Original Article

Efficacy and safety of pulmonary rehabilitation training on lung function, quality of life, and T cell immune function in patients with stable chronic obstructive pulmonary disease: a randomized controlled trial

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Background: Pulmonary rehabilitation training is an important means of stable chronic obstructive pulmonary disease (COPD). However, some people think that its effect is not satisfactory, and there is a lack of understanding of the effect of pulmonary rehabilitation training on T cell immune function. This study investigated the efficacy and safety of pulmonary rehabilitation training on lung function, quality of life and T cell immune function in stable COPD patients.

Methods: Seventy-two stable COPD patients recruited from the Outpatient department of Affiliated Hospital of Jiangnan University and Wuxi Huishan Rehabilitation Hospital, and divided them into experimental group (39 cases) and control group (33 cases) by random number table method. Both groups were received routine drug therapy, COPD knowledge education, and smoking cessation treatment. On this basis, the experimental group received daily pulmonary rehabilitation training, including pursed-lip breathing (PLB) training, abdominal breathing training, skeletal muscle training, and coughing and expectoration training. Lung function [percentage of forced expiratory volume in 1 second (FEV1%) and the percentage of FEV1/forced vital capacity (FEV1/FVC%)], quality of life [6-minute walk test (6MWT), COPD assessment test (CAT score)], and T lymphocyte subsets ($CD3^+$%, $CD4^+$%, $CD8^+$%, and $CD4^+$%/$CD8^+$%) levels were compared by independent sample *t*-test or paired *t*-test between the 2 groups before and after 12 weeks of treatment in a double-blind method.

Results: There were no remarkable differences in lung function indexes, 6MWT, CAT score, and T cell immune function between the 2 groups before treatment. After 12 weeks, all indexes in the experimental group (all $P<0.01$) and T lymphocyte subsets in the control group ($CD3^+$%, $CD4^+$%, $CD8^+$% and $CD4^+$%/$CD8^+$% were 0.010, 0.037, 0.021 and 0.016, respectively) were significantly better than before treatment, and there were no significant differences in lung function,6MWT, and CAT scores in the control group. After 12 weeks, all indexes in the experimental group were significantly better than those in the control group except $CD8^+$% (FEV1%, FEV1/FVC%, 6MWT, CAT score, $CD3^+$%, $CD4^+$% and $CD4^+$%/$CD8^+$% were 0.002, 0.009, <0.001, 0.007, 0.037, 0.046 and <0.001, respectively).

Conclusions: Pulmonary rehabilitation training can improve the lung function, quality of life, and T cell immune function of stable-phase COPD patients. Perhaps the recovery of T-cell immune function is the root of the patient's improvement.

Trial Registration: Chinese Clinical Trial Registry ChiCTR2100048419.

Keywords: Pulmonary rehabilitation training; chronic obstructive pulmonary disease (COPD); stable phase; lung function; T lymphocyte subsets

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Introduction

Chronic obstructive pulmonary disease (COPD) is a common disease of the elderly which seriously affects quality of life. It is likely the third most common cause of death in the world today (1), and has become a major public health problem worldwide. Clinically, COPD can be divided into acute exacerbation and stable phases. Acute exacerbation of COPD (AECOPD) is a continually worsening condition that can have a significant impact on a patient's health. This phase causes T lymphocyte activity "passivation" and leads to the decline of immune response function; the immune monitoring function is consequently reduced, followed by repeated chronic infection of viruses, bacteria, and other pathogenic microorganisms, which further damages lung function, forming a vicious circle. Thus, exercise ability and quality of life are further reduced (2,3).

The treatment of COPD in the stable period is mainly to prevent AECOPD, reduce the frequency of COPD attacks, and improve physiological function and patients' quality of life (4). Pulmonary rehabilitation training refers to individualized, multidisciplinary and comprehensive intervention measures for symptomatic chronic respiratory disease patients with decreased daily living ability. Its purpose is to improve the patient's symptoms, promote the recovery of the patient's lung function, improve their daily living ability, and optimize the patient's quality of life. It mainly includes four aspects: exercise therapy, family comprehensive intervention, psychological intervention and effect evaluation. Pulmonary rehabilitation training is an important means to treat stable COPD which can improve the symptoms of COPD. Exercise training is one of the most important components of any pulmonary rehabilitation program. Previous studies have shown that respiratory exercise training improves lung function in patients with stable COPD (5,6). In addition, respiratory muscle and skeletal muscle training have been shown to increase respiratory and circulatory endurance in sedentary COPD patients (7,8).

