatment sessions in PAG included pricking or poking, but no sensation like *de qi* was reported.

RANDOMIZATION

After obtaining informed consent, participants were registered at a randomization center by a clinical trial coordinator. They were stratified by age (<75 or ≥75 years)⁸ and then randomly assigned to the RAG or PAG using a computer-generated random allocation sequence with permuted block design.

PRIMARY OUTCOME MEASURE

We conducted the 6MWT using the standard method for assessment of severity of DOE.⁹ To rate breathlessness before and immediately after the 6MWT, a modified 10-point Borg category ratio scale was used, where 0 signified "breathing very well, barely breathless" and 10 signified "severely breathless"¹⁰ (Table 1). The score after the 6MWT was used in the analysis.

SECONDARY OUTCOME MEASURES

Secondary outcome measures in the present study included the 6MWD⁹; the lowest oxygen saturation during the 6MWT, which was monitored at 1-minute intervals with a saturation pulse oxygen meter; and forced expiratory volume in 1 second (FEV₁),

which was monitored using a computed spirometer according to the protocol for lung function measurements of the American Thoracic Society.¹¹ Quality of life of the patients was measured with the St George Respiratory Questionnaire (SGRQ).¹²

OTHER OUTCOME MEASURES

Other outcome measures included respiratory function, such as diffusing capacity of the lung for carbon monoxide (DLCO), residual volume, and total lung capacity. Arterial blood gas was measured under stable conditions. The maximum inspiratory mouth pressure and maximum expiratory mouth pressure were measured using a standard mouthpiece and a respiratory muscle strength testing device (Vitaropower KH115; Chest MI Co Ltd) according to the American Thoracic Society/European Respiratory Society.¹³ Body mass index (BMI; calculated as weight in kilograms divided by height in meters squared) and serum prealbumin levels were evaluated as indices of nutritional status. Evaluation of thorax mobility was made by measuring the difference of the girth of the chest between the residual volume level and total lung capacity level on the basis of the fourth intercostal using a tape measure. Dyspnea during activities of daily living was scored using the MRC dyspnea scale.⁶ Measurements were taken at baseline and after completion of the acupuncture treatment.

At the end of the intervention period, we asked the following question to all patients to ascertain the perception of the placebo needling. "Please select one of the following regarding treatment procedures you think you had been received: 1. Real acupuncture, 2. Placebo acupuncture, 3. Do not know."

STATISTICAL ANALYSIS

Statistical analysis in the present study was conducted by 2 biostatisticians (Y.A. and T.O.). The sample size of this study was computed based on the primary end point, which was a change in the Borg scale score at the end of the 6MWT. Calverley¹⁴ reported that the minimal clinically important difference in the Borg scale score in COPD patients was 2 units. Thus, the required sample size was estimated to be 60 patients, which was calculated to detect a minimal difference between means in the Borg scale score of 2.0 at a significance level of .05 with a power of 0.8.

All data are presented as mean (SD) or mean (95% CI). The difference between baseline and final volumes was compared using analysis of covariance with baseline values and age as covariates and treatment group as the factor of interest. All main analyses in the present study were performed with SAS statistical software, version 9.1.3 (SAS Institute, Inc).

RESULTS

STUDY RECRUITMENT AND FOLLOW-UP

Of the 111 patients who met the inclusion and exclusion criteria, 68 agreed to participate in the study. **Figure 2** shows the trial profile. Of those participants, 6 were unable to complete the study because they believed it was too difficult to continue (2 in the PAG and 1 in the RAG) or they had acute exacerbation of respiratory infections (3 in the RAG). Baseline characteristics of the patients in each group, including medications taken by the patients during the study, are listed in **Table 2**. All medications remained unchanged through the study period.

