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# Home-based prescribed pulmonary exercise improves exercise capacity and quality of life in patients with stable chronic obstructive pulmonary disease --Manuscript Draft--

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## 1 TITLE:

- 2 Effects of Home-Based Prescribed Pulmonary Exercise in Patients with Stable Chronic
- 3 Obstructive Pulmonary Disease

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#### **KEYWORDS:**

respiratory disease, traditional Chinese exercise, home-based rehabilitation, alternative intervention, functional exercise capacity, quality of life

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#### **SUMMARY:**

- Presented here is a protocol to investigate the effects of home-based prescribed pulmonary exercise in stable chronic obstructive pulmonary disease (COPD) patients, which is modified based on traditional Chinese exercises according to dyspnea and limited exercise capacity
- 40 observed in COPD patients.

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#### ABSTRACT:

- 43 As a systemic disease, chronic obstructive pulmonary disease (COPD) affects the respiratory
- 44 system, inducing restless and exercise dyspnea. It also impacts exercise capacity and forms a

vicious circle in which it further aggravates the condition of patients and accelerates disease progression. As a functional holistic exercise, traditional Chinese exercises (TCE) play an important role in the rehabilitation of COPD on the basis of adjusting the breath and performing coordinated movements. This study investigates the effects of prescribed pulmonary exercises that are modified from TCE. These modifications are based on dyspnea and limited exercise capacity, exercise capacity of upper and lower limbs, endurance exercise capacity, and quality of life in stable COPD patients. The goal is to determine the accessibility of these prescribed exercises in COPD rehabilitation. Participants are randomly divided into a nonexercise control group (CG) or prescribed pulmonary exercise group (PG) at a ratio of 1: 1. The PG receives intervention for 60 min twice per day, 7 days a week, for a total of 3 months. The intensity is measured using the Borg category-ratio 10 scale and with a heart-rate monitor. Then, an exercise capacity test and quality of life questionnaire are scheduled at 1 week before and after the formal intervention. After 3 months of intervention, the 30 s arm curl test, 30 s sit-to-stand test, 6 min walking test, and quality of life show significant improvement in COPD patients (p < 0.05). These findings indicate that prescribed pulmonary exercises can be applied as alternative, convenient, and effective home- and community-based exercises for stable COPD patients.

#### **INTRODUCTION:**

Chronic non-communicable diseases have gradually become the biggest threat to global health, accounting for 70% of global mortality. A majority of such deaths have been caused by four main diseases, while COPD ranks third and only falls behind cardiovascular disease and cancer. Moreover, the ranking of COPD in leading to years of life lost has risen from eleventh in 2007 to seventh in 2017<sup>1</sup>. This change indicates unsatisfactory effects of current treatments in the rehabilitation of COPD progression. More studies have recognized that COPD is not only a respiratory disease but also a complex, multi-systemic, and multi-complicative condition<sup>2,3</sup>. COPD complications (i.e., skeletal muscle dysfunction) exist in all stages of the disease and play an important role in progression and prognosis<sup>4</sup>. Considering interactions between the respiratory symptoms and exercise capacity, rehabilitation of exercise capacity has received a lot of attention.

Pulmonary rehabilitation as a comprehensive intervention program, including but not limited to exercise training, health education, and self-management, has demonstrated effectiveness on physical and psychological condition of COPD patients<sup>5</sup>. Among the different types of exercise training, aerobic exercise plays a critical role in the improvement of endurance performance and muscle power<sup>6</sup>. In contrast, resistance exercise shows advantages in the improvement of muscle strength and functional exercise capacity<sup>7</sup>. Moreover, the interventional mechanisms of these two exercise types are distinct. Compared to resistance exercise, aerobic exercise is more effective in modulating inflammatory cytokine levels and inducing oxidized phenotypes of the quadriceps<sup>8,9</sup>.

Although the effects of these two conventional exercises in pulmonary rehabilitation has been demonstrated, regardless of the location (in hospital or at home)<sup>10,11</sup>, implementation of

conventional exercise training is still limited due to the requirements of specific equipment, spacious room, and safety monitoring. These constraints not only inflict a burden on a patient's family but also to the healthcare system. Alternative interventions such as neuromuscular electrical stimulation and whole-body vibration training share the same constraints<sup>12,13</sup>.