At present, pursed-lip breathing (PLB) training, abdominal breathing training, and skeletal muscle training combined with general exercise training is widely used in stable COPD patients in China. With the aging of the population, many community hospitals have gradually introduced community rehabilitation treatment for common and frequently-occurring diseases, to the benefit of affected patients (9). For example, Wuxi Huishan Rehabilitation Hospital has conducted substantial community rehabilitation work according to the needs of patients. Pulmonary rehabilitation training is an important means of stable COPD. However, some people think that its effect is not satisfactory, and there is a lack of understanding of the effect of pulmonary rehabilitation training on T cell immune function.

We posited that pulmonary rehabilitation training influences the lifestyle of patients, and improvements of lung function and living ability of patients might be related to the improvement of T cell immune function. The purpose of this study was to investigate the effects of pulmonary rehabilitation training on lung function, quality of life, and T cell immune function in patients with stable COPD. We present the following article in accordance with the CONSORT reporting checklist (available at https://apm.amegroups.com/article/view/10.21037/apm-22-451/rc).

Methods

Patient recruitment

The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). This study was approved by the Ethics Committee of the Affiliated Hospital of Jiangnan University (No. 2018007), and Wuxi Huishan Rehabilitation Hospital was informed and agreed with the study. Informed consent was taken from all the patients.

Patients were enrolled in the Affiliated Hospital of Jiangnan University and Wuxi Huishan Rehabilitation Hospital. They all complied with the diagnostic criteria for stable COPD (10), and had no history of severe liver, kidney, endocrine, malignant tumor, mental illness, or severe cardiovascular disease. The study was a double-blind, two-parallel study and randomized controlled trial. Except for pulmonary rehabilitation exercise instructors or participants, all outcome assessments were blinded. Based on sample size calculations, 72 patients were divided into experimental group (39 cases) and control group (33 cases) in a 1:1 allocation ratio by random number table method. There were no significant differences in age, gender,

Table 1 Comparison of general data between the two groups

Demographic	Experimental	Control	χ^2/t	P value
Gender, n (%)			0.010	0.921
Male	22 (56.4)	19 (57.6)		
Female	17 (43.6)	14 (42.4)		
Age, years, mean (95% CI)	68.64 (65.97–71.41)	70.70 (67.64–73.61)	1.010	0.316
Level of education, n (%)			0.117	0.733
Primary school and below	15 (38.5)	14 (42.4)		
Secondary school and above	24 (61.5)	19 (57.6)		
BMI, mean (95% CI)	24.05 (22.26–25.69)	24.64 (22.70–26.61)	0.448	0.656
Smoking index, n (%)			0.717	0.397
<300	30 (76.9)	28 (84.8)		
≥300	9 (23.1)	5 (15.2)		
Course of disease, years, mean (95% CI)	11.74 (10.05–13.41)	12.70 (10.24–15.24)	0.633	0.529
GOLD stage, n (%)			0.093	0.760
I–II	25 (64.1)	20 (60.6)		
III–IV	14 (35.9)	13 (39.4)		

CI, confidence interval; BMI, body mass index; GOLD, Global Initiative for Chronic Obstructive Lung Disease.

education level, body mass index (BMI), smoking index, course of disease, and disease severity between the 2 groups (P>0.05) (*Table 1*).

Therapeutic methods

All participants received routine drug treatment according to their condition, such as inhaled bronchodilator, glucocorticoid, expectorant, and antitussive therapy. All patients received education about COPD knowledge, including giving up smoking, maintaining good living habits, and adhering to a reasonable diet. The experimental group received pulmonary rehabilitation training on the basis of the above treatment, as follows:

(I) PLB training: while either sitting or standing, the patient was instructed to relax, inhale slowly and deeply through the nose, hold the breath for 1–2 s, then contract the lips, and slowly exhale through the mouth. The ratio of exhalation and inhalation time was 2:1, 5–10 min/time, 3–4 times/day, and the speed was gradually accelerated.

(II) Abdominal breathing training: patients assumed a sitting, lying, or standing position. The patient was asked to relax their shoulders and upper chest, then place 1 hand in front of the chest, and the other hand on the upper abdomen. The aim of breathing was that the hands should not feel chest undulation, but rather the abdominal movement. When exhaling, the abdomen retracts and forces; while inhaling, the abdomen bulges against the pressure of hands. Inhalation should be deep and through the nose, and exhalation should be slow. The duration of exhalation was 1–2 times longer than that of inhalation; the training was conducted for 5 min/time, and gradually increased to 10–15 min/time, 3–4 times/day.