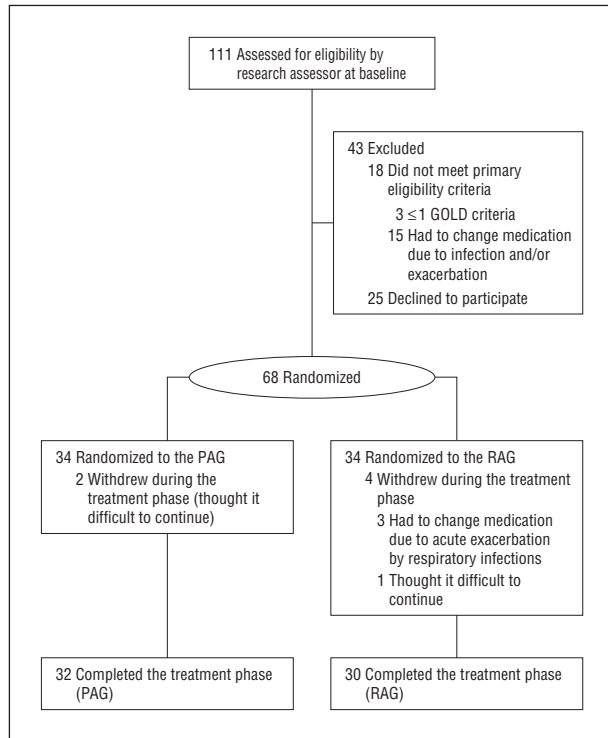


Figure 2. Study participant flow diagram. GOLD indicates Global Initiative for Chronic Obstructive Lung Disease; PAG, placebo acupuncture group; and RAG, real acupuncture group.

MAIN OUTCOME

After 12 weeks of treatment, the Borg scale score after the 6MWT improved from 5.5 (2.8) to 1.9 (1.5) in the RAG. On the other hand, no improvement was seen in the Borg scale score in the PAG before and after acupuncture treatment (4.2 [2.7] and 4.6 [2.8], respectively). The difference in the Borg scale score in the RAG (-3.6 [1.9]) was statistically significant compared with that in the PAG (0.4 [1.2]; mean difference by analysis of covariance, -3.58; 95% CI, -4.27 to -2.90) (**Table 3** and **Figure 3A**).

SECONDARY OUTCOMES

Significant improvement was found in the 6MWD, oxygen saturation during the 6MWT, and SGRQ results after treatment in the RAG of which the difference from the baseline was significantly greater than that in the PAG, whereas changes in the FEV₁ did not reach statistical significance (**Table 3**, **Table 4**, and **Figure 3B**).

OTHER OUTCOME MEASURES

Dyspnea During Activities of Daily Living

After 12 weeks of acupuncture, significant improvements in the MRC score were found in the RAG, with a significantly greater reduction in scores compared with the PAG (**Table 5**).

Nutritional Evaluation, Arterial Blood Gas, and Range of Motion in the Rib Cage

Improvement in the nutritional status (BMI and prealbumin level), arterial blood gas (PaO₂), and range of motion in the rib cage was found in the RAG of which the difference from the baseline showed a statistically significant difference compared with that in the PAG (**Table 5**).

Respiratory Function and Respiratory Muscle Strength

After 12 weeks of acupuncture, significant improvements in respiratory function (forced vital capacity, percentage of FEV₁, DLCO, and percentage of DLCO) and respiratory muscle strength (maximum expiratory mouth pressure and maximum inspiratory mouth pressure) were found in the RAG compared with the PAG (**Table 6**).

Perception of the Placebo Needling by the Patients

Regarding perception of the needling, 4, 2, and 26 patients in the PAG answered “real acupuncture,” “placebo acupuncture,” and “don’t know,” respectively. These responses were given in 2, 3, and 25 patients, respectively, in the RAG.

ADVERSE REACTIONS

The following minor adverse reactions were reported by some patients during the study: fatigue (4 in the RAG and 5 in the PAG), subcutaneous hemorrhage (5 in the RAG), dizziness (1 in the RAG and 2 in the PAG), and needle site pain (5 in the RAG). All events were minor reactions and patients recovered in a short time. No serious events due to acupuncture treatment were reported.

COMMENT

ACUPUNCTURE AND COPD

This is the first placebo-controlled, randomized study, to our knowledge, that demonstrated the efficacy of acupuncture treatment for improvement of DOE and exercise tolerance in patients with COPD. Although previous studies^{15,16} have evaluated efficacy of acupuncture on dyspnea of patients with COPD, participants in those studies had various diseases, such as bronchial asthma, interstitial pneumonia, cystic fibrosis, and COPD. It is therefore inconclusive whether acupuncture is capable of improving symptoms of COPD from these studies alone. The standardization of acupuncture points as used in the present study may be a strength because it may increase the reproducibility of the technique by other practitioners.

The mean reduction in the Borg scale score after the 6MWT, the main outcome of this study, and the increase in the 6MWD with the acupuncture procedure were significantly greater in the RAG than in the PAG.

