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REVIEW

Exercise Rehabilitation and Chronic Respiratory Diseases: Effects, Mechanisms, and Therapeutic Benefits

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Abstract: Chronic respiratory diseases (CRD), is a group of disorders, primarily chronic obstructive pulmonary disease and asthma, which are characterized by high prevalence and disability, recurrent acute exacerbations, and multiple comorbidities, resulting in exercise limitations and reduced health-related quality of life. Exercise training, an important tool in pulmonary rehabilitation, reduces adverse symptoms in patients by relieving respiratory limitations, increasing gas exchange, increasing central and peripheral hemodynamic forces, and enhancing skeletal muscle function. Aerobic, resistance, and high-intensity intermittent exercises, and other emerging forms such as aquatic exercise and Tai Chi effectively improve exercise capacity, physical fitness, and pulmonary function in patients with CRD. The underlying mechanisms include enhancement of the body's immune response, better control of the inflammatory response, and acceleration of the interaction between the vagus and sympathetic nerves to improve gas exchange. Here, we reviewed the new evidence of benefits and mechanisms of exercise intervention in the pulmonary rehabilitation of patients with chronic obstructive pulmonary disease, bronchial asthma, bronchiectasis, interstitial lung disease, and lung cancer.

Keywors: chronic respiratory disease, exercise training, chronic obstructive pulmonary disease, asthma, interstitial lung disease, bronchiectasis, lung cancer

Introduction

Chronic respiratory diseases (CRD) are a group of common disorders with lesions primarily occurring in the trachea, bronchi, alveoli, and chest cavity.[1] Over the last three decades, the incidence of CRD has been increasing yearly due to various factors such as environmental exposure, poor lifestyle habits, air pollution, occupational carcinogens, smoking, and alcohol consumption. In 2020, the World Health Organization (WHO) released a list of the top 10 deadly diseases worldwide, which include: chronic obstructive pulmonary disease (COPD), lower respiratory tract infections, and tracheal, bronchial, and lung cancers.[2] COPD, the third most deadly disease worldwide, accounts for 6% of all deaths. There were approximately 2.2 million cases of tracheal, bronchial and lung cancer worldwide in 2019, affecting 1.52 million men and 737,000 women, which is an increase of 23.3% from 2010.[3] Chronic and severe airway pathologies have caused a huge medical burden on countries worldwide, greatly affecting the quality of life of patients and becoming a major disease that plagues humanity.[4] Thus, there is an urgent need to find efficient and economical means for the prevention and rehabilitation in CRD and to compensate for the shortcomings in its prevention and control.

In 2007, the American College of Sports Medicine (ACSM) launched the Exercise is Medicine program, which aims to guide and encourage doctors to evaluate the exercise ability of patients when designing treatment plans and to promote the treatment and prevention of chronic diseases through scientific exercise. Exercise can promote health and combat diseases, by changing the abundance of biomolecules in the body and triggering functional changes in the body's tissues and organs.[5,6] Exercise reportedly regulates the body's immune response, among other things.[7] A large body of research

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data on sports medicine provides a scientific basis for formulating exercise programs in patients with respiratory diseases.[8] The typical characteristics of CRD are exertional dyspnea and exercise intolerance. Its physiological mechanisms include respiratory limitation, inadequate gas exchange, central and peripheral hemodynamic restriction, and decreased skeletal muscle function. In 2006, the American Thoracic Society (ATS) and European Respiratory Society (ERS) stated that active pulmonary rehabilitation can reduce the adverse symptoms of patients with CRD to a certain extent, effectively prevent exacerbations, and improve pulmonary function, exercise endurance and quality of life.[9] Exercise training is not only the cornerstone of lung rehabilitation, but also an economic and easy means of preventing and rehabilitating the diseases.[10,11]