Traditional Chinese exercises (TCE), including tai chi, liu zi jue, wu qin xi, ba duan jin, and yi jin jing, belong to the self-exercise category, which focuses on adjustment of the breath accompanied with coordinated movement. These exercises also rely on psychological-physiological-morphological mechanisms to achieve health-related fitness. Previous studies have shown that 1) TCE as a low-and medium-intensity aerobic exercise induces a maximum heart rate of 43%–49%<sup>14</sup>, 2) exercise intensity ranges from 1.5 to 2.6 metabolic equivalents of energy (METs)<sup>15</sup>, and 3) it exerts positive effects in patients with stable COPD through clinical and family rehabilitation<sup>16-19</sup>. Compared to conventional exercise training, the advantage of TCE is that it is easy to execute at home without any equipment or spatial constraints.

As a modified TCE, the prescribed pulmonary exercise described in this protocol has been developed from the theory of traditional Chinese medicine and aims at the rehabilitation of COPD dyspnea and exercise capacity. Previous studies have showed significant improvements in the exercise capacity (assessed by 6 min walking test, 6MWT), daily life (Zhongshan COPD questionnaire for quality of life), and systemic inflammation levels in COPD patients after prescribed pulmonary exercise. However, the effects of prescribed pulmonary exercise on the exercise capacity of upper and lower limbs and quality of life in COPD patients is still unclear.

This study compares 3 months of usual medicinal treatment without exercise intervention (control group, CG) vs. 3 months of prescribed pulmonary exercise intervention (PG) in stable COPD patients to investigate the effects of prescribed pulmonary exercise. The effects on upper limb exercise capacity are evaluated by the 30 s arm curl test, effects on lower limb exercise capacity evaluated by the 30 s sit-to-stand test (30 s SST), effects on endurance exercise capacity evaluated by the 6 min walking test (6MWT), and effects on quality of life evaluated by St. George's Respiratory Questionnaire (SGRQ).

#### PROTOCOL:

The protocol has been approved by the Ethics Committee of Yueyang Hospital of Integrated Traditional Chinese and Western Medicine affiliated with Shanghai University of Traditional Chinese Medicine (Shanghai, China).

#### 1. Video construction and study design

1.1. Construct a video of the prescribed pulmonary exercise. Our video was based on the TCE video issued by the General Administration of Sport of China.

1.1.1. In the video, have a member of the research team in a spacious place display and give a general introduction to the different characteristics of the prescribed pulmonary exercises.

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134 1.1.2. Have the member simulate the exercises in different dimensions to clarify their

135 characteristics.

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- NOTE: The video used here is in Chinese. The person in the video is of normal weight and is a
- middle-aged female in good physical shape, from Shanghai University of Traditional Chinese Medicine. The video structure and contents can be seen in **Figure 1.**

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1.2. Use a parallel-designed single-blind randomized controlled trial to determine the effect of
 prescribed pulmonary exercise on COPD patients.

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1.2.1. Obtain written, informed consent and collect basic characteristics including age, sex, body mass index (BMI), duration, and disease grade from recruited participants.

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1.2.2. Randomize the divided participants into two groups at a 1:1 ratio according to a random number table.

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NOTE: Random numbers should be generated using a computer and enclosed in an opaque envelope by an independent individual who does not participate to achieve allocation concealment.

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2. Power calculation

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2.1. Conduct a power analysis using analysis software of choice to determine the minimal
 sample size necessary to obtain statistical results.

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2.1.1. Choose an appropriate statistical test according to the study design.

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2.1.2. Select an assumed mean difference of the changes in quality of life after 3 months of
 intervention of prescribed pulmonary disease. This can be based on any previous work that may
 have been done.

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2.1.3. Select an assumed standard deviation (SD), as well as an appropriate alpha and powervalue.

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2.2. Using a previous study as a reference (if possible) and considering the study design, definean assumed drop-out rate.

- NOTE: The power analysis of this study was based on an independent t-test assuming equal
- variance. Based on the minimal clinical important difference of the total SGRQ and item
- scores<sup>21</sup>, the assumed mean difference was set at 4 scores, and the assumed SD in both groups
- was set at 3.6 scores according to previous studies<sup>17</sup>. The two-side significance level was set at
- an alpha-level of 0.05, and a power of 0.8. Results of the power calculation revealed that a total
- of 28 participants were needed (14/group). Considering a drop-out rate of about 15%, we

177 planned to recruit 34 participants (17/group) (Figure 2).