Table 2. Baseline Patient Characteristics of Full Analysis Set

Characteristic	PAG (n = 34)	RAG (n = 34)	Mean Difference
Sex			
Male	32	31	
Female	2	3	
Age, mean (SD), y	72.5 (7.4)	72.7 (6.8)	0.1
MRC score, mean (SD)	2.9 (1.1)	3.3 (1.0)	0.4
Brinkman index, mean (SD)	1433.9 (759.8)	1292.5 (526.4)	-141.4
GOLD criteria			
I	0	0	
II	13	6	
III	8	16	
IV	13	12	
GOLD stage, mean (SD)	3.0 (0.9)	3.2 (0.7)	0.2
Home oxygen therapy	11	9	
β_2 -Agonist			
Salbutamol sulfate	5	6	
Salmeterol xinafoate	7	12	
Tulobuterol hydrochloride	13	8	
Anticholinergic			
Oxipropium bromide	2	2	
Tiotropium bromide hydrate	29	30	
Inhaled corticosteroid			
Fluticasone propionate	11	16	
Beclomethasone dipropionate	4	1	
Budesonide	4	4	
Ciclesonide	0	1	
Salmeterol xinafoate and fluticasone propionate	1	2	
Oral corticosteroid			
Prednisolone	3	3	
Exercise capacity			
6MWT post-Borg scale score, mean (SD)	4.1 (2.7)	5.5 (2.8)	1.3
6MWD, mean (SD), m	404.5 (109.5)	358.7 (132.5)	-45.9
SpO ₂ , mean (SD), % lowest rate	88.4 (6.1)	86.4 (6.7)	-2.1
Pulmonary function, mean (SD)			
VC, L	3.1 (0.7)	2.8 (0.5)	-0.3
IC, L	1.9 (0.5)	1.8 (0.4)	-0.1
ERV, L	1.3 (0.3)	1.1 (0.4)	-0.2
FVC, L	3.0 (0.7)	2.8 (0.6)	-0.2
FEV ₁ , L	1.2 (0.4)	1.0 (0.3)	-0.2
FEV ₁ , % predicted	48.0 (16.5)	44.5 (16.3)	-3.5

Abbreviations: 6MWD, 6-minute walk distance; 6MWT, 6-minute walk test; ERV, expiratory reserve volume; FEV₁, forced expiratory volume in 1 second; FVC, forced vital capacity; GOLD, Global Initiative for Chronic Obstructive Lung Disease; IC, inspiratory capacity; MRC, Medical Research Council; PAG, placebo acupuncture group; RAG, real acupuncture group; SpO₂, oxygen saturation as measured by pulse oximetry; VC, vital capacity.

These improvements in the Borg scale score and the 6MWD during the 6MWT were in line with studies¹⁷ that suggest clinically important differences in COPD. Previous review articles^{18,19} indicated that the reduction in the Borg scale score and the increase in the 6MWD with standard care, such as rehabilitation or exercise, was 1.1 to 3.6 U and 54 to 80 m, respectively. Thus, our results are comparable to or better than these interventions. Also, the increase in lowest oxygen saturation during the 6MWT after real acupuncture was found. These results indicate the efficacy of acupuncture for improving exercise capacity.

POSSIBLE MECHANISM UNDERLYING THE EFFECT OF ACUPUNCTURE ON DYSPNEA

Several factors are thought to relate to DOE in patients with COPD, including dynamic hyperinflation, hypoxemia, hypercapnia, and limitation of rib cage move-

ment. Increased workload causes fatigue and dysfunction of accessory muscles, and at the end of exercise in patients with COPD, when dyspnea intensity reaches intolerable levels, the inspiratory muscles are maximally shortened, and thoracic displacement is greatly constrained.²⁰ These phenomena lead to accumulation of various algogenic or sensitizing substances under ischemic conditions, which consequently cause muscle fatigue and pain. Kawakita et al²¹ reported that acupuncture suppressed electromyogram activity of the muscle that was experimentally hyperactivated by repeated eccentric contraction. We therefore speculate that a similar phenomenon is evoked in the accessory respiratory muscles by needling on the acupuncture points on the rib cage. Decreased muscle tone consequently caused the recovery of the muscle strength in the rib cage, resulting in the increased mobility in the rib cage. Relaxation of accessory respiratory muscles may also contribute to rib cage motion. In fact, the present study showed increases in

Table 3. Mean (SD) Changes in the Main Outcome Measure and Exercise Capacity

Exercise Capacity	Baseline	After 12 wk	Change From Baseline to Posttreatment Measurements	Mean Difference (95% CI)
Borg scale score				
PAG				-3.58 (-4.27 to -2.90)
≥75 (n = 14)	4.0 (2.4)	4.2 (2.7)	0.3 (1.3)	
<75 (n = 18)	4.4 (3.0)	4.9 (2.8)	0.5 (1.2)	
Total	4.2 (2.7)	4.6 (2.8)	0.4 (1.2)	
RAG				
≥75 (n = 12)	4.1 (2.2)	1.3 (0.9)	-2.8 (1.6)	
<75 (n = 18)	6.4 (2.9)	2.3 (1.8)	-4.2 (1.9)	
Total	5.5 (2.8)	1.9 (1.5)	-3.6 (1.9)	
6MWD, m				78.68 (54.16 to 103.21)
PAG	405.2 (111.2)	385.8 (118.3)	-19.4 (48.7)	
RAG	373.2 (115.2)	436.7 (101.0)	63.5 (49.9)	
SpO ₂ , % lowest rate				4.73 (3.49 to 5.96)
PAG	88.3 (6.1)	86.7 (6.7)	-1.6 (2.2)	
RAG	86.0 (7.0)	89.5 (5.2)	3.5 (2.9)	