(III) Skeletal muscle training: The difficulty and speed of this exercise was adjusted from easy to difficult and from fast to slow depending on the specific situation of patients. The first section was upper limb muscle training. Patients' were shown how to bend their upper limbs in the form of fists, and make fists alternately in front of the syncline, inhale when punching, exhale when withdrawing, inhale when slowly lifting up the arm, and exhale when slowly lowering the arm, with 30 repetitions comprising a set, and 2–3 sets completed a day. The second section was chest expansion training. The patient performed alternate leg lunges, hands in fist shape, and both upper limbs stretched horizontally to both sides. They were instructed to inhale when stretching, exhale when withdrawing, with 30 repetitions comprising a set, and 2–3 sets completed a day. The third section was lower limb muscle training. The patient was asked to assume a standing position, lift their legs alternately at a right angle, and maintain the lift for 2–3 s. They inhaled when lifting the legs, and exhaled when the legs dropped, with 30 repetitions comprising a set, and 2–3 sets completed a day. The fourth section was training to relax. From a supine position, the patient tensed the muscles of the body on the inhale and relaxed them on the exhale, with 30 repetitions comprising a set, and 2–3 sets completed a day.

(IV) Coughing and expectoration training: If there was sputum retention, sputum drainage practice was increased as appropriate; the patient was taught to correctly implement the steps of cough, and improve the effectiveness of cough. With the forced expiratory technique, the patient was instructed to exhale deeply through the mouth, form a high-speed airflow, and make "ha" sound, so that the peripheral sputum was loosened and gathered into the large airway, and could be discharged as soon as possible by effective coughing. If the patient's physical strength was feeble, a percussion beat playing method could be used. A family member would arrange 5 fingers close together, the palm slightly bent into an arched shape, and perform rhythmic percussion on the patient's chest and back. Cough expulsion training could also be performed after aerosol inhalation.

Patients visited the hospital twice a week for collective training and experience exchange, as well as guidance, error correction, and supervision, and self-training was conducted every other day.

6-minute walk test (6MWT) is used as an alternative to cardiopulmonary exercise tests because it is cost-effective, easy to perform and is commonly used in clinical practice to determine exercise capacity in patients with chronic lung disease. COPD Assessment Test (CAT) score can help doctors evaluate the impact of COPD on patients' health and daily life. Therefore, we use these two indicators to evaluate patients' exercise ability and quality of life. Lung function, 6MWT, CAT score, and T lymphocyte subsets were measured at baseline and 12 weeks later in both groups. Lung function was measured by MasterScope-diffusion Jaeger® lung function meter (Hoechberg, Germany). Observations included the percentage of forced expiratory volume in 1 second (FEV1%) and the percentage of FEV1/forced vital capacity (FEV1/FVC%). Both 6MWT and CAT scores were completed by 2–3 professionally trained respiratory therapists, of which 6MWT was performed on a long corridor with 50 m of flat ground. For the T cell immune function test, fasting venous blood was extracted from patients in 2 groups before and after treatment, and the levels of T lymphocyte subsets $CD3^+$%, $CD4^+$%, $CD8^+$%, and $CD4^+$%/$CD8^+$% were measured by flow cytometry. FEV1%, FEV1/FVC%, 6MWT, CAT score, and T lymphocyte subsets were the primary outcome measures, and secondary were adverse events.

Statistical analysis

The software SPSS 22.0 (IBM Corp., Armonk, NY, USA) was used for statistical analysis. Interval data were presented with means and 95% confidence intervals (CI). Comparison between 2 groups was conducted with independent sample *t*-test, and the comparison of each group before and after treatment was conducted with a paired *t*-test. The chi-square test was used to compare frequencies. Statistical significance was considered when $P<0.05$.

Results

Patients were enrolled from August 2020 to October 2021. Study flow diagram see *Figure 1*.

Comparison of general data between the two groups

There were no significant differences in age, gender, education level, BMI, smoking index, course of disease, and disease severity between the 2 groups ($P>0.05$) (*Table 1*).

Comparison of lung function, 6MWT, and CAT scores between the two groups before and after treatment

There was no significant difference in the indexes of the control group before and after treatment, all $P>0.05$; in the experimental group, all indexes were significantly improved after treatment (all $P<0.01$) (*Table 2*).

There was no significant difference in each index between the 2 groups before treatment. After treatment, there were remarkable differences in the indexes between the 2 groups: FEV1% (t=3.256, P=0.002), FEV1/FVC% (t=2.702, P=0.009), 6MWT (t=3.797, P<0.001), CAT score (t=−2.800, P=0.007) (*Figure 2*).

Comparison of T lymphocyte subsets before and after treatment between two groups

All of $CD3^+$%, $CD4^+$%, and $CD4^+$%/$CD8^+$% after pulmonary rehabilitation training in experimental group were significantly higher than before training, while $CD8^+$% was significantly lower than before training, and the differences were remarkable (P<0.01). The indexes of T lymphocyte subsets in the control group were also better after treatment than before treatment, and the differences were also remarkable (P<0.05) (*Table 3*).