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## 3. Participant recruitment

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181 NOTE: Participant recruitment in this example was conducted in the Department of Respiratory, 182 Yueyang Hospital of Integrated Traditional Chinese and Western Medicine, Shanghai University of Traditional Chinese Medicine.

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187 NOTE: The COPD diagnosis was based on the guidelines of the Global Initiative for Chronic 188 Obstructive Lung Disease (GOLD) (forced expiratory volume in 1 second (FEV 1)/forced vital 189 capacity (FVC) < 0.7, FEV1 < 80% the predicted value)<sup>5</sup>.

3.1. Recruit patients with stable COPD between the ages of 40 and 80.

190

191 3.2. Exclude participants who have regularly exercised in the past 6 months (>2x per week 192 for >60 min each). Also, exclude participants in acute exacerbation as well as those that have 193 serious cardiovascular diseases or musculoskeletal disorders that could affect exercise 194 intervention and testing programs.

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3.3. Ask participants for written consent after informing them about possible discomfort and risks during the training sessions and testing. The possible discomfort and risks include but are not limited to sourness of muscle, dizzy, dyspnea, and falling.

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## 4. Training

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4.1. Give training instructions 3x within 2 weeks to PG participants before the formal training session. Ask participants to study the complete action and breathing requirements of each intervention.

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4.2. Deliver the video of the prescribed pulmonary exercises and the exercise record brochure to all participants.

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4.3. Instruct PG participants to perform the prescribed pulmonary exercises in accordance with the intervention program (60 min each, 2x per day, 7 days a week, for a total of 3 months).

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NOTE: On Sunday afternoons, ask participants to gather in the hospital to perform exercises under the supervision and instruction of physiotherapists, and for the remaining 6 days to perform exercises at home.

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216 4.3.1. Instruct PG participants to perform a warm-up exercise for 10 min, mainly focusing on 217 dynamic flexibility exercises of involved muscle groups and stretching muscles.

218

219 4.3.2. Instruct PG participants to perform prescribed pulmonary exercises for 40 min, which is 220 composed of six characteristics including the "hu" and "si" sounds in liu zi jue, "pushing up the

- sky to regulate the triple warmer" and "drawing a bow to shoot a vulture" in ba duan jin, "the crane actions" in wu gin xi, and "cross-armed iron staff" in yi jin jing<sup>22</sup>.
- 223
- NOTE: Evaluate the exercise intensity using the Borg category-ratio 10 (Borg CR-10) and ask
- participants to maintain a level of dyspnea in the range of 4 to 6<sup>23</sup>. In the hospital, the Borg CR-
- 226 10 and heart rate monitor<sup>2</sup> are both used to evaluate exercise intensity.

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228 4.3.3. Instruct PG participants to perform a cool-down exercise for 10 min, mainly focusing on stretching and relaxing the muscles.

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4.4. Ask participants to record detailed information after each exercise session in the exercise
 record brochure, including details about exercise method, time, duration, intensity, and site.

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5. Outcome assessment

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NOTE: Conduct an assessment session within 7 days before and after the formal intervention.

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238 5.1. Assessment of height, weight, and body composition

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5.1.1. Ask participants to remove all items and metal objects from their clothing and bodies.

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5.1.2. Ask participants to stand barefoot on the corresponding positions of the electrode pads with their back to the instrument column. Wait briefly for the apparatus to automatically print data including height, weight, body fat, and BMI.

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246 5.2. Six minute walking test (6MWT)

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5.2.1. Perform the 6MWT in accordance with the technical standard described by European
 Respiratory Society/American Thoracic Society (ERS/ATS)<sup>24</sup>.

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5.2.2. Explain the test procedure and inform participants that temporary rest is available when
 discomfort or exhaustion arises. Encourage participants to walk as fast as they can during the 6
 min duration.

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255 5.2.3. Prior to the test, inquire participants about their levels of dyspnea using the Borg CR10.

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5.2.4. Ask participants to walk back and forth as quickly as possible in a marked, 30 m straight
 line. Standardized phrases of encouragement are used for each minute.

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5.2.5. After 6 min, ask participants to stand stationary, then record their distance in meters and
 levels of dyspnea.

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263 5.2.6. After a 30 min rest, instruct participants to perform the test a second time.