Recently, the effectiveness of exercise interventions in improving COPD, interstitial lung disease, asthma, and pulmonary fibrosis has been confirmed. In 2013, the ATS and ERS published an official exercise rehabilitation program guideline for people with CRD: endurance training 3–5 times/week of 20–60 min duration each, with gradually increasing intensity and a target of > 70% of the expected maximum heart rate.[12] The British Thoracic Society (BTS) also provides guidelines for resistance training programs: resistance/strength training of 2–4 sets/session, with 10–15 reps/set and 30–60 min/session, and a recommended interval of at least 48 h between training sessions.[13] Additionally, individualized exercise programs should be developed according to the patient's specific situation. For patients with severe diseases, high-intensity interval training (HIIT) can be used as an alternative because of their ability to perform high-intensity exercises for a short period with sufficient rest in between.[14]

In this study we have reviewed the rehabilitative effects of exercise on COPD, bronchial asthma, bronchiectasis, interstitial lung disease, and lung cancer, and elucidated the mechanisms underlying the pathophysiological changes. We hope that this study will provide guidance for the application and practice of exercise rehabilitation in chronic lung diseases, as well as for the in-depth exploration of the pathological mechanism of exercise in improving lung diseases in the future. Furthermore, we aim to raise public awareness of pulmonary rehabilitation and facilitate the promotion and application of pulmonary rehabilitation methods.

Exercise and COPD

COPD is a common condition characterized by persistent airflow limitation and a series of clinical manifestations such as progressive decline in lung function, including chronic cough, sputum, and shortness of breath, and skeletal muscle dysfunction. It can progress to severe pulmonary heart disease or respiratory failure, with high mortality.[15] A large number of randomized controlled trials have recently provided evidence regarding the efficacy of exercise training interventions in patients with COPD. Resistance training can improve patients' exercise tolerance, muscle strength, and arm function, while aerobic exercises can improve patients' maximum oxygen consumption, neurological control of heart rate, and quality of life. The following table summarizes the researches on exercise interventions to improve COPD patients in the last decade (Table 1).

The body of patients with COPD is reportedly in a chronic inflammatory state with impaired intrinsic immunity.[25] This disease often worsens due to airway infections, with 22–40% of patients with COPD experiencing at least one moderate or severe exacerbation each year. Furthermore, the mortality rate is > 15% within 3 months of hospitalization for acute exacerbations.[26] Regular exercise can reportedly enhance the immune response of patients and control the body's inflammatory response. In animal studies, aerobic exercise was found to prevent the increase in macrophage and neutrophil count in mice with COPD;[27] a similar trend was found in population trials, with a significant reduction in eosinophil count in vivo after 6 weeks of endurance and strength training.[28] The benefits of exercise training on the innate immunity were demonstrated by Fernandes 2018 et al[29] who identified a significant increase in $CD4^+$ T-cells, improved immune response, and a reduction in exacerbations and hospitalizations after 12 weeks of exercise training in patients with COPD.[29] Thus, we hypothesized that the exercise-induced improvement of the intrinsic immune response would subsequently lead to the activation of the adaptive immune response. Wang et al determined that aerobic exercises upregulated interleukin (IL)-10 and chemokine (CXCL)-1 levels in bronchoalveolar lavage fluid (BALF), downregulated transforming growth factor (TGF)-β, IL-1β and tumor necrosis factor (TNF)-α levels in BALF, upregulated IL-10 levels in serum, and activated Sirt1 expression. These in turn suppressed the inflammatory responses and attenuated the oxidative stress in mice.[27] In a population trial, aerobic exercise reduced the serum expression of TNF-α, IL-4, IL-6

Table 1 Studies Related to the Rehabilitative Effects of Exercise Interventions in Patients with COPD

