



# Tai Chi and Pulmonary Rehabilitation Compared for Treatment-Naive Patients With COPD

## A Randomized Controlled Trial

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**BACKGROUND:** In COPD, functional status is improved by pulmonary rehabilitation (PR) but requires specific facilities. Tai Chi, which combines psychological treatment and physical exercise and requires no special equipment, is widely practiced in China and is becoming increasingly popular in the rest of the world. We hypothesized that Tai Chi is equivalent (ie, difference less than  $\pm 4$  St. George's Respiratory Questionnaire [SGRQ] points) to PR.

**METHODS:** A total of 120 patients (mean FEV<sub>1</sub>,  $1.11 \pm 0.42$  L; 43.6% predicted) bronchodilator-naive patients were studied. Two weeks after starting indacaterol 150  $\mu$ g once daily, they randomly received either standard PR thrice weekly or group Tai Chi five times weekly, for 12 weeks. The primary end point was change in SGRQ prior to and following the exercise intervention; measurements were also made 12 weeks after the end of the intervention.

**RESULTS:** The between-group difference for SGRQ at the end of the exercise interventions was  $-0.48$  (95% CI PR vs Tai Chi,  $-3.6$  to  $2.6$ ;  $P = .76$ ), excluding a difference exceeding the minimal clinically important difference. Twelve weeks later, the between-group difference for SGRQ was  $4.5$  (95% CI,  $1.9$  to  $7.0$ ;  $P < .001$ ), favoring Tai Chi. Similar trends were observed for 6-min walk distance; no change in FEV<sub>1</sub> was observed.

**CONCLUSIONS:** Tai Chi is equivalent to PR for improving SGRQ in COPD. Twelve weeks after exercise cessation, a clinically significant difference in SGRQ emerged favoring Tai Chi. Tai Chi is an appropriate substitute for PR.

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**KEY WORDS:** COPD; indacaterol; pulmonary rehabilitation; Tai Chi

**ABBREVIATIONS:** 6MWD = 6-min walk distance; MCID = minimal clinically important difference; mMRC = modified Medical Research Council dyspnea score; PR = pulmonary rehabilitation; SGRQ = St. George's Respiratory Questionnaire

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Drs Zhong and Luo contributed equally to the study.

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COPD is a progressive lung condition and a common cause of adult mortality globally.<sup>1</sup> In the absence of a therapy that can reverse parenchymal lung damage, the most effective treatment for improving quality of life and exercise performance is pulmonary rehabilitation (PR).<sup>2-5</sup> Although PR is highly effective in completers, a center/gymnasium-based approach limits provision, and the benefits wane after course completion.<sup>2</sup>

Tai Chi is a Chinese recreational exercise that is gradually becoming more popular worldwide.<sup>6-8</sup> Tai Chi improves symptoms in several chronic diseases, including fibromyalgia<sup>8</sup> and Parkinson's disease.<sup>7</sup> Pilot

studies have shown that Tai Chi represents a significant exercise load compared with standard exercise modalities, suggesting that Tai Chi could, as with PR, improve physical function and quality of life in patients with COPD.<sup>9,10</sup> However, there has been no large-scale comparison of Tai Chi with conventional PR, which precludes an unqualified rollout of Tai Chi to replace PR. We therefore undertook a comparison of Tai Chi and PR against a background of standardized bronchodilator use to test the hypothesis that Tai Chi and PR were of equivalent benefit in COPD, judged by using the St. George's Respiratory Questionnaire (SGRQ).

## Patients and Methods

### Overview

The study was undertaken at Xing-Ning People's Hospital and was approved by the ethics committee of First Affiliated Hospital of Guangzhou Medical University; participants provided written informed consent. Patients were recruited from the community (using advertisements) based on their age, smoking history, and symptoms (cough/breathlessness); patients were bronchodilator naive. Eligible patients were aged between 40 and 80 years with postbronchodilator FEV<sub>1</sub>  $\geq$  25% and  $<$  80% of predicted and FEV<sub>1</sub>/vital capacity  $<$  0.7.

Measurements were made prior to and following a 2-week run-in period when indacaterol 150  $\mu$ g once daily was started (visits 2 and 3). Patients were randomized at visit 2 to receive 12 weeks of either Tai Chi or center-based rehabilitation, after which further measurements (visit 6) were made. Indacaterol was continued for an additional 12 weeks, after which final measurements were made (visit 9). Intermediate visits were also conducted (e-Fig 1) but are not reported for clarity.

### Intervention

Tai Chi was taught as a 24 form Yang style; instruction was given 5 days per week for 1 h for 12 weeks. Initially, patients were taught two to three movements each day and typically took 2 weeks to master them; at this point, each instructor supervised two to three participants. Thereafter, the participants were able to join larger group training in which a single instructor provided instructions that were relayed to all group members in the hall by real-time video streaming. At the end of the 12-week period, participants were encouraged to continue Tai Chi, either alone or via a community group; however, no assistance was provided by the investigators during this period. Inherent to the group nature of Tai Chi practice, the exercise did not become more strenuous over the training period although participants became more accomplished at performing it. A video of the larger Tai Chi group

undertaking Tai Chi may be viewed online (Videos). This group also received educational input.