5	5.3. 30 second arm curl test
) 7 }	NOTE: The 30 s arm curl test was carried out according to the senior fitness test manual <sup>25</sup> .
	5.3.1. Explain and demonstrate the test procedure and inform participants that the test should be performed as quickly as possible during a 30 s duration.
	NOTE: The test is initiated from the down position to the arm curl position, and the wrist should not move during the motion.
	5.3.2. Ask participants to sit on a 43 cm tall straight-back armless chair with their backs upright and feet flat on the ground.
	5.3.3. Ask participants to perform the arm curl motion 1–2x to familiarize.
	5.3.4. Ask participants to hold the dumbbells (8 lbs for men, 5 lbs for women) using the dominant hand.
	5.3.5. On the signal "go", instruct participants to curl the weight through a full range of motion as many times as possible in 30 s. A researcher should stand to the side to time and record the results.
	5.4. 30 second sit-to-stand test
	NOTE: The 30 s SST was performed according to the senior fitness test manual <sup>25</sup> .
	5.4.1. Place a chair with the backrest leaning against a wall.
	5.4.2. Explain and demonstrate the test procedure and inform participants that the test should be performed as quickly as possible in 30 s.
	NOTE: The test is initiated from a seating position, with feet separated and knee flexed at about 90°.
	5.4.3. Ask participants to sit in the middle of the chair with back straight, arms crossed on the chest and placed on the opposite shoulder.
	5.4.4. Ask participants to perform the sitting up motion 1–2x to familiarize.
	5.4.5. On the signal "go", instruct participants to stand up and sit down as many times as possible in 30 s. A researcher should stand to the side to time and record the results.
	NOTE: If participants conduct more than half of the motion at the end of the 30 s duration, this counts as a full motion.

5.5. Questionnaire for quality of life 5.5.1. Ask participants to complete the SGRQ to assess quality of life. The SGRQ consists of three subdomains including symptoms (cough, cough, asthma attacks, etc.), activity (climbing, dressing, housework, etc.), and impact (anxiety, pain, insecurity, etc.)<sup>26,27</sup>. 5.5.2. Calculate final SGRQ scores (total and sub-domains) per previous protocols, using analysis software of choice<sup>26,27</sup>. NOTE: Participants who display deficiency of knowledge or defects in vision should complete the questionnaire with the help of staff. 6. Statistical analysis 6.1. Carry out statistical analysis using software of choice. 6.2. Conduct normality and variance homogeneity tests for continuous data. 6.3. Conduct two paired t-tests or a Wilcoxon rank-sum test to analyze differences within the group according to data normality and variance. 6.4. Calculate the changes after 3 months of intervention as post-values minus pre-values. 6.5. Conduct an independent t-test or Mann-Whitney U test to analyze differences between the group according to change-value normality and variance. 6.6. Conduct a chi-squared ( $\chi^2$ ) test for category data. NOTE: Conduct a two-sided test and use p < 0.05 as the significance cut-off value. **REPRESENTATIVE RESULTS:** The protocol above describes a randomized controlled trial to investigate whether prescribed pulmonary exercise improves exercise capacity and quality of life in stable COPD patients. While 44 participants were recruited, only 37 (84%) participants completed the study (CG = 19, PG = 18). Thus, data analysis was carried out using the 37 participants, and the two groups showed no significant differences in basic characteristics including age, sex, BMI, duration, and disease grade (Table 1). After 3 months of intervention, repetition of: the 30 s arm curl test increased from 21.3 ± 4.4 to 22.9  $\pm$  4; the 30 s SST increased from 16.8  $\pm$  1 to 19.7  $\pm$  3.5 (p = 0.001, Figure 3); and the distance in meters of 6MWT increased from  $501.26 \pm 74.08$  to  $535.78 \pm 55.09$  (p = 0.005) in PG.

Between-group comparisons found that the improvement of exercise capacity in PG was

significantly different from CG (p < 0.01). In addition, the activity score of SGRQ in CG showed a significant increase (p = 0.01), while the total and item scores of SGRQ in PG showed significant decreases (p < 0.01, **Figure 4**). Between-group comparisons showed that improvement of SGRQ in the PG was significantly different from that in the CG (p < 0.01).

#### FIGURE AND TABLE LEGENDS:

**Figure 1: Main characteristics of prescribed pulmonary exercises.** These pictures were originally published in Liu et al.<sup>22</sup>

**Figure 2: Schematic diagram of the protocol**. The pre- and post-tests are similar. Further details are given in the text.