Abbreviations: 6MWD, 6-minute walk distance; PAG, placebo acupuncture group; RAG, real acupuncture group; SpO₂, oxygen saturation as measured by pulse oximetry.

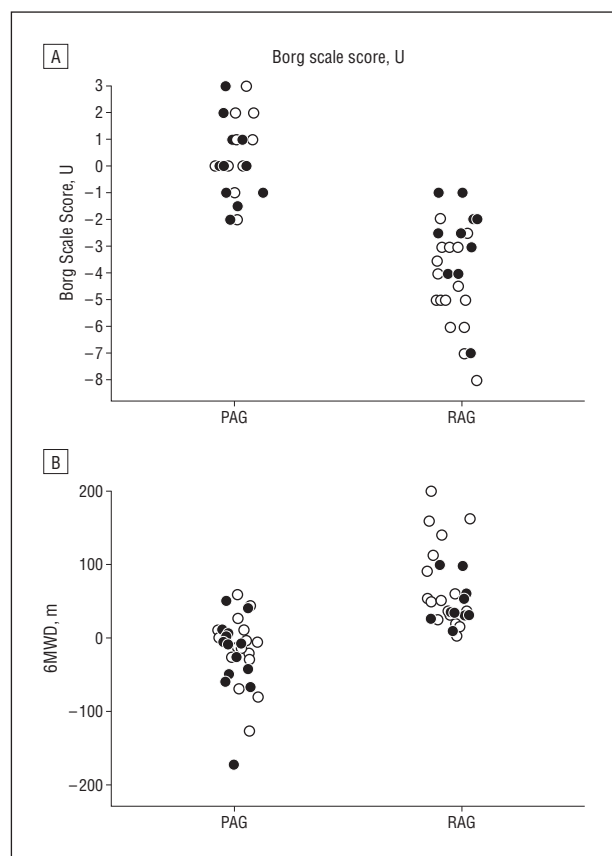


Figure 3. Differences in the Borg scale score and 6-minute walk distance (6MWD) test in the placebo acupuncture group (PAG) and the real acupuncture group (RAG). Differences in the Borg scale score (A) and 6MWD (B) between baseline and at the end of the intervention. Open circles indicate patients younger than 75 years; closed circles, patients 75 years or older. Estimated mean differences (95% CIs) (error bars) were -3.58 (-4.27 to -2.90) and 78.68 (54.16 to 103.21) for the Borg scale score and 6MWD, respectively.

maximum inspiratory mouth pressure, maximum expiratory mouth pressure, and range of motion in the rib cage at the end of acupuncture treatment.

In this study, vital capacity, FVC, percentage of FEV₁, and percentage of DLCO significantly increased after acupuncture treatment. These findings suggest that acupuncture treatment might improve DOE and exercise endurance, at least to some extent, through the improvement of pulmonary function. It is not clear why acupuncture improves pulmonary function; however, we speculate that the relaxation of hyperactivated respiratory muscles and the correction of the autonomic tone might cause the beneficial effect on pulmonary function.²² Further investigations are needed to clarify this.

QUALITY OF LIFE AND ACUPUNCTURE

In the present study, the total score on the SGRQ was significantly decreased by -16.0 U in patients in the RAG. Jones²³ reported that the minimal clinically important difference for the total SGRQ score is 4 U or more; therefore, the effect of acupuncture on health-related quality of life was satisfactory in this study. Previous studies^{24,25} indicate that exercise capacity is an important determinant of quality of life in patients with COPD. The exercise capacity enhanced by acupuncture in the present study may have contributed to the improvement in the SGRQ. The GOLD guidelines emphasize that the overall approach to managing stable COPD should be individualized to address symptoms and improve quality of life.¹ Our results indicate that dyspnea and quality of life of patients in the RAG were markedly improved, suggesting that acupuncture is a useful modality to manage stable COPD.