The PR program was based on standard UK practice; at study initiation, the training used was supervised and checked by an experienced British physiotherapist (B. M.). Briefly, a 12-week program with 1-h training session (with warm-up and cool-down phases as well) thrice weekly was used. Participants undertook a mixture of approximately 50% resistance exercises (arm and leg weights aiming for a target 70%-80% of their one-repetition maximum), hybrid (rowing machine), and 50% progressive aerobic whole body exercise (eg, cycle or treadmill) in addition to educational sessions. For the aerobic exercise, the patient's level of dyspnea was recorded after each exercise session and was titrated to achieve a BORG rating of perceived dyspnea level of 4 to 6. At the end of the program, participants received verbal encouragement to remain as physically active as possible. Further details may be found in e-Appendix 1.

### Measurements

The SGRQ, the primary end point, was measured at visits 2, 3, 6, and 9; secondary measures made at the same time points were FEV<sub>1</sub> (as % predicted) and 6-min walk distance (6MWD), and the primary comparison was made between the start and finish of exercise training (visit 3 to visit 6). SGRQ was administered by using a Mandarin version of the questionnaire,<sup>11</sup> and spirometry was performed by using a hand-held spirometer (microQuark, COSMED) in line with American Thoracic Society guidelines. We also measured the modified Medical Research Council dyspnea score (mMRC), short physical performance battery score,<sup>12</sup> height, mass (allowing calculation of BMI), fat-free mass by bioimpedance (BCA-1A, Member Enterprise of Tongfang Co, Ltd),<sup>13</sup> and quadriceps maximum voluntary contraction force in the dominant leg,<sup>14</sup> as well as data concerning hospital admission/ED attendance. Physical activity over 7 days (ActiGraph) was measured at screening (visit 1) and, not to overburden patients to finish, at visit 6 (ie, starting 11 weeks after starting the training intervention) and visit 9 (ie, starting 11 weeks after finishing the training intervention).

In the absence of pilot data, a formal power calculation was not possible; however, based on the earlier research of Casaburi et al,<sup>15</sup> in which a statistically significant improvement in SGRQ following tiotropium and PR had been observed, we aimed to recruit sufficient participants to have 50 "completers" in each group. Projecting an approximate 20% dropout, 60 patients were specified a priori in each group.

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## Statistical Analysis

All subjects who were randomized to study and received  $\geq 1$  dose of indacaterol were retained in the full analysis set, which was analyzed by the intention-to-treat method. The number of missing visits (or incomplete data collection at a visit) was small (e-Table 1). No

attempt was made to impute missing data but rather the last observation was carried forward. Pre-post comparisons were made by using Student *t* tests, having ascertained that the data were normally distributed, and changes between groups were assessed by ANOVA (SPSS version 13).

## Results

Recruitment and retention data are shown in Figure 1; demographic data at baseline are presented in Table 1. Through a protocol violation, one patient (of 120) used a bronchodilator between consent and visit 1. There were no statistically significant differences between groups at baseline. Both groups had high compliance in terms of attendance rate (present days/total expected days):  $91 \pm 1\%$  for the Tai Chi group and  $87 \pm 2\%$  for the PR group.

### Comparison of Tai Chi vs PR (Visit 3 vs Visit 6)

Principal outcomes are shown in Table 2 as a function of treatment allocation; significant improvements were seen in both groups, with the exception of FEV<sub>1</sub>.

However, when between-group changes were considered, we observed no difference in total SGRQ, spirometry, 6MWD, or mMRC score. The between-group difference for PR and Tai Chi for SGRQ was  $-0.48$  (95% CI,  $-3.6$  to  $2.6$ ;  $P = .76$ ); for 6MWD, it was  $0.78$  m (95% CI,  $-10.8$  to  $12.8$ ;  $P = .89$ ). No differences were observed for FEV<sub>1</sub>.

### Preservation of Benefit: PR Compared With Tai Chi (Performance at Visit 9)

At visit 9, compared with visit 6, the Tai Chi group demonstrated further improvement in SGRQ, mMRC, and 6MWD; in contrast, the PR group showed no further improvement in SGRQ or mMRC and exhibited a small but statistically significant fall in 6MWD (e-Table 2). The between-group difference between PR