Type of Movement	Author & Year	Movement Frequency	Duration	Movement Form	Exercise Intensity	Improvement Indicators
Resistance exercises	Chen Y et al 2018[16]	3 times/ week	12 weeks	Elastic band and self-weight	Varies with each person	Muscle strength↑ Sports endurance↑
	Silva CMDSE et al 2018[17]	3 times/ week	8 weeks	Free weight (Dumbbell)	50% 1RM	Motor ability↑ Upper limb muscle strength↑ Quality of life↑
	Calik-Kutukcu E et al 2017[18]	3 times/ week	8 weeks	Free weight	40–50% 1RM	Peripheral muscle strength↑ Arm motility↑ ADL performance↑ Satisfaction with activity performance↑ Respiratory distress and arm fatigue perception↓
	Zambom-Ferraresi F et al 2015[19]	2 times/ week	12 weeks	Equipment	50–70% 1RM	Maximum muscle strength ↑ Motor ability↑ Quality of life↑
	Nyberg A et al 2015[20]	3 times/ week	8 weeks	Elastic band and self-weight	Varies with each person	Upper limb activity endurance↑ Muscle function↑
Aerobic exercises	Gallo-Silva B et al 2019[21]	3 times/ week	8 weeks	Aerobic interval training in water	Medium-high intensity (Borg rating of 4–6)	Self-regulating heart rate↑ Quality of life↑ Functional capacity↑
	Santos C et al 2015[22]	3 times/ week	8 weeks	Treadmill and bicycles	60/80% Wmax	HRQOL↑ Symptom control↑ Exercise tolerance↑
	De Sousa Pinto JM et al 2014[23]	2 times/ week	12 weeks	Walking, stair climbing, cycling, and treadmill walking	Varies with each person	Quality of life↑ Motor ability↑ Breathing difficulties for activities of daily living↓
	Pleguezuelos E et al 2013[24]	Daily	1 year	City walk	Low intensity	Motor ability↑

Abbreviations: COPD, chronic obstructive pulmonary disease; 1RM, one-repetition maximum; Wmax, workload maximum; ADL, activity of daily living; HRQOL, health-related quality of life. ↑, upward arrow represents a positive improvement in function; ↓, downward pointing arrow represents symptom relief.

and C-reactive protein (CRP).[30] These results suggest that exercise training is an effective strategy for reducing pulmonary and systemic inflammation, alleviating symptoms, and preventing disease progression in patients with COPD.

Exercise and Bronchial Asthma

The Global Initiative for Asthma[31] guidelines defines bronchial asthma as a heterogeneous disease characterized by chronic airway inflammation and hyperresponsiveness with varying degrees of airflow limitation, including cough, wheezing, chest tightness, dyspnea, and other clinical manifestations. It is one of the most common and serious CRDs affecting human health worldwide.[32]

Reduction or even elimination of physical activity is advised in patients with asthma to avoid symptom deterioration or exercise-induced bronchoconstriction. However, the reduction in physical activity leads to decreased fitness and exercise tolerance,[33,34] making asthmatics more prone to fatigue and breathing difficulties during exercise; ultimately, this leads to exercise avoidance.[35] In addition, steroid used to treat asthma can also lead to a decrease in muscle endurance.[36] The primary goals of asthma treatment proposed by the GINA are to control symptoms, reduce future risks, and improve the quality of life.[32] Current common clinical treatments include the use of bronchodilators and anti-inflammatory drugs; however, their efficacy is not satisfactorily adequate. Therefore, it is necessary to find an active and effective non-pharmacological treatment option.[37] As an important part of pulmonary rehabilitation, exercise training is a new non-pharmacological therapy used in some clinical studies. The following table summarizes the researches on exercise interventions to improve patients of bronchial asthma in the last decade (Table 2).

Asthmatics are capable of physical activity, and moderate physical activity can reportedly improve their health status.[47] The limitation of exercise capacity is sometimes more due to skeletal muscle dysfunction than due to airflow limitation. A large number of population-based trials have shown that aerobic exercise is beneficial in patients with asthma; the lung function is enhanced by improving the forced vital capacity (FVC), forced expiratory volume of 1st second (FEV1), peak expiratory flow (PEF), and other indicators.[48–50] Furthermore, it helps better control the asthmatic symptoms [51–53] and improves bronchial hyperresponsiveness,[54–56] aerobic capacity, quality of life, anxiety, and depression.[52,57–60] Physical activity and conventional therapy can effectively improve the quality of life and asthma control in patients with nocturnal deterioration.[61] Several epidemiological studies have shown an association between asthma and obesity; weight loss improves asthma control in overweight and obese patients.[62] However, exercise regimen formulations differ in exercise-induced asthma; it is necessary to consider the safety, feasibility, scientific nature, and focus of the regimen.