NUTRITIONAL DISORDER AND ACUPUNCTURE

Malnutrition is one of the major problems in patients with COPD.^{1,26,27} A nutritional disorder leads to loss of body weight and muscle volume,²⁶ resulting in decreased strength of the respiratory muscles and intolerance to exercise.²⁸ Our study clearly demonstrated that reduced

Table 4. Mean (SD) Changes in St George Respiratory Questionnaire Scores

Scale	Baseline	After 12 wk	Change From Baseline to Posttreatment Measurements	Mean Difference (95% CI)
Total				-15.7 (-20.3 to -11.2)
PAG	40.8 (15.4)	41.1 (16.0)	0.3 (7.9)	
RAG	46.2 (14.2)	30.2 (15.7)	-16.0 (9.7)	
Symptom				-24.7 (-32.2 to -17.1)
PAG	53.2 (20.6)	50.5 (14.4)	-2.6 (14.4)	
RAG	54.7 (18.9)	26.9 (17.7)	-27.8 (17.3)	
Activity				-16.2 (-22.8 to -9.61)
SAG	53.1 (19.0)	55.9 (19.6)	2.8 (13.1)	
RAG	58.6 (16.9)	44.6 (22.0)	-14.0 (13.6)	
Impact				-12.1 (-16.7 to -7.59)
PAG	26.7 (15.5)	26.8 (16.1)	0.1 (8.2)	
RAG	33.5 (15.2)	20.5 (15.1)	-13.0 (9.6)	

Abbreviations: PAG, placebo acupuncture group; RAG, real acupuncture group.

Table 5. Mean (SD) Changes in the Other Outcome Measures

Outcome Measure	Baseline	After 12 wk	Change From Baseline to Posttreatment Measurements	Mean Difference (95% CI)
Medical Research Council				-0.78 (-1.11 to -0.44)
PAG	2.9 (1.1)	2.8 (1.2)	-0.1 (0.5)	
RAG	3.2 (0.9)	2.3 (1.1)	-0.9 (0.8)	
BMI				1.16 (0.77 to 1.55)
PAG	21.3 (3.9)	21.1 (3.6)	-0.2 (0.5)	
RAG	21.7 (3.9)	22.7 (4.0)	1.0 (1.0)	
Prealbumin level, g/dL				2.84 (0.93 to 4.76)
PAG	23.4 (3.7)	22.9 (4.6)	-0.5 (2.6)	
RAG	23.0 (4.9)	25.4 (6.7)	2.4 (4.7)	
pH				0.001 (-0.01 to 0.01)
PAG	7.41 (0.02)	7.41 (0.02)	0.003 (0.02)	
RAG	7.42 (0.02)	7.42 (0.03)	0.004 (0.03)	
PaCO ₂				-0.40 (-2.12 to 1.31)
PAG				
mm Hg	41.8 (4.5)	41.5 (4.9)	-0.32 (3.3)	
kPa	5.56 (0.6)	5.53 (0.7)		
RAG				
mm Hg	40.2 (3.7)	39.5 (4.8)	-0.72 (3.4)	
kPa	5.36 (0.5)	5.26 (0.5)		
PaO ₂				11.18 (4.70 to 17.66)
PAG				
mm Hg	78.3 (11.8)	74.5 (12.3)	-3.84 (13.3)	
kPa	10.5 (1.6)	9.90 (1.7)		
RAG				
mm Hg	70.9 (11.7)	78.2 (12.7)	7.34 (12.1)	
kPa	9.5 (0.6)	10.42(1.7)		
Bicarbonate, mEq/L				-0.37 (-1.11 to 0.36)
PAG	25.8 (2.1)	25.7 (2.2)	-0.10 (1.5)	
RAG	25.5 (1.9)	25.1 (2.2)	-0.47 (1.4)	
Rib cage ROM, cm				3.20 (2.28 to 4.12)
PAG	3.7 (1.6)	3.6 (1.8)	-0.1 (1.5)	
RAG	2.3 (1.5)	5.4 (2.6)	3.1 (2.1)	

Abbreviations: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); PAG, placebo acupuncture group; RAG, real acupuncture group; ROM, range of motion.

SI conversion factors: To convert albumin to grams per liter, multiply by 10; and to convert bicarbonate to millimoles per liter, multiply by 1.0.