Figure 3: Exercise capacity before and after 3 months of intervention. CG = control group; PG = prescribed pulmonary disease; 30 s SST = 30 seconds sit-to-stand test. Data are expressed as mean  $\pm$  SD. Within-group comparisons were calculated using the paired sample t-test (\*\*p < 0.01, meaning that the comparisons were significant within groups).

Figure 4: Quality of life before and after 3 months of intervention. CG = control group; PG = prescribed pulmonary disease; SGRQ = St. George's Respiratory Questionnaire. Data are expressed as mean  $\pm$  SD. Within-group comparisons were calculated using the paired sample t-test (\*p < 0.05, \*\*p < 0.01, meaning that the comparisons were significant within groups).

**Table 1: Basic characteristics**. CG = control group; PG = prescribed pulmonary exercise group; AECOPD = acute exacerbation of chronic obstructive pulmonary disease.

## **DISCUSSION:**

In this study, a modified TCE referred to as prescribed pulmonary exercise is used in an intervention program, and a number of fitness tests are used to investigate the effects of home-based prescribed pulmonary exercise on exercise capacity and quality of life in stable COPD patients. The main finding is that many improvements occurred in upper and lower limb exercise capacity, endurance exercise capacity, and quality of life after 3 months of intervention. The results indicate that prescribed pulmonary exercise as a COPD-targeted and easy-to-study TCM can be used in home- and community-based COPD rehabilitation programs.

The completion rate of 84% after 3 months of intervention in this study is comparable to 90% in a previous study that adopted tai chi in COPD patients. The intervention program is 60 min each, once per day, 7 days a week (2 days in the hospital and 5 days at home), for a total of 12 weeks<sup>28</sup>. However, another study that applied the ba duan jin exercise as an intervention in COPD patients (age:  $73.12 \pm 1.33$ , FEV1%pred:  $36.75 \pm 2.11$ ) only led to a completion rate of 65%, which was once per day, 4x per week, for a total of 6 months<sup>19</sup>. This may be attributed to the patients' ages, in which all were above 70 years old, and that the FEV1%pred were all under 40%. In addition, a longer intervention with only four repetitions of instructions may be a

reason for higher drop-out rates. Surprisingly, a study using liu zi jue as an intervention (with a similar program to the ba duan jin study mentioned above) reached a 94% complete rate<sup>16</sup>. It can be speculated that the duration of intervention and age of participants minimally affects the complete rate, while the type of intervention and severity of disease affects influences it comparatively more. However, a systemic and comprehensive method should be developed to investigate the possible factors affecting attrition rates when TCE is used as an intervention.

Elderly COPD patients may have difficulties with sustaining stable conditions during the 3 months of intervention. Researchers should be aware of the risk of acute exacerbation due to possible climate changes and various injuries due to training and testing. However, no injury or discomfort related to training or testing occurred during the intervention period among these participants. Modifications can be made regarding the specific motions in prescribed pulmonary disease according to the abilities of participants. Regarding the home-based intervention regime, the quality of accomplishment and compliance of participants is hard to guarantee. Therefore, the prescribed pulmonary exercise video, exercise record brochure registered by participants themselves, and encouragement and instruction from therapists play an irreplaceable role in the accomplishment of intervention.

During the upper limb exercise capacity test, it is important to avoid errors in the measurement procedure including activity of upper arm, movement of the wrist, and incomplete extension intermittent with the flexion, which ensures that participants perform maximally. Possible errors in lower limb exercise capacity are important to avoid, which are mainly present during the process of knee flexion intermittent with the extension. For this reason, it is valuable to require warm-up and familiarization exercises.

Furthermore, endurance exercise capacity was evaluated by 6MWT in an unobstructed 30 m straightway, which is more commonly used in clinical evaluation. Previous studies have found that the 6 min stepper test performed with no technical and spatial limitations can be used as a valid clinical exercise tolerance test for COPD patients. In this case, the results significantly correlated with the distance evaluated by 6MWT<sup>29</sup>. In particular, reproducibility and sensitivity of the 6 min stepper test used in COPD patients were demonstrated<sup>30</sup>. Considering that it is feasible, reliable, and easy to perform and requires minimal space, the 6MWT should be considered when evaluating the endurance exercise capacity of COPD patients.