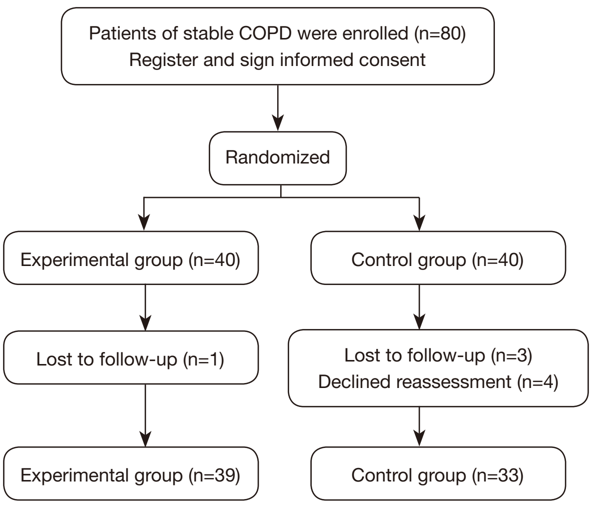


Figure 1 Study flow diagram. COPD, chronic obstructive pulmonary disease.

Comparison between the 2 groups before treatment, $CD3^+$% (t=−0.425, P=0.672), $CD4^+$% (t=−0.202, P=0.840), $CD8^+$% (t=−0.081, P=0.936) and $CD4^+$%/$CD8^+$% (t=−0.251, P=0.803) had no significant difference. After 12 weeks, there were remarkable differences in $CD3^+$% (t=2.125, P=0.037), $CD4^+$% (t=2.029, P=0.046), and $CD4^+$%/$CD8^+$% (t=4.513, P<0.001) between the 2 groups. There was no significant difference in $CD8^+$% (t=−0.486, P=0.629) (*Figure 3*).

Comparison of T cell subsets expression before and after pulmonary rehabilitation training of 1 patient in the experimental group. The upper part of the figure shows the expression of $CD3^+$% (30.4%), $CD4^+$% (29.0%), and $CD8^+$% (69.1%) before treatment. The lower part shows the recovery of passivated T lymphocytes after pulmonary rehabilitation training, and the expression of T cell subsets is $CD3^+$% (48.1%), $CD4^+$% (33.0%) and $CD8^+$% (54.6%) (*Figure 4*).

Comparison of adverse events such as acute exacerbation between the two groups

There were 3 cases of acute exacerbation in the control group during the observation period, which were improved after outpatient treatment and oral anti-infective drugs. There was no acute exacerbation in the experimental group. There was no significant difference in the results of chi-

Table 2 Comparison of lung function, 6MWT and CAT scores between the two groups before and after treatment

Groups	Indexes	Before treatment		After treatment		t	P value
		Mean (SD)	95% CI	Mean (SD)	95% CI		
Experimental (n=39)	FEV1%	47.31 (9.38)	44.44–50.13	55.62 (9.02)	52.95–58.38	−13.463	<0.001
	FEV1/FVC%	48.21 (9.32)	45.67–52.09	54.95 (10.09)	53.03–59.45	−7.459	<0.001
	CAT scores	23.33 (5.83)	21.00–24.94	18.69 (5.81)	16.30–21.05	10.774	<0.001
	6MWT (m)	286.67 (31.87)	277.70–299.69	317.79 (34.43)	305.06–329.33	−11.226	<0.001
Control (n=33)	FEV1%	47.91 (10.05)	44.58–51.21	48.18 (10.35)	44.67–51.52	−0.497	0.623
	FEV1/FVC%	48.15 (9.97)	44.78–51.55	48.55 (9.93)	45.15–52.00	−0.457	0.651
	CAT scores	22.67 (5.82)	20.73–24.51	22.42 (5.42)	20.64–24.18	0.631	0.533
	6MWT (m)	284.09 (33.10)	273.22–296.09	287.03 (34.05)	275.70–299.64	−1.223	0.230

6MWT, 6-minute walk test; CAT, COPD Assessment Test; COPD, chronic obstructive pulmonary disease; CI, confidence interval; SD, standard deviation; FEV1%, percentage of forced expiratory volume in 1 second; FVC, forced vital capacity.