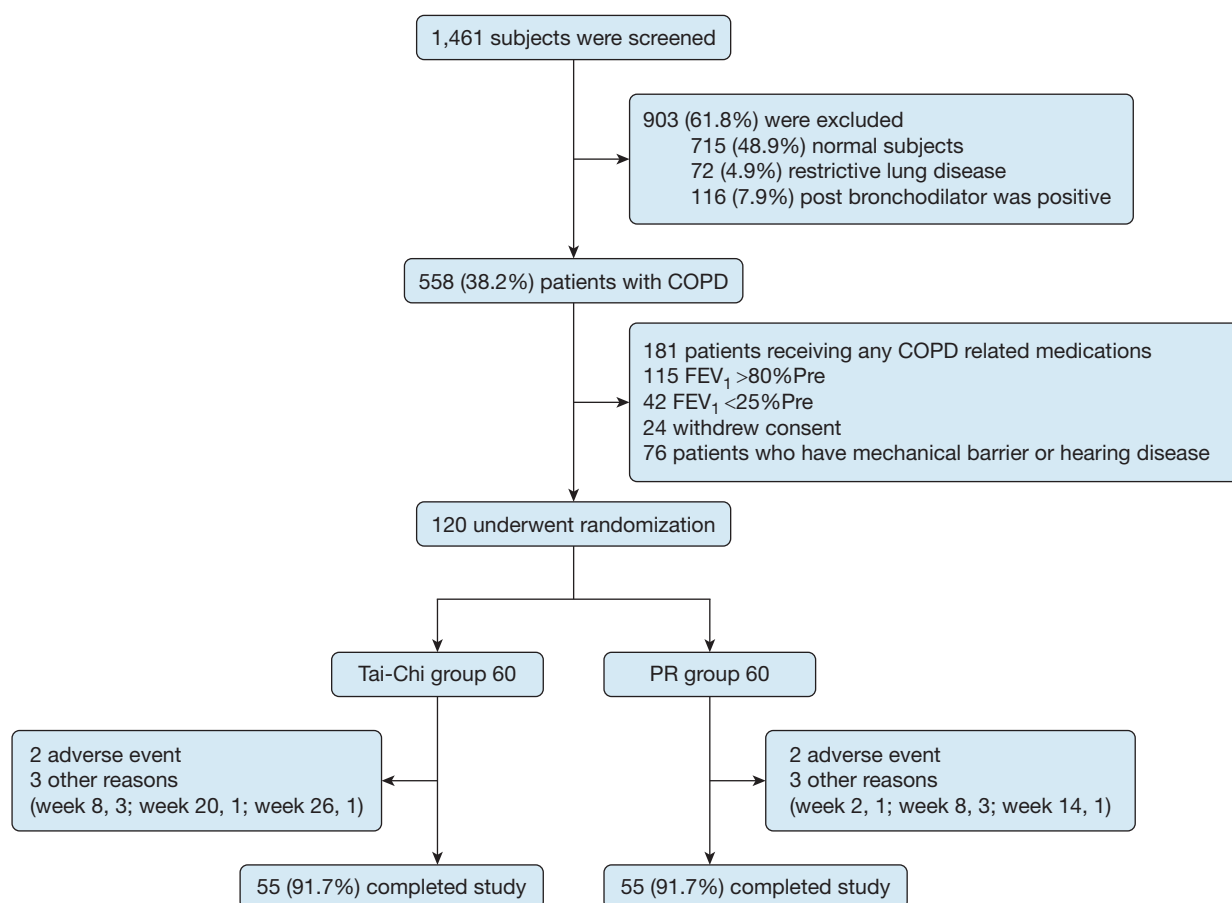


Figure 1 – Flow of participants through study. PR = pulmonary rehabilitation.

**TABLE 1 ] Descriptive Data of Participants Prior to Initiation of Indacaterol (V2)**

Variable	Tai Chi Group (n = 60)	PR Group (n = 60)	Statistics	P Value
Currently smoking?				
Yes	26 (43.3%)	25 (41.7%)	$\chi^2 = 0.03$	.853
No	34 (56.7%)	35 (58.3%)		
No. of cigarettes per day	12.1 $\pm$ 8.3	14.6 $\pm$ 10.8	$t = 0.92$	.36
Prior use of rescue salbutamol within 1 y				
No	58 (96.7%)	59 (98.3%)		
Yes	2 (3.3%)	1 (1.7%)		
Current use of indacaterol or other bronchodilators				
Yes	0	1 (1.7%)		
No	60 (100%)	59 (98.3%)		
Weight, kg	56.0 $\pm$ 8.7	53.9 $\pm$ 9.1	$t = 1.26$	.209
BMI, kg/m <sup>2</sup>	21.1 $\pm$ 3.1	20.3 $\pm$ 3.2	$t = 1.49$	.137
Blood pressure, mm Hg				
Systolic	133 $\pm$ 19.3	129 $\pm$ 18.0	$t = 1.05$	.295
Diastolic	76 $\pm$ 12.5	75 $\pm$ 11.8	$t = 0.47$	.637
Heart rate, beats/min	84.9 $\pm$ 13.8	85.0 $\pm$ 13.8	$t = -0.05$	.963
Respiratory rate, breaths/min	22.3 $\pm$ 3.5	21.9 $\pm$ 4.1	$t = 0.58$	.566
Predose FEV <sub>1</sub> , L	1.10 $\pm$ 0.36	1.10 $\pm$ 0.47	$t = 0.02$	.988
Predose FEV <sub>1</sub> , % predicted	44.3 $\pm$ 13.5	42.8 $\pm$ 15.8	$t = 0.59$	.556
Predose FVC, L	2.32 $\pm$ 0.57	2.31 $\pm$ 0.64	$t = 0.08$	.937
Predose FVC, % predicted	72.4 $\pm$ 14.6	70.3 $\pm$ 15.9	$t = 0.72$	.47
Predose FEV <sub>1</sub> /FVC	47.0 $\pm$ 9.39	46.5 $\pm$ 10.68	$t = 0.22$	.824
Postdose FEV <sub>1</sub> , L	1.21 $\pm$ 0.36	1.21 $\pm$ 0.46	$t = 0.03$	.976
Postdose FEV <sub>1</sub> , % predicted	48.7 $\pm$ 13.4	47.1 $\pm$ 15.4	$t = 0.59$	.554
Postdose FVC, L	2.56 $\pm$ 0.55	2.53 $\pm$ 0.58	$t = 0.24$	.807
Postdose FVC, % predicted	79.7 $\pm$ 13.7	77.3 $\pm$ 13.8	$t = 0.98$	.328
Postdose FEV <sub>1</sub> /FVC	47.4 $\pm$ 10.9	46.8 $\pm$ 10.8	$t = 0.30$	.765
6MWD, m	545 $\pm$ 59.4	528 $\pm$ 69.3	$t = 1.50$	.137
SGRQ				
Symptoms	61.4 $\pm$ 13.7	63.1 $\pm$ 15.8	$t = -0.62$	.538
Activity	50.6 $\pm$ 21.4	53.7 $\pm$ 22.3	$t = -0.77$	.444
Impacts	39.8 $\pm$ 19.3	38.3 $\pm$ 19.2	$t = 0.41$	.681
Total	46.7 $\pm$ 17.5	47.0 $\pm$ 17.0	$t = -0.10$	.921
mMRC scale (0-4)	1.70 $\pm$ 0.72	1.83 $\pm$ 0.69	$t = -1.03$	.304
SPPB (of 12)	12 $\pm$ 0	12 $\pm$ 0		
Mean physical activity (step count)	7,992 $\pm$ 3,894	7,005 $\pm$ 3,619	$t = 1.43$	.157
FFMI, kg/m <sup>2</sup>	15.3 $\pm$ 1.3	15.0 $\pm$ 1.3	$t = 1.32$	.19
QMVC, kg	32.1 $\pm$ 8.3	30.5 $\pm$ 7.4	$t = 1.15$	.253