At present, it is widely accepted that bronchial asthma is closely related to inflammation, immunity, genetics, and the environment. The airway inflammatory response is the central link in triggering bronchial asthma, which is dominated by eosinophil and mast cell infiltration and an enhanced T helper cell 2 (Th2)-type response.[63,64] Exercises may reportedly have a protective effect by reducing airway inflammation and increasing the bronchial patency.[65,66] In animal models, appropriate aerobic exercise training downregulated IgE and IgG levels in the early stages and reduced the inflammatory factor release, which alleviated the symptoms of acute allergic asthma.[67] Recently, aerobic exercise has been found to effectively reduce airway eosinophilic expression, which in turn reduces the inflammation, inhaled glucocorticoid (ICS) dosage, and acute exacerbations, under the premise of standardizing and optimizing ICS medication.[68] Aerobic training can also positively modulate airway inflammation and remodeling mediators. Patient's FeNO and sputum eosinophil counts were reduced with aerobic exercise interventions, which was more pronounced in patients with higher levels of

Table 2 Studies Related to the Rehabilitative Effects of Exercise Interventions in Patients with Bronchial Asthma

Type of Movement	Author & Year	Movement Frequency	Duration	Movement Form	Exercise Intensity	Improvement Indicators
Resistance exercises	Chung et al 2021[38]	5 days/week	12 weeks	Equipment	50–60% PImax	Inspiratory muscle strength↑ Asthma control↑ Functional capacity↑ Physical activity↑
	Sanz-Santiago et al 2020[39]	3 days/week	12 weeks	Equipment	From 40% of 5RM lifting ability at the start of the program to 60% of 5RM at the end of the program	Cardiorespiratory fitness↑ Muscle strength↑
	Freitas et al 2018[40]	2 times/ week	3 months	Equipment	50–70% 1RM	Daily life physical activity↑ Sleep efficiency↑ Depression↓ Asthma symptoms↓

(*Continued*)

Table 2 (Continued).

Type of Movement	Author & Year	Movement Frequency	Duration	Movement Form	Exercise Intensity	Improvement Indicators
Aerobic exercises	O'Neill & Dogra 2021[41]	3 times/ week	6 weeks	HIIT	10% Wpeak for 1 min and 90% Wpeak for 1 min, repeated 10 times	Asthma control↑ Exertional dyspnea↑ Exercise enjoyment↑
	Winn et al 2021[42]	3 times/ week	6 months	HIIT	>90% age-predicted HRmax	Cardiorespiratory fitness↑ BMI↓
	Evaristo et al 2020[43]	2 times/ week	2 weeks	Treadmill	60% HRmax	Asthma control↑ Use of rescue medication↓
	Sanz-Santiago et al 2020[39]	3 days/week	12 weeks	Aerobic cycle	HR of VT1 measured at baseline	Cardiorespiratory fitness↑ Muscle strength↑
	Zhang & Yang 2019[44]	3 times / week	6 weeks	Aerobic circuit training		Clinical symptoms↑ QoL↑
	Jaakkola et al 2019[45]	≥3 times / week	24 weeks	Different forms	70–80% HRmax	Asthma control↑ Shortness of breath↓
	Freitas et al 2018[40]	2 times/ week	3 months	Bike Treadmill Elliptical machine	50–75% VO2 Max	Daily life physical activity↑ Sleep efficiency↑ Depression↓ Asthma symptoms↓
	Carew & Cox 2018[46]	1 time/week	6 weeks	Swimming Football Basketball		FVC%↑ PEF%↑ Asthma symptoms↓
	Toennesen et al 2018[60]	3 times/ week	8 weeks	HIIT (Indoor spinning bikes)	<30% maximal intensity <60% maximal intensity >90% maximal intensity	Asthma control↑ QoL↑
	Abdelbasset et al 2018[48]	3 times/ week	10 weeks	Walking on a treadmill	50–70% HRmax	Pulmonary functions↑ Aerobic capacity↑ PQoL↑
	Franca-Pinto et al 2015[54]	2 times/ week	12 weeks	Treadmill	Vigorous training (based on the AnT and the RCP)	Motor ability↑ QoL↑

Abbreviations: PImax, maximal inspiratory pressure; Wpeak, peak power output; 5RM, five-repetition maximum; 1RM, one-repetition maximum; VT1, ventilation threshold; HIIT, high-intensity interval training; BMI, body mass index; QoL, quality of life; HRmax, heart rate maximum; PEF, peak expiratory flow; PQoL, pediatric quality of life; AnT, anaerobic threshold; RCP, respiratory compensation point. ↑, upward arrow represents a positive improvement in function; ↓, downward pointing arrow represents symptom relief.

inflammation.[52,55,69] Together, these findings suggest that aerobic training can be an effective adjunct to medication use in patients with asthma.