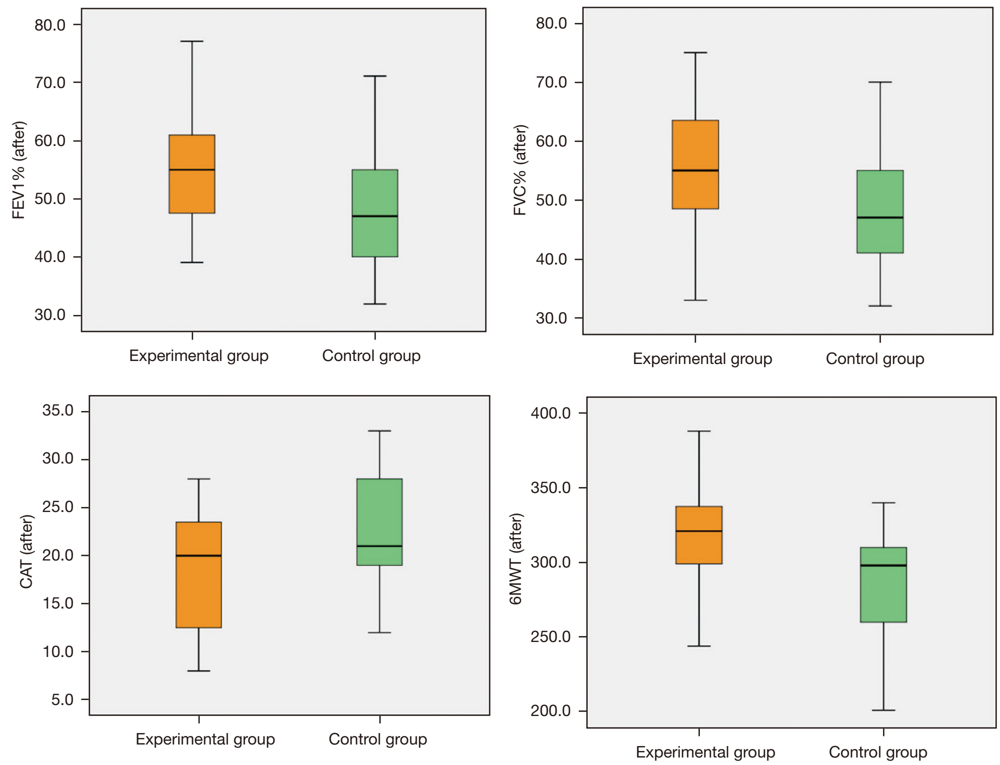


Figure 2 Comparison of lung function, 6MWT, and CAT scores between the two groups after treatment. FEV1%, percentage of forced expiratory volume in 1 second; FVC%, the percentage of FEV1/forced vital capacity; 6MWT, 6-minute walk test; CAT, COPD Assessment Test; COPD, chronic obstructive pulmonary disease.

Table 3 Comparison of T lymphocyte subsets between the two groups before and after treatment

Groups	Indexes	Before treatment		After treatment		*t*	P value
		Mean (SD)	95% CI	Mean (SD)	95% CI		
Experimental (n=39)	$CD3^+$%	43.18 (9.91)	40.03–46.34	51.23 (10.97)	47.69–54.70	–9.733	<0.001
	$CD4^+$%	30.64 (11.17)	27.28–34.00	38.28 (12.50)	34.29–42.13	–15.746	<0.001
	$CD8^+$%	29.77 (11.35)	26.13–33.26	27.67 (11.29)	24.00–31.00	10.856	<0.001
	$CD4^+$%/$CD8^+$%	1.05 (0.22)	0.99–1.13	1.47 (0.39)	1.37–1.61	–11.392	<0.001
Control (n=33)	$CD3^+$%	44.24 (11.31)	40.73–47.76	45.48 (11.96)	41.97–49.24	–2.747	0.010
	$CD4^+$%	31.21 (12.76)	27.15–35.60	32.21 (12.82)	28.00–36.58	–2.181	0.037
	$CD8^+$%	30.00 (12.96)	25.70–34.15	29.03 (12.52)	24.94–33.06	2.424	0.021
	$CD4^+$%/$CD8^+$%	1.06 (0.16)	1.01–1.12	1.14 (0.18)	1.08–1.20	–2.539	0.016

CI, confidence interval; SD, standard deviation.

square test (χ^2=3.700, P=0.054). In addition, there were no adverse reactions such as vertigo, palpitation, and dyspnea aggravation during the pulmonary rehabilitation training in the experimental group.

Discussion

Airflow limitation is the characteristic feature of COPD (11). The main reasons for airflow limitation include the following: spasmodic contraction, thickening, and