BMI and prealbumin level in COPD patients were recovered after 12 weeks of acupuncture. It was reported that acupuncture at ST36 (*Zusanli*) and CV12 (*Zhongwan*) ac-

celerates gastric emptying,²⁹ which may consequently facilitate food ingestion. We therefore suggest that improvement in gastrointestinal function and reduced

Table 6. Mean (SD) Changes in the Respiratory Functions and the Respiratory Muscle Strength

Respiratory Variable	Baseline	After 12 wk	Change From Baseline to Posttreatment Measurements	Mean Difference (95% CI)
VC, L				0.09 (−0.07 to 0.25)
PAG	3.1 (0.7)	3.1 (0.7)	−0.03 (0.3)	
RAG	2.9 (0.5)	2.9 (0.6)	0.06 (0.4)	
IC, L				0.10 (−0.05 to 0.25)
PAG	1.9 (0.5)	1.9 (0.5)	−0.01 (0.2)	
RAG	1.8 (0.4)	1.9 (0.5)	0.09 (0.4)	
FVC, L				0.24 (0.14 to 0.35)
PAG	3.0 (0.7)	2.9 (0.6)	−0.10 (0.2)	
RAG	2.8 (0.5)	2.9 (0.5)	0.14 (0.2)	
FEV ₁ , L				0.09 (−0.02 to 0.20)
PAG	1.1 (0.3)	1.1 (0.3)	−0.04 (0.2)	
RAG	1.0 (0.3)	1.1 (0.3)	0.07 (0.3)	
FEV ₁ , % predicted				4.20 (0.04 to 8.37)
PAG	47.9 (16.5)	46.9 (17.7)	−1.00 (4.8)	
RAG	46.0 (16.6)	49.2 (19.5)	3.17 (10.7)	
FRC, L				−0.02 (−0.28 to 0.24)
PAG	4.1 (0.9)	4.1 (0.8)	−0.02 (0.5)	
RAG	3.7 (0.8)	3.6 (0.8)	−0.04 (0.5)	
TLC, L				0.01 (−0.31 to 0.33)
PAG	6.0 (1.1)	6.0 (1.0)	−0.02 (0.6)	
RAG	5.5 (0.9)	5.5 (0.9)	−0.01 (0.7)	
RV/TLC, %				−0.89 (−4.12 to 2.31)
PAG	47.5 (8.8)	47.2 (8.8)	−0.21 (4.8)	
RAG	46.7 (6.1)	45.6 (7.2)	−1.10 (7.6)	
Dlco, mL/min/mm Hg				1.20 (0.14 to 2.26)
PAG	10.1 (4.3)	9.6 (5.1)	−0.52 (2.1)	
RAG	9.8 (5.5)	10.4 (5.5)	0.68 (2.1)	
Dlco/VA, mL/min/mm Hg/L				0.24 (−0.01 to 0.48)
PAG	2.3 (1.2)	2.2 (1.2)	−0.12 (0.3)	
RAG	2.3 (1.5)	2.4 (1.4)	0.12 (0.6)	
MEP, H ₂ O cm				36.09 (26.41 to 45.77)
PAG	63.5 (21.5)	61.8 (22.9)	−1.70 (12.2)	
RAG	59.5 (21.6)	93.9 (32.2)	34.4 (24.3)	
MIP, H ₂ O cm				14.83 (8.49 to 21.16)
PAG	56.4 (20.6)	55.4 (19.5)	−1.0 (11.9)	
RAG	60.8 (20.6)	74.6 (15.8)	13.8 (13.0)	

Abbreviations: DLCO, carbon monoxide diffusing capacity; FEV₁, forced expiratory volume in 1 second; FRC, functional residual capacity; FVC, forced vital capacity; IC, inspiratory capacity; L, liter; MEP, maximum expiratory mouth pressure; MIP, maximum inspiratory mouth pressure; PAG, placebo acupuncture group; RAG, real acupuncture group; RV, residual volume; TLC, total lung capacity; VA, alveolar volume; VC, vital capacity.

dyspnea during mealtime may facilitate food intake, resulting in a better nutritional condition of the patient. In addition, reduction in energy expenditure in the respiratory muscles, which was derived from relaxation of the muscles, reduction in oxygen consumption, and improvement in DOE, may contribute to the improvement in nutritional status.

STUDY LIMITATIONS

Our study has some limitations. First, most patients were already taking standard medication for COPD because it was practically impossible to recruit those who are not receiving medication. Although the baseline medications were not significantly different between the RAG and PAG, changes in outcome measures in the present trial may have been achieved not only by acupuncture but also by additional or synergic effects of medication. Second, this study was performed in a relatively short period without follow-up evaluation. Acupuncture was

shown to improve BMI, MRC criteria, and 6MWD, but another study should be performed to confirm the long-term effect of acupuncture on COPD. Finally, this study was performed as a placebo-controlled, randomized trial using placebo acupuncture. Although no significant difference was found in the proportion of patients regarding perception of real and placebo needling, we were unable to mask the acupuncture therapists, which might influence the results based on their attitudes.

CONCLUSIONS

We demonstrated clinically relevant improvements in DOE (Borg scale), nutrition status (including BMI), airflow obstruction, exercise capacity, and health-related quality of life after 3 months of acupuncture treatment. Randomized trials with larger sample sizes and longer-term interventions with follow-up evaluations are necessary to confirm the usefulness of acupuncture in COPD treatment.