Exercise and Bronchiectasis

Bronchiectasis is a recurrent suppurative infection caused by various factors. Small- and medium-sized bronchi are repeatedly damaged and blocked, which destroys the wall structure and results in bronchial abnormalities and persistent dilation. The clinical manifestations include chronic cough, massive expectoration, and intermittent hemoptysis. If not treated promptly, it can lead to pulmonary heart disease and respiratory failure.[70] Secondary problems such as decreased peripheral muscular endurance and activity also cause significant damage to a patient's personal and social life.[71] Current clinical treatments focus on the acute exacerbation phase and are based on the principles of suppressing acute and chronic bronchial infections, improving mucociliary clearance, reducing the impact of structural lung disease, preventing deterioration, reducing symptoms, and improving the quality of life.[72]

Bronchiectasis is not an uncontrollable or unpreventable respiratory disease, and the risk of acute exacerbation can be reduced by preventive interventions and increased awareness of self-management during the stable phase.[73] Several population-based trials have demonstrated the benefits of exercise interventions in patients with bronchiectasis. The following table summarizes recent studies on exercise interventions that have improved the condition of patients with bronchiectasis (Table 3). The findings indicate that resistance training and aerobic exercises of the upper and lower extremities can increase exercise capacity and endurance, enhance peripheral and respiratory muscle strength, improve lung function, reduce dyspnea, and raise the quality of life.[74–76] However, maintaining these benefits is challenging; as exercise cycles increase, patient compliance decreases, and the positive cumulative effect decreases accordingly.[77,78] A great deal of experimentation and research is still warranted to reach a consensus on how long exercise training can maintain the improvement and what type of exercise training is easy for patients to adhere to.

The inefficient clearance of mucus and microorganisms and inflammation progression are the main causes of irreversible lesions in bronchiectasis. Regular exercise training can alter the autonomic balance of mucociliary clearance and accelerate vagal and sympathetic interactions for the recovery of gas exchange capacity.[83] Inflammatory progression results in a large cellular infiltration in the airway epithelium.[84] Neutrophil-mediated immune responses, which secrete excessive amounts of matrix metalloproteinases 8 and 9 (MMP-8 and MMP-9), lead to continuous airway destruction.[85] Furthermore, the patient's serum, bronchoalveolar lavage fluid, and lung tissue showed increased levels of chemokines and pro-inflammatory cytokines, such as IL-8 and IL-17.[86,87] Currently, there is a lack of investigation into the underlying mechanism by which exercise improves bronchiectasis; however, numerous studies have confirmed that exercise training can reduce the levels of inflammatory markers in the body[88] and inhibit neutrophil hyperactivation.[89] Therefore, it can be hypothesized that exercise prevents or inhibits disease progression by reducing airway inflammation and modulating the functional activity of immune cells. However, further studies are needed to clarify these mechanisms.

Table 3 Studies Related to the Rehabilitative Effects of Exercise Interventions in Patients with Bronchiectasis

Type of Movement	Author & Year	Movement Frequency	Duration	Movement Form	Exercise Intensity	Improvement Indicators
Resistance exercises	Cedeño de Jesús S et al 2022[74]	3–5 days/week	8 weeks	Equipment	Varies with each person	Motor ability↑ Walking distance↑ Breathing difficulties↓
	Araújo AS et al 2022[79]	3 times/week	3 months	Equipment and barbells	Starting at 50% 1RM, the load was increased by 10% per week until 80% 1RM was reached	Physical fitness↑ QoL↑
	José A et al 2021[75]	3 times/week	8 weeks	Elastic band	70% maximum isometric autonomous contraction	Motor ability↑ QoL↑ Quadriceps muscle strength↑
	Deniz S et al 2021[80]	2 times/week	8 weeks	Incremental load resistance	Varies with each person	Motor ability↑ QoL↑
	Patel S et al 2019[81]	3 times/week	8 weeks	Equipment and free weights	60% 1RM	Motor ability↑ HRQoL↑ Breathing difficulties↓
	Pehlivan E et al 2019[77]	2 times /week	2 months	Free weight		Physical activity level↑ Lung function↑

(*Continued*)

Table 3 (Continued).