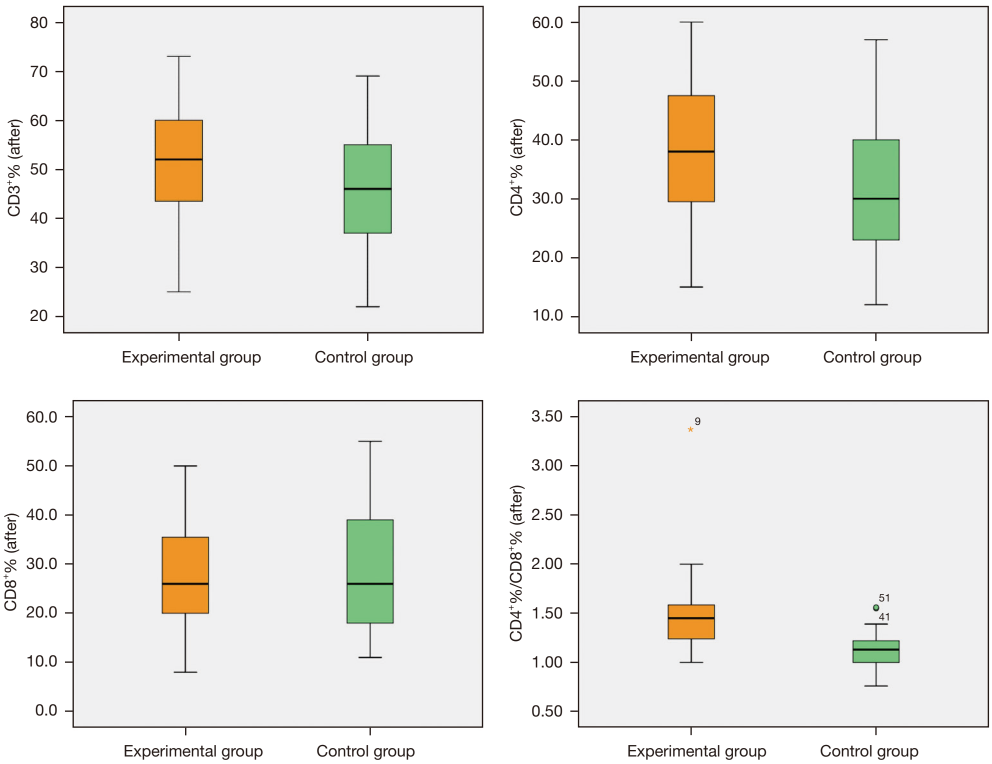


Figure 3 Comparison of T lymphocyte subsets after treatment between the two groups.

hypertrophy of airway smooth muscle, increased secretions blocking the lumen, the destruction of alveolar structure weakening the ability to open small airways, and the decrease of respiratory muscle function such as the diaphragm due to over inflated lungs. In COPD, the large, medium, and small airways are involved, and all aspects of lung functions are damaged (12). Patients with COPD present with persistent dyspnea and irreversible airflow obstruction which can ultimately result in the inability to perform everyday activities and significantly reduce quality of life.

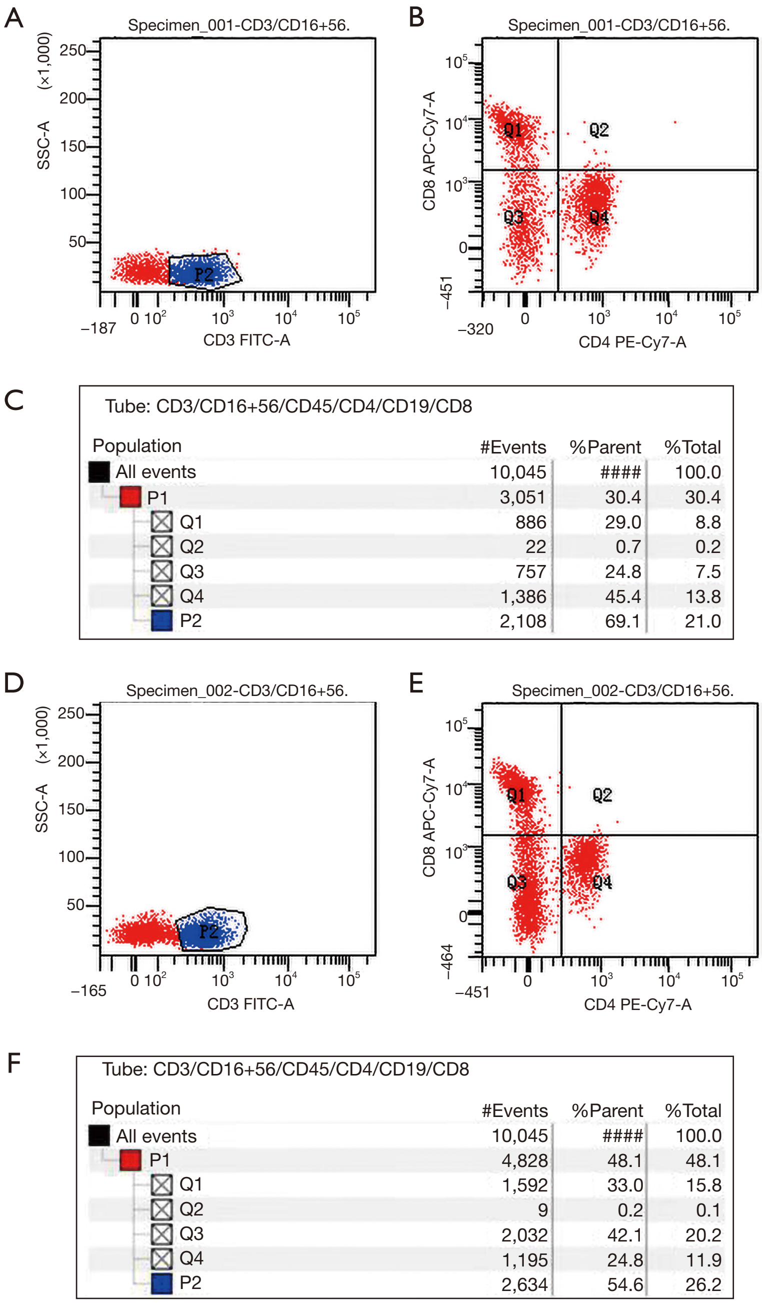
Lung function is indispensable to the evaluation of stable COPD. The FEV1 is the main index of lung function impairment, and the FEV1/FVC% is an important index to judge airway obstruction (13). However, COPD is also a systemic disease. It is not sufficiently comprehensive to evaluate patients only by FEV1 and other pulmonary function indexes. The BODE score system, namely body mass index (BMI), airflow obstruction (AO), dyspnea (D), and exercise ability (E), can better reflect the patients' whole body status and prognosis (14).