Accepted for Publication: March 5, 2012.

Published Online: May 14, 2012. doi:10.1001/archinternmed.2012.1233

Author Affiliations: Department of Respiratory Medicine, Graduate School of Medicine, Kyoto University, Kyoto (Drs M. Suzuki, Muro, Sato, and Mishima), Division of Respiratory Medicine, Respiratory Disease Center Kitano Hospital, The Tazuke Kofukai Medical Research Institute, Osaka (Drs M. Suzuki, Aihara, Matsumoto, S. Suzuki, Itotani, Ishitoko, Takemura, Ueda, Kagioka, and Fukui), Biostatistics Group, Center for Product Evaluation, Pharmaceuticals and Medical Devices Agency, Tokyo (Ms Ando), Epidemiology and Biostatistics Laboratory, Faculty of Culture and Information Science, Doshisha University, Kyoto (Dr Omori), Department of Respiratory Medicine, Ako City Hospital, Ako City (Dr Shiota), Department of Respiratory Medicine, Hyogo Prefectural Amagasaki Hospital, Hyogo (Drs Endo, Hara, and Hirabayashi), and Department of Clinical Acupuncture and Moxibustion, Meiji University of Integrative Medicine, Kyoto (Dr M. Suzuki), Japan.

Correspondence: Masao Suzuki, LAc, PhD, Department of Clinical Acupuncture and Moxibustion, Meiji University of Integrative Medicine, Hiyoshi-cho, Nantan city, Kyoto, Japan (masuzuki@meiji-u.ac.jp).

Author Contributions: *Study concept and design:* M. Suzuki, Muro, Ando, Omori, Fukui, and Mishima. *Acquisition of data:* M. Suzuki, Shiota, Endo, Sato, Aihara, Matsumoto, S. Suzuki, Itotani, Ishitoko, Hara, Takemura, Ueda, Kagioka, Hirabayashi, and Fukui. *Analysis and interpretation of data:* Muro, Ando, Omori, Fukui, and Mishima. *Drafting of the manuscript:* M. Suzuki, Muro, Ando, Fukui, and Mishima. *Critical revision of the manuscript for important intellectual content:* M. Suzuki, Muro, Omori, Shiota, Endo, Sato, Aihara, Matsumoto, S. Suzuki, Itotani, Ishitoko, Hara, Takemura, Ueda, Kagioka, Hirabayashi, Fukui, and Mishima. *Statistical analysis:* Ando and Omori. *Obtained funding:* M. Suzuki. *Administrative, technical, and material support:* Muro, Endo, Sato, Hara, Hirabayashi, Fukui, and Mishima. *Study supervision:* Muro, Hirabayashi, Fukui, and Mishima.

Financial Disclosure: None reported.

Funding/Support: This trial was funded by the Grants-in-Aid for scientific research from the Japan Society of Acupuncture and Moxibustion (JSAM).

Role of the Sponsors: The JSAM had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; and preparation, review, or approval of the manuscript.

Disclaimer: The contents of this publication are solely the responsibility of the authors and do not necessarily represent the official views of JSAM or pharmaceuticals and medical devices agency.

Previous Presentation: The results of the study were presented at the International Conference of American Thoracic Society; May 19, 2010; New Orleans, Louisiana. This study received an American Thoracic Society Travel Award.

Additional Contributions: Professor Naoto Ishizaki (Department of Clinical Acupuncture and Moxibustion, Meiji University of Integrative Medicine) provided administrative support and assistance with manuscript preparation.