6MWD = 6-min walk distance; FFMI = fat-free mass index; mMRC = modified Medical Research Council dyspnea score; PR = pulmonary rehabilitation; QMVC = quadriceps maximum voluntary contraction force; SGRQ = St. George's Respiratory Questionnaire; SPPB = short physical performance battery score; V = visit.

and Tai Chi for SGRQ was 4.5 (95% CI, 1.9 to 7.0;  $P < .001$ ); for 6MWD, it was -22.7 m (95% CI, -34.6 to -10.9;  $P < .001$ ) and for mMRC, the score was 0.32 (95% CI, 0.15 to 0.49;  $P < .001$ ). All favored Tai Chi.

Because mMRC is a categorical variable, we calculated the proportion in each group; a one-point decrease was observed between visits 6 and 9 in 20 (33.3%) patients in the Tai Chi group and in five (8.3%) patients in the PR

**TABLE 2 ] Primary, Secondary, and Selected Exploratory End Points at V3, V6, and V9 According to Treatment Group Allocation**

Variable	Tai Chi Group				P Value	PR Group				F Value	P Value
	V3	V6	V9	F		V3	V6	V9			
SGRQ, total	31.3 ± 13.6	16.1 ± 10.9 <sup>a</sup>	12.4 ± 7.9 <sup>a</sup>	44.9	< .001	29.8 ± 11.1	13.5 ± 8.2 <sup>a</sup>	14.8 ± 9.9 <sup>a</sup>	25.4	< .001	
SGRQ, symptoms	50.0 ± 14.0	30.8 ± 14.9 <sup>a</sup>	27.6±12.3 <sup>a</sup>	41.6	< .001	49.7 ± 15.6	25.3 ± 12.7 <sup>a</sup>	30.0 ± 13.3 <sup>a</sup>	36.4	< .001	
SGRQ, activity	40.4 ± 17.9	18.8 ± 14.5 <sup>a</sup>	12.8 ± 11.2 <sup>a</sup>	53.1	< .001	39.6 ± 17.2	19.5 ± 13.6 <sup>a</sup>	21.7 ± 18.9 <sup>a</sup>	17.8	< .001	
SGRQ, impacts	21.6 ± 14.8	11.2 ± 9.6 <sup>a</sup>	8.8 ± 7.1 <sup>a</sup>	21.5	< .001	19.8 ± 11.2	7.3 ± 7.3 <sup>a</sup>	7.6 ± 7.1 <sup>a</sup>	16.9	< .001	
6MWD, m	561 ± 57.9	580 ± 52.5	588 ± 53 <sup>a</sup>	3.4	.035	541 ± 67	564 ± 68	547 ± 70	1.1	.335	
FEV <sub>1</sub> , L	1.1 ± 0.4	1.2 ± 0.42	1.1 ± 0.4	0.2	.822	1.2 ± 0.5	1.3 ± 0.5	1.3 ± 0.5	0.1	.908	
FVC, L	2.4 ± 0.6	2.5 ± 0.6	2.4 ± 0.6	0.3	.748	2.4 ± 0.6	2.4 ± 0.7	2.4 ± 0.6	0.2	.845	
mMRC	1.5 ± 0.7	1.0 ± 0.6 <sup>a</sup>	0.7 ± 0.6 <sup>a,b</sup>	23.2	< .001	1.5 ± 0.6	0.9 ± 0.7 <sup>a</sup>	0.9 ± 0.7 <sup>a</sup>	10.9	< .001	
QMVC, kg	33.1 ± 8.5	36.9 ± 10.9 <sup>a</sup>	40.2 ± 10 <sup>a</sup>	8	< .001	31.8 ± 7.8	36.7 ± 1.2 <sup>a</sup>	36.7 ± 8.5 <sup>a</sup>	5.3	.006	

See Table 1 legend for expansion of abbreviations.