Regarding the results of this study, improvement of the arm curl test was similar to a previous study that used 8 weeks of resistance exercise (pre:  $10.3 \pm 2.4$ , post:  $12.4 \pm 2.6$ ) and pulmonary rehabilitation combined with resistance exercise (pre:  $10.9 \pm 2.5$ , post:  $12.4 \pm 2.8$ ) in COPD patients<sup>31</sup>. The improvement of the sit-to-stand test was also consistent with a previous study that used home- and hospital-based resistance exercise programs<sup>32,33</sup>. Finally, improvement of the 6MWT achieved minimal clinical significance difference (MCID) of  $33 \text{ m}^{11}$ . The speculated reason is that many different angles and contraction modes of isometric and isotonic exercise are contained in prescribed pulmonary exercise, which can effectively stimulate muscle contraction and achieve training effects. However, less attention was paid to the effects of TCE on skeletal muscle function in COPD patients; thus, more studies should be conducted to

investigate the accurate effects and related mechanisms.

 In addition, the limitations include concerns regarding the evaluation of quality of life. Although SGRQ is often used as a COPD-specific questionnaire to speculate prognosis and development of the disease<sup>5</sup>, the outcome is susceptible to subjective awareness and patients' level of literacy. Hence, a specialized staff is crucial to the quality of life evaluation. The results in this study showed significantly decreases in SGRQ scores and surpassed the MCID of four scores<sup>21</sup>. The results are consistent with previous studies that applied tai chi, Liuzijue, Yijinjing, and Baduanjin as interventions in COPD patients<sup>16,18,19,34</sup>. In addition, a recent meta-analysis found similar improvements in quality of life of COPD patients when home- or hospital-based rehabilitation were applied<sup>35</sup>.

In conclusion, prescribed pulmonary exercise can be performed in clinics, homes, and in the community to improve the exercise capacity and quality of life in stable COPD patients. Further research is required to fully explore the effectiveness in COPD patients of different severity and the long-term outcomes in stable COPD patients.

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#### **DISCLOSURES:**

The authors have nothing to disclose.

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#### Characteristics of intervention



#### Summary of content

0:00

#### Preparatory



- Two feet open as the shoulder width
- Inhaling with two palms holding up in front of the abdomen
- Exhaling with two palms holding down in front of the abdomen



#### Hu Zi Jue

- Two feet open as the shoulder width
- Inhaling with two palms holding up in front of the abdomen
- Flip palms inward and cross in front of abdomen
- Exhaling with the sound of "hu" and gradually extended the elbow to the position of upper limbs like holding a ball



#### 2:03 Si Zi J

- Two feet open as the shoulder width
- Inhaling with two palms holding up in front of the chest
- Adduction shoulders with the two palms standing and opposite
- Inhaling with head reclining and scapula adducting
- Exhaling with the sound of "si" and push forward two palms



Pushing up the sky to regulate the triple warmer

- Two feet open as the shoulder width
- Inhaling with two palms holding up in front of the chest
- Continue to lift until the two arms straight, and keep the eyes staring at palms
- Exhaling with the two palms falling down on the sides of body



6 Drawing a bow to shoot a vulture

- Two feet open as the shoulder width
- Adducted the shoulder and flexed the elbow with both hands crossed in the front of chest
- Left motion: Exhaling with the left elbow stretching to the side and the right limb performing like a bow-like movement in the squatting position
- Right motion: Contrary to the left





8:09 The crane actions

- Two feet open as the shoulder width
- Crane Stretch: Exhaling with two upper limbs and one lower limb stretching back
- Crane flies: Inhaling with two upper limbs abducting and one legs flexing