Type of Movement	Author & Year	Movement Frequency	Duration	Movement Form	Exercise Intensity	Improvement Indicators
Aerobic exercises	Cedeño de Jesús S et al 2022[74]	3–5 days/week	8 weeks	Walking and bicycles	Varies with each person	Motor ability↑ Walking distance↑ Sports endurance↑ Breathing difficulties↓
	Araújo AS et al 2022[79]	3 times/week	3 months	Treadmill	80% VO2 Max	Physical fitness↑ QoL↑
	José A et al 2021[75]	3 days/week	8 weeks	Step training	Achieve 60–80% of the maximum step cadence	Motor ability↑ Exercise tolerance↑ QoL↑
	Deniz S et al 2021[80]	2 times/week	8 weeks	Treadmill and bicycles	60–90% HRmax	Motor ability↑ QoL↑
	Dos Santos DO et al 2018[82]	2 times/week	12 weeks	Treadmill and bicycles	80% VO2 Max	Breathing difficulties↓
	Zanini A et al 2015[78]	3 days/week	3 weeks	Treadmill and bicycles	60–70% HRmax	HRQoL↑ Motor ability↑ Breathing difficulties↓
	Van Zeller M et al 2012[76]	3 times/week	12 weeks	Bicycles	60% Wmax	FVC↑

Abbreviations: HRQoL, health-related quality of life; FVC, forced vital capacity; Wmax, workload maximum; VO2 Max, peak oxygen consumption; ↑, upward arrow represents a positive improvement in function; ↓, downward pointing arrow represents symptom relief.

Exercise and Interstitial Lung Disease

Interstitial lung disease (ILD) is a diverse group of CRDs characterized by dyspnea, exercise-induced hypoxemia,[90] and exercise intolerance.[91,92] It can severely limit the ability of patients to maintain even moderate levels of functional physical activity, including those of daily living and employment.[93]

ILD differs from other respiratory diseases because it causes significant EIH, which often makes it difficult for patients to achieve adequate exercise intensity.[90] The standard exercise program for COPD is effective for ILD. After aerobic exercise training, the 6-minute walking distance (6MWD) of patients with ILD increased significantly, and the clinical cardiopulmonary function improved conspicuously.[94–96] An increase in 6MWD reportedly coincides with a decrease in patient-reported fatigue,[97] which subsequently improves a patient's health-related quality of life (HRQoL).[98] During exercise training, transcutaneous oxygen saturation (SpO2) and degree of dyspnea should be monitored in real time. If EIH or dyspnea is difficult to control, the following training strategies or methods should be considered: interval training, supplemental oxygen, transnasal high-flow oxygen therapy, noninvasive ventilation, alternative exercises (Nordic walking or downhill training), and the use of energy-saving techniques and equipment. Owing to the difficulty in implementing an exercise program in the late stages of uncontrolled symptoms, all patients with ILD should be started on exercise training as early as possible.[91] The intervention plans and results of exercise intervention on patients of ILD are summarized in the following table (Table 4).