<sup>a</sup> $P < .05$  compared with V3.

<sup>b</sup> $P < .05$  compared with V6.

group ( $\chi^2$  test,  $P = .001$ ). No differences were observed for FEV<sub>1</sub>. The overall progression of the main parameters is shown in Figure 2, and the subanalysis of different SGRQ domains is shown in e-Table 3. The overall message conveyed by analysis of visit 9 data was also confirmed if the point of comparison was the start of exercise (visit 3) as opposed to the end (visit 6) (e-Table 4).

### Quadriceps Strength

Data regarding quadriceps strength are shown in Figure 2. No differences were noted between PR and Tai Chi at the end of the exercise intervention (visit 6). However, between visits 6 and 9, quadriceps strength differed between groups, and by visit 9, the group difference between PR and Tai Chi for quadriceps maximum voluntary contraction force was  $-3.3$  kg (95% CI,  $-5.2$  to  $-1.4$ ;  $P < .001$ ). Physical activity showed a slight benefit in favor of Tai Chi, and thus this group had a significantly higher step count at visit 9 (e-Table 5):  $7,907 \pm 3,568$  steps/d for Tai Chi and  $6,558 \pm 3,137$  steps/d for PR ( $P = .03$ ).

### Effect of Indacaterol and Adverse Events

The effect of indacaterol is shown in e-Table 6. No difference in adverse events was observed between the groups (e-Table 7).

### Discussion

With concurrent long-acting inhaled  $\beta$ -agonist use, both PR and Tai Chi conferred substantial benefits as judged by using a treatment-specific quality of life measure and performance on a 6MWD test. Although neither training approach differed from the other by more than the minimal clinically important difference (MCID) of 4 SGRQ points, 12 weeks after discontinuation of formal training, improvements emerged in favor of Tai Chi in SGRQ score, 6MWD, mMRC dyspnea score, and quadriceps strength. We concluded that Tai Chi is equivalent to PR and may confer more sustained benefit.

### Critique of the Method

The choice of SGRQ as the primary outcome measure requires justification. The efficacy of COPD treatments is often judged by change in FEV<sub>1</sub>; however, based on earlier findings,<sup>4</sup> we did not expect either PR or Tai Chi to affect FEV<sub>1</sub>. We could have used an exercise outcome measure, but there would have been a danger that the exercise modality chosen for evaluation might have favored one or other intervention through a learning effect. For this