11:40 Cross-armed iron staff

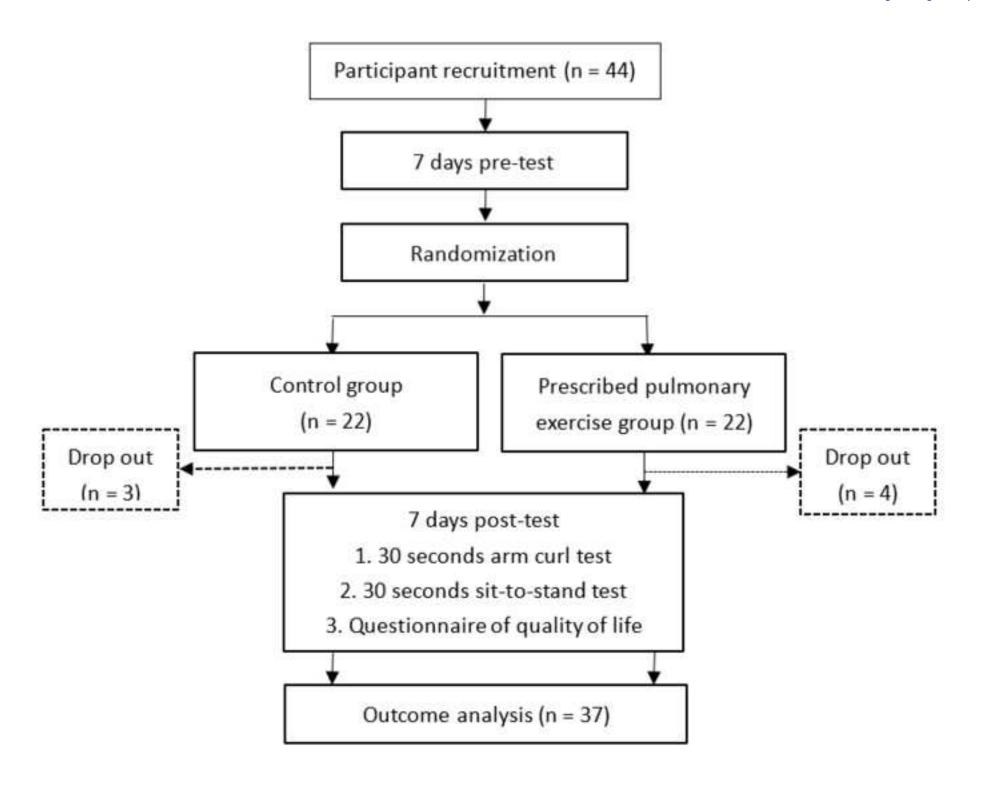
- Two feet open as the shoulder width
- Inhaling with the shoulders abduction and body-lifting
- Exhaling with the shoulders falling down and body-downing