The main aim when treating interstitial pneumonia is to control alveolar inflammation. This can be achieved with glucocorticoids, which have strong anti-inflammatory effects and can induce lymphocyte apoptosis. These immunosuppressive effects prevent the lethality of excessive inflammation and increases the risk of infection and cancer. In addition, long-term use negatively affects the immune system and leads to secondary infections.[107] Studies on the effects of exercise training on the patient's immune system in patients with ILD are limited. Exercise is reportedly effective in

Table 4 Studies Related to the Rehabilitative Effects of Exercise Interventions in Patients with ILD

Type of Movement	Author & Year	Movement Frequency	Duration	Movement Form	Exercise Intensity	Improvement Indicators
Resistance exercises	Jarosch et al 2020[99]	3–6 times /week	3 weeks	Free weight	15–20RM	Exercise capacity↑ Disease-specific QoL↑
	Sciriha et al 2019[100]	2 times/week	12 weeks	Free weights		Dyspnoea↓ Health status↑ Fatigue↓
	Perez-Bogerd et al 2018[101]	3 times/week	6 months	Multi-gym device	70% 1RM	Exercise tolerance↑ Health status↑ Muscle force↑
	Naz et al 2018[102]	2 times/week	12 weeks	Free weights	Borg scale (4–6)	Functional capacity↑ Dyspnoea↓ QoL↑ Muscle strength↑ Anxiety and fatigue↑
	Dowman et al 2017[103]	2 times/week	8 weeks	Dumbbell	10–12 RM	Exercise capacity↑ Symptoms↓ HRQoL↑
	Tonelli et al 2017[104]	6 hours/week	4 weeks	Light weights Resistance bands	Varies with each person	Exercise performance↑ HRQoL↑
Aerobic exercises	Essam et al 2022[105]	3 times /week	6 weeks	Arm ergometer Treadmill	50–76% HRmax	Functional exercise capacity↑ Dyspnoea↓ Oxygen saturation↑ HRQoL↑
	Brunetti et al 2021[106]	5 times/week	3–4 weeks	Continuous cycling	50–70% of the maximal load	Dyspnoea↓ Exercise capacity↑ Fatigue↓
	Jarosch et al 2020[99]	3–6 times /week	3 weeks	Interval cycle training	60% −100% Wpeak	Exercise capacity↑ Disease-specific QoL↑
	Sciriha et al 2019[100]	2 times/week	12 weeks	Treadmill Stationary bike	70% resting heart rate	Functional capacity↑ Dyspnoea↓ Health status↑ Fatigue↓
	Perez-Bogerd et al 2018[101]	3 times/week	6 months	Cycle ergometer	60–85% Wmax	Exercise tolerance↑ Health status↑
	Naz et al 2018[102]	2 time/week	12 weeks	Treadmill	70% Wmax	Functional capacity↑ Dyspnoea↓ QoL↑ Oxygenation↑ Anxiety and fatigue↓
	Tonelli et al 2017[104]	6 hours/week	4 weeks	Treadmill Stationary bikes	Varies with each person	Exercise performance↑ HRQoL↑
	Dowman et al 2017[103]	2 times /week	8 weeks	Cycling Walking	70% Wmax 80% Wmax	Exercise capacity↑ Symptoms↓ HRQoL↑
	Keyser et al 2015[97]	3 times/week	10 weeks	Treadmill	70–80% HRmax	Fatigue↓ Physical activity↑

Abbreviations: ILD, Interstitial Lung Disease; RM, repetition maximum; ↑, upward arrow represents a positive improvement in function; ↓, downward pointing arrow represents symptom relief.

improving the function of the body's immune system.[108] Perhaps, exercise could possibly reduce lung inflammation and glucocorticoid-induced damage to the immune system.

Exercise and Lung Cancer

Lung cancer is one of the most common malignancies worldwide and the leading cause of cancer-related deaths.[109] The WHO classifies lung cancer into two broad histological subtypes: non-small cell lung cancer (NSCLC) and small cell lung cancer (SCLC). NSCLC accounts for about 85–88% of the cases and SCLC accounts for about 12–15%.[110] Long-term smoking, presence of excessive carcinogens in the work environment, ionizing radiation, lack of physical activity, genetics, and previous chronic lung infections are strongly associated with the development of lung cancer.[111] Patients often present with symptoms such as cough, hemoptysis, fever, chest pain, shortness of breath, enlarged supraclavicular lymph nodes, and hoarseness of voice. The mainstay of clinical treatments include surgery, drug therapy, chemotherapy, targeted therapy, radiation therapy, interventional therapy and Chinese medicine.[112–115]