As a supplement to the cardiopulmonary exercise test, the 6MWT can be utilized for risk assessment before cardiopulmonary rehabilitation, formulation of exercise prescription, and evaluation of rehabilitation effect. It can better replicate the patient's daily physiological state, reflect their daily living ability, and is simple, safe, easy to operate, and easily tolerated by patients (15).

The CAT score is a questionnaire completed by the patients themselves, which is mainly used to evaluate the health status of COPD patients. It covers symptoms, activity ability, psychological and sleep status, social influences, and other aspects, and can more comprehensively reflect the quality of life in COPD patients than the dyspnea score alone (16).

In 2013, the American Thoracic Society (ATS) and the European Respiratory Society (ERS) defined pulmonary rehabilitation as an individualized comprehensive intervention based on a full and comprehensive evaluation of the patient. It includes exercise training, respiratory training, education, nutritional interventions, psychological support, and behavioral interventions to improve the physical and mental health of patients with COPD and promote long-term health-enhancing behaviors (17).

Pulmonary rehabilitation training is an important component in the treatment of COPD. At present, it mainly focuses on traditional abdominal breathing, PLB,



C. Tube: CD3/CD16+56/CD45/CD4/CD19/CD8

Population	#Events	%Parent	%Total
All events	10,045	####	100.0
P1	3,051	30.4	30.4
Q1	886	29.0	8.8
Q2	22	0.7	0.2
Q3	757	24.8	7.5
Q4	1,386	45.4	13.8
P2	2,108	69.1	21.0

F. Tube: CD3/CD16+56/CD45/CD4/CD19/CD8

Population	#Events	%Parent	%Total
All events	10,045	####	100.0
P1	4,828	48.1	48.1
Q1	1,592	33.0	15.8
Q2	9	0.2	0.1
Q3	2,032	42.1	20.2
Q4	1,195	24.8	11.9
P2	2,634	54.6	26.2

Figure 4 Passivated T lymphocytes were recovered after pulmonary rehabilitation training in the experimental group.

and skeletal muscle training (18). Pulmonary rehabilitation training reduces respiratory exertion by training patients' coordinated movement of respiratory muscle groups, reducing muscle fixation and rigidity, improving exercise endurance and ability, and improving gas exchange efficiency (19).

The PLB technique can increase lip resistance, slow down breathing frequency, extend expiratory and inspiratory time, increase vital capacity, increase airway pressure, especially small airway pressure, avoid premature closure and stenosis of small airway during exhalation, promote residual air discharge in the lung, and effectively improve gas exchange. Patients with severe and extremely severe COPD can improve their dyspnea and respiratory muscle function by lip contraction breathing training (20).

Abdominal breathing can compensate for a lack of chest breathing. It can reconfigure the unreasonably shallow and quick breathing pattern, extend the expiratory time in order to improve the tidal volume, reduce dead space, increase the vital capacity and alveolar ventilation, reduce the power consumption of the breath, and enable patients to cough and achieve expectoration drainage effectively, alleviate symptoms such as difficult breathing, shortness of breath, wheezing, and strengthen the function of patients with pulmonary ventilation function and gas exchange, to ameliorate hypoxia (21). Abdominal breathing can also expand the chest volume, reestablish sufficient heart diastole, thereby improving myocardial blood and oxygen supply, and preventing heart failure (22).