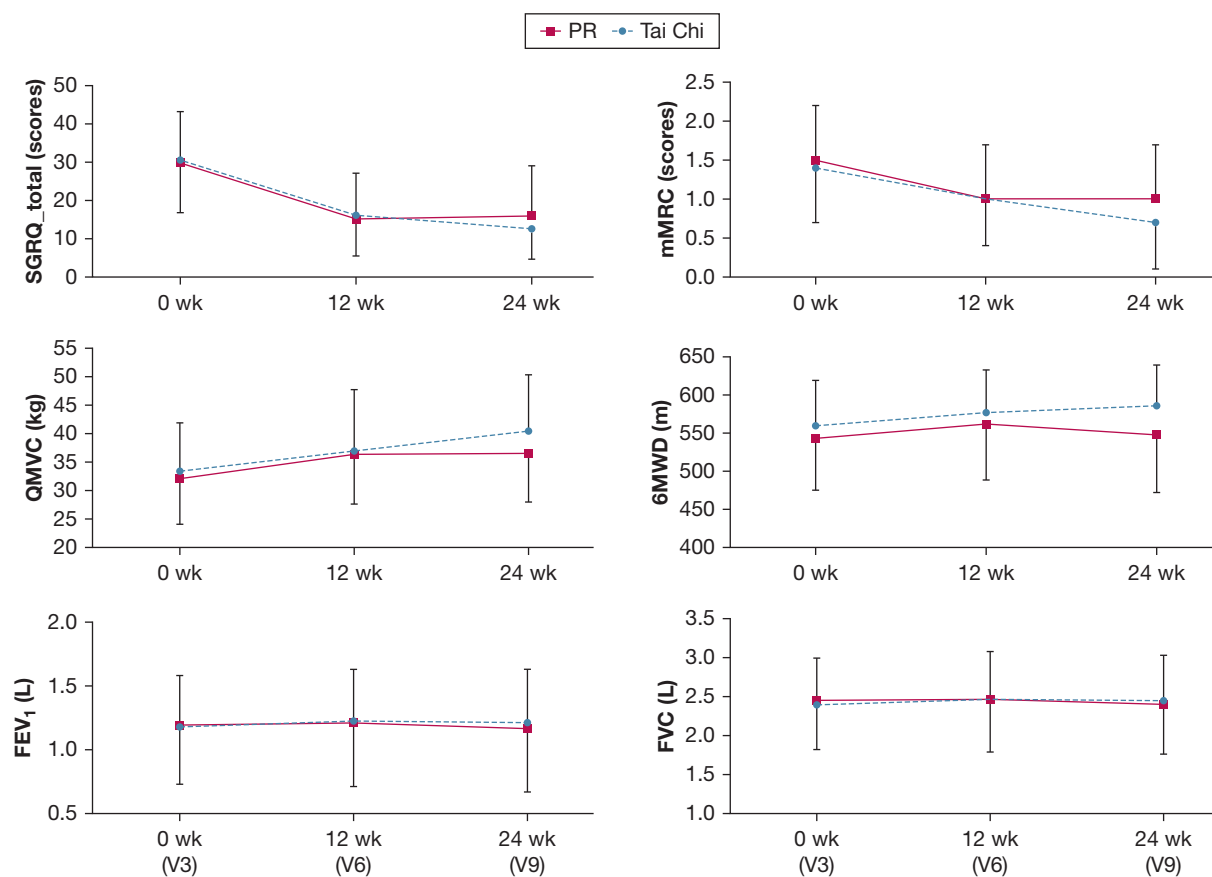


Figure 2 – Main parameters of interest as a function of visit and treatment allocation. V2 and V3 were the introduction of indacaterol 150 µg once daily (all participants). V3 to V6 were treatment with Tai Chi or Western-style PR according to treatment allocation, and V6 to V9 represent the continuation phase with indacaterol alone. 6MWD = 6-min walk distance; MCID = minimal clinically important difference; mMRC = modified Medical Research Council dyspnea score; SGRQ = St. George's Respiratory Questionnaire; V = visit. See Figure 1 legend for expansion of other abbreviation. Solid line represents PR, dashed lines represent Tai Chi.

reason, we did not undertake specific cardiopulmonary exercise testing because this testing is closer in concept to formal PR than Tai Chi. Conversely, SGRQ is widely used as an end point in COPD clinical trials and has recently been recognized as a valid co-primary end point in trials of new medicines by the US Food and Drug Administration (<http://www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm071575.pdf>). The choice of an MCID of 4 represents an agreed consensus in the COPD field.<sup>16</sup> One criticism of using the SGRQ is that it is susceptible to influence by other nonexercise-related features such as interaction with study staff, as well as social and educational interventions. This concern is further sharpened by the observation that gains in 6MWD did not reach the MCID for either intervention. Thus, it is possible that (considered as a group) these study participants were not sufficiently disabled to maximally profit from either PR or TC.

Ideally, the assessment team would have been blinded to treatment allocation as was done by Holland et al.<sup>17</sup> However, in a rural Chinese environment in which, by definition it was impossible to blind patients and their caregivers to treatment allocation, we felt that this approach was not practical. In addition, particularly had the study been assessor blinded, the visit 3 measures might have been better made before randomization.

Medicine costs may represent a significant burden for patients in China, particularly in remote countryside areas (eg, Xing-Ning), where the monthly family income is typically 2000 RMB (approximately \$250)<sup>18</sup>; thus, many patients are bronchodilator naive. Therefore, given the impressive (at least judged according to SGRQ) results conferred by both PR and Tai Chi, we speculate that it would be useful to conduct a four-way study comparing the effects of bronchodilators and Tai Chi both separately and together; nevertheless, we



predict that by permitting more intense exercise, bronchodilators and exercise would be complementary rather than alternative therapies.

We lacked data to power the study for superiority of Tai Chi over PR. However, the intention in any case was to seek evidence of equivalence because a preference for Tai Chi would then be justified on the grounds of convenience and probably cost, although we did not undertake a health economic analysis. We submit that equivalence was demonstrated by 95% CI showing the difference in SGRQ between groups lay between 4 and -4. Furthermore, beyond the cost of initially educating participants, Tai Chi requires nothing except a small flat space that may, depending on the weather, be either indoor or outdoor.

Compared with European patients, the participants were relatively well functioning (Table 1). Specifically, despite being, on average, in grade III COPD according to the Global Initiative for Chronic Obstructive Lung Disease scoring, their 6MWD exceeded 500 m; in the multicenter study reported by Waschki et al,<sup>19</sup> however, participants achieved a mean 6MWD of 364 m and an SGRQ of 54 with a daily step count of 4,725 compared with an SGRQ of 46 and a step count > 7,000 in this cohort despite having a similar FEV<sub>1</sub>. Two possibilities may explain this discrepancy. First, the patients studied by Waschki et al<sup>19</sup> were mainly those referred for hospital care (rather than being mainly recruited from community, as was the case in the present study), and they therefore may have been self-selected to be more symptomatic. Second, most patients in the present study were farmers who have to work to create income because they generally do not have a pension or other government benefits. Similar observations were made by Pitta et al<sup>20</sup> comparing Brazilian and Austrian patients with COPD.

It may be argued that 12 weeks of PR is longer than usual, at least for the United Kingdom,<sup>21,22</sup> although longer training periods are used in some European centers.<sup>4</sup> We choose to use 12 weeks for two reasons: first, to ensure that patients would have sufficient time to learn Tai Chi and second, to guarantee that we had given an adequate exposure to PR to ensure a fair comparison. We acknowledge that our protocol required patients to attend five times weekly for Tai Chi as opposed to thrice weekly for PR; thus, Tai Chi could be viewed as more burdensome for the patients in the sense that greater exposure is required to achieve an equivalent change in the SGRQ.

Lastly, we acknowledge that Tai Chi can be taught in different forms and even in the 24 form Yang style it is possible to have individualized instruction with, for example, greater focus on lower limb weight-bearing, either by single-leg maneuvers or by moving one's center of gravity lower. In the present trial, after small-group learning of the maneuvers, patients joined a larger Tai Chi class; thus, this form of individualized instruction was not possible (although training intensity may nevertheless have increased as participants became more proficient). Conversely, with PR, the tasks are programmed to become more demanding as the program proceeds. It is therefore possible that a personalized Tai Chi program may have resulted in greater benefits, but the present study lacks data that could support that speculation. Nevertheless, this possibility does not detract from our conclusion that a group Tai Chi program can provide equivalent benefit to a conventional Western PR program.