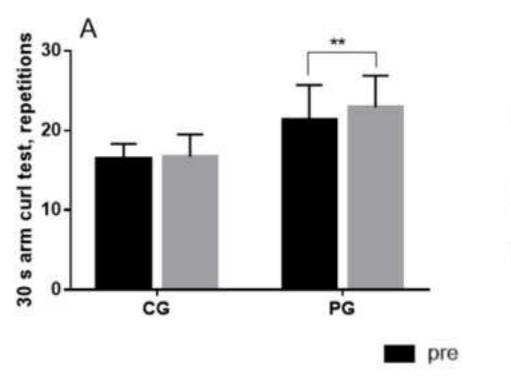


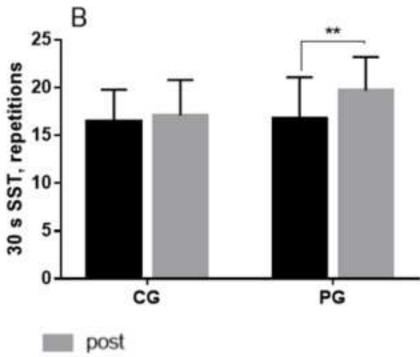
12:09 Ending motion

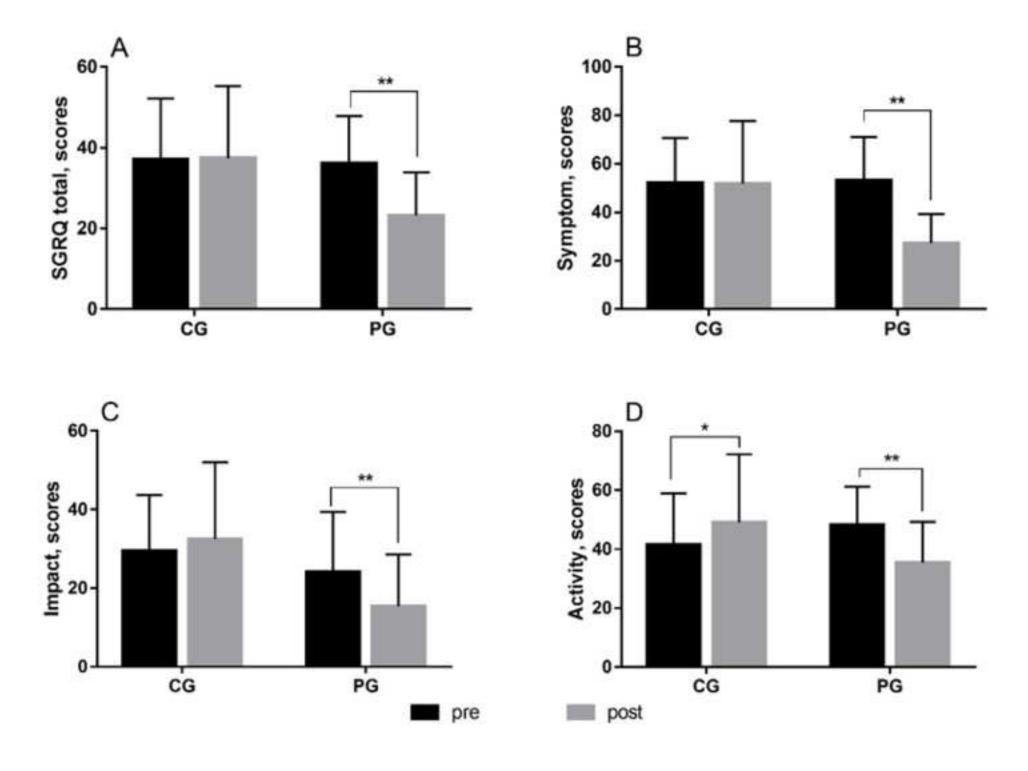
- Two feet open as the shoulder width
- Both hands lifting on the side of body and falling down in the front of chest
- Inhaling while lifting, exhaling while falling

12:53









Parameter	CG (n=19)	PG (n=18)	P-value
Age (years)	64.58 ± 9.06	66.11 ± 9.08	0.61
Sex			
male (n/%)	14 (74%)	15 (83%)	0.69
female (n/ %)	5 (26%)	3 (17%)	0.09
BMI (kg/m <sup>2</sup> )	22.90 ± 3.71	25.22 ± 0.82	0.61
Disease duration (years)	11.12 ± 4.66	10.28 ± 5.67	0.64
AECOPD (repetitions)	1.16 ± 0.21	$1.06 \pm 0.31$	0.5
Disease grade			
I (n/%)	2 (11%)	1 (6%)	
II (n/%)	11 (58%)	10 (55%)	0.64
III (n/%)	5 (26%)	7 (39%)	0.64
IV (n/%)	1 (5%)	0 (0)	
Treatments			
Long-acting cholinergic (n/%) Inhaled corticosteroids	9 (47%)	9 (50%)	0.76
associated with long-acting $\beta$ 2-agonists (n/%)	9 (47%)	7 (39%)	0.76
No treatments (n/%)	1 (6%)	2 (11%)	
Comorbidities			
Hypertension (n/%)	10 (53%)	9 (50%)	
Diabetes (n/%)	5 (26%)	6 (33%)	0.88
No comorbidities (n/%)	4 (21%)	3 (17%)	

Name of Material/Equipment	Company	Catalogue number
4643a	Tanita	
Borg CR10	None	
PASS 15.0	NCSS, LLC	
Polar team 2	Polar	
SGRQ software	Developed by Peking Union Medical C	ollege
SPSS 24.0	IBM Corporation	

## **Comments/Description**

Used for the evaluation of height, weight, and body mass index
Used for the evaluation of dyapnea
Used for power calculation
Used for supervising the heart rate of participants
Used for calculating the score of quality of life
Used for statistical analysis



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Best regards, Weibing Wu

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- 2. We require that the portions of the manuscript you intend to film be highlighted before we can accept it; please do so. It looks like sections 4, 5, and 6 tell a reasonable story and are roughly 2.75 pages; would those work?

**Answer:** Thanks for your suggestion. The portions intended to film have been highlighted in the manuscript.

3. Both the SGRQ and program you provided are in Chinese; we would require both to be in English. As it would probably be unreasonable to rewrite the program (unless an English-language version already exists), could you provide a reference that describes the analysis process in 5.5.2?

**Answer:** Actually, the SGRQ and program used in this study was translated from the English version developed by Jone PW in 1992. Therefore, we provided a reference to support the questionnaire in 5.1.1. Thanks for your understanding.