REFERENCES

1. Global Initiative for Chronic Obstructive Lung Disease. Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease updated 2009. [http://www.goldcopd.org/Guideline item](http://www.goldcopd.org/Guideline%20item). Accessed January 11, 2010.
2. Mahler DA, Tomlinson D, Olmstead EM, Tosteson AN, O'Connor GT. Changes in dyspnea, health status, and lung function in chronic airway disease. *Am J Respir Crit Care Med*. 1995;151(1):61-65.
3. Cohen AJ, Menter A, Hale L. Acupuncture: role in comprehensive cancer care—a primer for the oncologist and review of the literature. *Integr Cancer Ther*. 2005;4(2):131-143.
4. Jobst KA. A critical analysis of acupuncture in pulmonary disease: efficacy and safety of the acupuncture needle. *J Altern Complement Med*. 1995;1(1):57-85.
5. Suzuki M, Namura K, Ohno Y, et al. The effect of acupuncture in the treatment of chronic obstructive pulmonary disease. *J Altern Complement Med*. 2008;14(9):1097-1105.
6. Brooks SM. Surveillance for respiratory hazard. *ATS News*. 1982;8:12-16.
7. Park J, White A, Stevinson C, Ernst E, James M. Validating a new non-penetrating sham acupuncture device: two randomised controlled trials. *Acupunct Med*. 2002;20(4):168-174.
8. Couser JI Jr, Guthmann R, Hamadeh MA, Kane CS. Pulmonary rehabilitation improves exercise capacity in older elderly patients with COPD. *Chest*. 1995;107(3):730-734.
9. ATS Committee on Proficiency Standards for Clinical Pulmonary Function Laboratories. ATS statement: guidelines for the six-minute walk test. *Am J Respir Crit Care Med*. 2002;166(1):111-117.
10. Borg GA. Psychophysical bases of perceived exertion. *Med Sci Sports Exerc*. 1982;14(5):377-381.
11. American Thoracic Society. Standardization of spirometry, 1994 update. *Am J Respir Crit Care Med*. 1995;152(3):1107-1136.
12. Jones PW, Quirk FH, Baveystock CM, Littlejohns P. A self-complete measure of health status for chronic airflow limitation: the St George's Respiratory Questionnaire. *Am Rev Respir Dis*. 1992;145(6):1321-1327.
13. American Thoracic Society/European Respiratory Society. ATS/ERS Statement on respiratory muscle testing. *Am J Respir Crit Care Med*. 2002;166(4):518-624.
14. Calverley PM. Minimal clinically important difference: exacerbations of COPD. *COPD*. 2005;2(1):143-148.
15. Jobst K, Chen JH, McPherson K, et al. Controlled trial of acupuncture for disabling breathlessness. *Lancet*. 1986;2(8521-22):1416-1419.
16. Lewith GT, Prescott P, Davis CL. Can a standardized acupuncture technique palliate disabling breathlessness? a single-blind, placebo-controlled crossover study. *Chest*. 2004;125(5):1783-1790.
17. Wise RA, Brown CD. Minimal clinically important differences in the six-minute walk test and the incremental shuttle walking test. *COPD*. 2005;2(1):125-129.
18. Ries AL. Minimally clinically important difference for the UCSD Shortness of Breath Questionnaire, Borg scale, and visual analog scale. *COPD*. 2005;2(1):105-110.
19. Sciruba F, Criner GJ, Lee SM, et al; National Emphysema Treatment Trial Research Group. Six-minute walk distance in chronic obstructive pulmonary disease: reproducibility and effect of walking course layout and length. *Am J Respir Crit Care Med*. 2003;167(11):1522-1527.
20. O'Donnell DE, Banzett RB, Carrieri-Kohlman V, et al. Pathophysiology of dyspnea in chronic obstructive pulmonary disease: a roundtable. *Proc Am Thorac Soc*. 2007;4(2):145-168.
21. Kawakita K, Itoh K, Okada K. Experimental model of trigger points using eccentric exercise. *J Musculoskeletal Pain*. 2008;16:29-35.
22. Burnstock G. Acupuncture: a novel hypothesis for the involvement of purinergic signalling. *Med Hypotheses*. 2009;73(4):470-472.
23. Jones PW. St George's Respiratory Questionnaire: MCID. *COPD*. 2005;2(1):75-79.
24. Hajiro T, Nishimura K, Tsukino M, Ikeda A, Oga T. Stages of disease severity and factors that affect the health status of patients with chronic obstructive pulmonary disease. *Respir Med*. 2000;94(9):841-846.
25. Lacasse Y, Goldstein R, Lasserson TJ, Martin S. Pulmonary rehabilitation for chronic obstructive pulmonary disease. *Cochrane Database Syst Rev*. 2006;(4):CD003793.
26. Schols AM, Slangen J, Volovics L, Wouters EF. Weight loss is a reversible factor in the prognosis of chronic obstructive pulmonary disease. *Am J Respir Crit Care Med*. 1998;157(6 pt 1):1791-1797.
27. Celli BR, Cote CG, Marin JM, et al. The body-mass index, airflow obstruction, dyspnea, and exercise capacity index in chronic obstructive pulmonary disease. *N Engl J Med*. 2004;350(10):1005-1012.
28. Creutzberg E. Anabolic steroids in acute and chronic disease. In: Wouters EFM, Schols AMWJ, eds. *Nutrition and Metabolism in Chronic Respiratory Disease* [European respiratory monograph]. Lausanne, Switzerland: European Respiratory Society Journals Ltd; 2003.
29. Takahashi T. Acupuncture for functional gastrointestinal disorders. *J Gastroenterol*. 2006;41(5):408-417.