### Significance of the Findings

The significance of our findings depends on the MCID of the parameters measured. The primary end point was SGRQ, and MCID for this measure is conventionally considered to be 4 points.<sup>16</sup> For 6MWD, a range of MCID have been reported between 25 and 54 m,<sup>23,24</sup> with recent larger data sets favoring the smaller number.<sup>25</sup> We are not aware of published MCIDs for mMRC dyspnea score or quadriceps strength.

Previous studies of Tai Chi in COPD, and other chronic conditions prevalent in the elderly, when considered together<sup>6</sup> reportedly show improvements both in walking distance and, again consistent with our data, knee extensor strength. Because we did not seek to tailor our Tai Chi program specifically for patients with respiratory disability, it is conceptually possible that classes as described here could simultaneously treat both patients with COPD and those with other conditions.

Our aim was to show equivalence of PR and Tai Chi at the end of the exercise intervention, and we achieved this goal because the mean difference in change in total SGRQ between treatment allocation was 0.48 point ( $P = \text{NS}$ ) and, importantly, the 95% CI was within the MCID of  $\pm 4$  points. Reassuringly, because PR is known to increase 6MWD, the difference in change in 6MWD conferred by the two exercise interventions was also both statistically nonsignificant and, in addition, had CIs that also excluded a clinically important difference. This

finding should encourage the use of Tai Chi as a substitute for PR because it suggests the effect of Tai Chi may confer, through mechanisms currently unknown, benefits that are not exclusively physical. We note that Tai Chi is not the only low-cost intervention that could substitute for PR, although it is one that is familiar to the Chinese population. In a meta-analysis, Alison and McKeough<sup>26</sup> highlighted other potentially beneficial approaches (walking, stepping, and the sit-to-stand maneuver).

The period after the exercise intervention proved illuminating, as a statistically significant between-group difference emerged for SGRQ with a magnitude (4.5 points) that exceeded the MCID; the 95% CI encompassed magnitudes of difference that, although remaining statistically significant, did not exceed the MCID, however. Consistent with this finding, statistically but not clinically significant differences in favor of the Tai Chi group were observed for exercise performance (6MWD), dyspnea, and quadriceps strength. We speculate that improved quadriceps function is the reason for improvement in the other parameters for the following reasons. First, it is entirely plausible that Tai Chi, which involves periods supporting oneself with one leg, acts as an (anabolic) training stimulus; consistent with this theory, we previously showed that Tai Chi, but not treadmill exercise, induces quadriceps fatigue,<sup>9</sup> and quadriceps fatigue is known to predict a positive response to strength training.<sup>27,28</sup> Second, we have previously shown that classic PR produces an increase in quadriceps strength that is related to the magnitude of improvement

in exercise performance.<sup>29</sup> Third, quadriceps weakness is associated with dyspnea in a general adult population<sup>30</sup> and specifically with impaired physical function in COPD.<sup>12</sup> The improvement in quadriceps function may have occurred during the formal training period. However, it is also likely that the Tai Chi group continued to some extent to practice after the end of the training period, which would have been more difficult for the PR group who lacked access to gymnasium equipment. It is conceded, however, that we could have offered the PR group more vigorous and practical advice as to how they could retain the benefits conferred by PR without having to use specialist exercise equipment.

The study population was unusual in that they were bronchodilator naive. In some cases, this situation occurred because they had not yet received a diagnosis of COPD; it is also possible that access to bronchodilators was limited in some cases by finance. This problem is also recognized globally,<sup>31</sup> and we speculate that Tai Chi may have potential as a low-cost initial therapy in COPD.

## Conclusions

Judged by using the primary end point of SGRQ, these data exclude a clinically meaningful difference at 12 weeks between classic PR and Tai Chi. Twelve weeks after the end of the intervention, a significant difference in SGRQ was observed favoring the Tai Chi group; this observation, supported also by improvements in dyspnea and exercise performance, suggests that Tai Chi could be substituted for PR in the treatment of COPD with greater convenience for patients.



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**Additional information:** The e-Appendix, e-Figure, e-Tables, and Videos can be found in the Supplemental Materials section of the online article.