Skeletal muscle training can also rectify abnormal breathing patterns, increase effective ventilation, enhance respiratory muscle and limb muscle strength, improve the ability of the respiratory tract to clear secretions, contribute to the good exchange of gas, and improve cardiopulmonary function (23,24). At the same time, skeletal muscle training can improve tense, despairing, anxious, and other bad emotions, is conducive to enhancing patient the confidence in their successful treatment, improve treatment compliance, reduce symptoms, and improve the quality of life (25,26). In addition, cough sputum training is simple and easy to perform, which can promote drainage of airway secretions, smooth the airway, reduce lung inflammation, improve the immune function, and reduce acute exacerbation of COPD.

Autoimmunity plays an important role in the course of COPD. It is a chronic progressive disease, patients often experience reduced immune function due to repeated infection, hypoxia, anxiety, depression, and other factors. At the same time, the inflammatory environment in the lungs and the whole body, which lead to the exposure of certain autoimmune antigens, is also associated with progression of the disease (27). The human immune system includes the innate immune system and the adaptive immune system. The innate immune defenses of the lung include epithelial barriers, mucociliary clearance, antimicrobial peptides, and complements (28). The adaptive immune system includes B cell-mediated humoral immunity and T cell-mediated cellular immunity.

The T cells play an immunomodulatory role through different functional T cell subsets. A decrease in the number of $CD3^+$ T cells can reflect a decrease in the total number of T cells. The $CD4^+$ T cells are helper T cells, which can produce cytokines, assist B cells to produce antibodies, and assist other lymphocyte functions. The $CD8^+$ T cells are cytotoxic cells, which can reduce the function of synthesis and secretion of antibodies by inhibiting the activity of B lymphocytes. The constant ratio of $CD4^+/CD8^+$ T cells can maintain the normal immune function of the body, and plays an important role in regulating and maintaining the immune balance. Decrease of CD3, CD4, and CD4/CD8 levels or increase of $CD8^+$ T cell count indicate decreased immune function (29,30). Patients with COPD often show similar changes.

Our study found that through routine drug therapy, COPD knowledge education, and smoking cessation treatment, the T cell immune function of COPD stable patients shifted towards improvement, and the pulmonary rehabilitation training on this basis in the experimental group made such improvements more obvious.

First, the change of lifestyle is the most important factor. Viruses, bacteria in the airway, and smoking changed the presentation of patients' own antigens, while smoking cessation treatment and pulmonary rehabilitation training may have reversed such presentation (31). Study has shown that obesity is associated with immune dysfunction, and excess fat in COPD patients may be the key factor for decreased T cell activation (32), while pulmonary rehabilitation training changes the lifestyle of patients and reduces body fat. Second, pulmonary rehabilitation training can improve the airflow obstruction, dyspnea, and exercise ability of patients, so that the structure and function of the lung are improved (33). In addition, aerobic exercise promotes the improvement of cellular immune function of the body, and pulmonary rehabilitation training reverses the inflammatory response of COPD airways and the whole body, leading to the abnormal improvement of inflammatory factors such as a variety of cytokines, proteases, and oxygen free radicals, which reduces the risk of infection and improves the T cell immune function of COPD patients (34).

From this study, it can be observed that continuous regular pulmonary rehabilitation training can improve lung function, subjective feeling, quality of life, and T cell immune function of stable COPD patients. The pulmonary ventilation function of the experimental group patients was obviously protected, and the 6MWT and CAT scores were obviously improved. In the control group, T cell function was also improved due to lifestyle changes such as smoking cessation. The BMI was not included in the observation index due to the relatively short observation period of the patients involved in the study (35-37).

Conclusions

At present, PLB training, abdominal breathing training, coughing and expectoration training, and skeletal muscle training combined with general exercise training is widely used in stable COPD patients. Continued and regular pulmonary rehabilitation training is of great significance to improve the rehabilitation quality of COPD patients in the stable phase. It can promote the recovery of respiratory function, improve respiratory muscle and skeletal muscle function, reduce oxygen consumption, improve respiratory efficiency, enhance sputum expulsion ability, improve anxiety, depression, and other negative emotions, improve T cell immune function of the body, maintain the stability of the disease, improve the quality of life, and the prognosis of stable COPD patients.

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Footnote

Reporting Checklist: The authors have completed the CONSORT reporting checklist. Available at https://apm.amegroups.com/article/view/10.21037/apm-22-451/rc

Trial Protocol: Available at https://apm.amegroups.com/article/view/10.21037/apm-22-451/tp

Data Sharing Statement: Available at https://apm.amegroups.com/article/view/10.21037/apm-22-451/dss

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Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). This study was approved by the Ethics Committee of the Affiliated Hospital of Jiangnan University (No. 2018007), and Wuxi Huishan Rehabilitation Hospital was informed and agreed with the study. Informed consents were provided by all participants.

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