## References

- Lozano R, Naghavi M, Foreman K, et al. Global and regional mortality from 235 causes of death for 20 age groups in 1990 and 2010: a systematic analysis for the Global Burden of Disease Study 2010. *Lancet*. 2012;380(9859):2095-2128.
- Griffiths TL, Burr ML, Campbell IA, et al. Results at 1 year of outpatient multidisciplinary pulmonary rehabilitation: a randomised controlled trial. *Lancet*. 2000;355(9201):362-368.
- Griffiths TL, Phillips CJ, Davies S, et al. Cost effectiveness of an outpatient multidisciplinary pulmonary rehabilitation programme. *Thorax*. 2001;56(10):779-784.
- Troosters T, Gosselink R, Decramer M. Short- and long-term effects of outpatient rehabilitation in patients with chronic obstructive pulmonary disease: a randomized trial. *Am J Med*. 2000;109(3):207-212.
- McGavin CR, Gupta SP, Lloyd EL, et al. Physical rehabilitation for the chronic bronchitic: results of a controlled trial of exercises in the home. *Thorax*. 1977;32(3):307-311.
- Chen YW, Hunt MA, Campbell KL, et al. The effect of Tai Chi on four chronic conditions—cancer, osteoarthritis, heart failure and chronic obstructive pulmonary disease: a systematic review and meta-analyses. *Br J Sports Med*. 2016;50(7):397-407.
- Li F, Harmer P, Fitzgerald K, et al. Tai chi and postural stability in patients with Parkinson's disease. *N Engl J Med*. 2012;366(6):511-519.
- Wang C, Schmid CH, Rones R, et al. A randomized trial of tai chi for fibromyalgia. *N Engl J Med*. 2010;363(8):743-754.
- Qiu ZH, Guo HX, Lu G, et al. Physiological responses to Tai Chi in stable patients with COPD. *Respir Physiol Neurobiol*. 2016;221:30-34.
- Niu R, He R, Luo BL, et al. The effect of tai chi on chronic obstructive pulmonary disease: a pilot randomised study of lung function, exercise capacity and diaphragm strength. *Heart Lung Circ*. 2014;23(4):347-352.
- Jones PW, Quirk FH, Baveystock CM, et al. 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.
- Patel MS, Mohan D, Andersson YM, et al. Phenotypic characteristics associated with reduced short physical performance battery score in COPD. *Chest*. 2014;145(5):1016-1024.
- Steiner MC, Barton RL, Singh SJ, et al. Bedside methods versus dual energy X-ray absorptiometry for body composition measurement in COPD. *Eur Respir J*. 2002;19(4):626-631.
- Seymour JM, Spruit MA, Hopkinson NS, et al. The prevalence of quadriceps weakness in COPD and the relationship with disease severity. *Eur Respir J*. 2010;36(1):81-88.
- Casaburi R, Kukafka D, Cooper CB, et al. Improvement in exercise tolerance with the combination of tiotropium and pulmonary rehabilitation in patients with COPD. *Chest*. 2005;127(3):809-817.
- Jones PW. St. George's Respiratory Questionnaire: MCID. *COPD*. 2005;2(1):75-79.
- Holland AE, Mahal A, Hill CJ, et al. Home-based rehabilitation for COPD using minimal resources: a randomised, controlled equivalence trial. *Thorax*. 2017;72(1):57-65.
- China NHAFPCotPsRo. per capita income in rural. *China Family Development Report*. 2015;8:100.
- Waschki B, Spruit MA, Watz H, et al. Physical activity monitoring in COPD: compliance and associations with clinical characteristics in a multicenter study. *Respir Med*. 2012;106(4):522-530.
- Pitta F, Breyer MK, Hernandez NA, et al. Comparison of daily physical activity between COPD patients from Central Europe and South America. *Respir Med*. 2009;103(3):421-426.
- Green RH, Singh SJ, Williams J, et al. A randomised controlled trial of four weeks versus seven weeks of pulmonary rehabilitation in chronic obstructive pulmonary disease. *Thorax*. 2001;56(2):143-145.
- Sewell L, Singh SJ, Williams JE, et al. How long should outpatient pulmonary rehabilitation be? A randomised controlled trial of 4 weeks versus 7 weeks. *Thorax*. 2006;61(9):767-771.
- Holland AE, Hill CJ, Rasekaba T, et al. Updating the minimal important difference for six-minute walk distance in patients with chronic obstructive pulmonary disease. *Arch Phys Med Rehabil*. 2010;91(2):221-225.
- Redelmeier DA, Bayoumi AM, Goldstein RS, et al. Interpreting small differences in functional status: the six minute walk test in chronic lung disease patients. *Am J Respir Crit Care Med*. 1997;155(4):1278-1282.
- Polkey MI, Spruit MA, Edwards LD, et al. Six-minute-walk test in chronic obstructive pulmonary disease: minimal clinically important difference for death or hospitalization. *Am J Respir Crit Care Med*. 2013;187(4):382-386.
- Alison JA, McKeough ZJ. Pulmonary rehabilitation for COPD: are programs with minimal exercise equipment effective? *J Thorac Dis*. 2014;6(11):1606-1614.
- Mador MJ, Mogri M, Patel A. Contractile fatigue of the quadriceps muscle predicts improvement in exercise performance after pulmonary rehabilitation. *J Cardiopulm Rehabil Prev*. 2014;34(1):54-61.
- Burtin C, Saey D, Saglam M, et al. Effectiveness of exercise training in patients with COPD: the role of muscle fatigue. *Eur Respir J*. 2012;40(2):338-344.
- Seymour JM, Moore L, Jolley CJ, et al. Outpatient pulmonary rehabilitation following acute exacerbations of COPD. *Thorax*. 2010;65(5):423-428.
- Kelly JL, Elkin SL, Fluxman J, et al. Breathlessness and skeletal muscle weakness in patients undergoing lung health screening in primary care. *COPD*. 2013;10(1):40-54.
- Gnatiuc L, Buist AS, Kato B, et al. Gaps in using bronchodilators, inhaled corticosteroids and influenza vaccine among 23 high- and low-income sites. *Int J Tuberc Lung Dis*. 2015;19(1):21-30.