Currently, pneumonectomy is the most effective treatment for stages I, II, and IIIA of NSCLC and offers the best prospects for long-term survival.[112] Compared with healthy individuals, the physical activity level of patients with NSCLC is lower and further declines within 6 months of diagnosis.[116] In particular, reduced lung function increases the risk of surgery in patients with operable diseases.[117] Some patients were excluded from surgical treatment because of poor preoperative evaluations.[118] We conducted a study of patients who underwent pneumonectomy. Preoperative rehabilitation for patients undergoing pneumonectomy became a landmark study. After four weeks of aerobic exercise and respiratory training, the lung function improved in patients who could not undergo surgery due to poor pulmonary function tests; this greatly increased their chances of undergoing surgery.[119] A study conducted by the University of California, determined that HIIT for two to six weeks may be the best perioperative exercise program; however, there is heterogeneity in the intensity and duration.[120] In some population-based trials, exercise interventions benefited patients both preoperatively and postoperatively, with improved muscle mass, strength, and sleep quality after resistance training.[121,122] Aerobic exercise improves exercise tolerance and cardiorespiratory fitness and reduces postoperative respiratory morbidity, length of hospital stay, cancer fatigue, anxiety, and depression;[123–126] both are beneficial for lung function, exercise capacity, cancer pain reduction, quality of life, and life extension.[127–129] The summary of exercise intervention to improve various indicators of lung cancer patients is shown in Table 5.

In recent years, immunotherapy has rapidly developed as an effective clinical strategy in cancer treatment. It is based on the tumor escape mechanism by manipulating the immune system to reactivate the anti-tumor immune response and overcome immune escape.[138] However, the antitumor mechanisms of exercise may be related to immune regulation. In a high-intensity training model of rats, the toxicity and activity of natural killer (NK) cells in rats increased.[139] Pedersen et al found that the tumor volume and pro-inflammatory cytokines (IL-1a and iNOS) in Lewis lung cancer (I)mice running voluntarily decreased significantly, and that the NK and T cell activity markers were upregulated.[140] Similar effects were observed in other populations.[141] Owing to the important role of NK cells in antitumor immunity,[142] the ultimate benefits of exercise training may have clinical significance in cancer treatment. In several prospective randomized studies on postoperative patients with NSCLC, 16 weeks of Tai Chi training significantly promoted the proliferation and cytotoxicity of peripheral blood mononuclear cells and maintained stable T1 to T2 ratios and cortisol levels.[143,144] More and more results of studies related to exercise immunity and anti-cancer progression suggest that exercise is an effective adjunct to existing anti-cancer therapies.

Conclusions

Exercise training-based pulmonary rehabilitation is effective in alleviating the symptoms of several CRDs, improving cardiovascular and muscle function, enhancing tolerance to physical activity, and improving the quality of life. Moderate-intensity aerobic exercise, resistance training, and HIIT are the most common forms of pulmonary rehabilitation exercises. Tai chi, yoga, aquatic exercise, and whole-body vibration training are also emerging forms of exercise that are gradually being used in the development of individualized pulmonary rehabilitation exercise programs. Although some patients may not respond adequately or respond inconsistently to specific training programs, published guidelines emphasize that pulmonary rehabilitation can benefit patients with stable respiratory disease symptoms. High-quality

Table 5 Studies Related to the Rehabilitative Effects of Exercise Interventions in Patients with Lung Cancer

Type of Movement	Author & Year	Movement Frequency	Duration	Movement Form	Exercise Intensity	Improvement Indicators
Resistance exercises	Machado et al 2023[130]	2 times/week	2–6 weeks	Free weight	RPE Borg CR-10 (3–5, moderate to strong)	HRQoL↑ Lower limb functional strength↑ Fatigue↓
	Mikkelsen et al 2022[131]	2 times/week	12 weeks	Free weight	Varies with each person	Physical function↑ Lower body muscle strength↑ Psychological well-being↑ Lean body mass↑
	Scott et al 2021[132]	3 times/week	16 weeks	Equipment and free weights	50–85% maximal strength	Maximal strength↑ Body composition↑
	Messaggi-Sartor et al 2019[133]	3 times/week	8 weeks	Free weight	30–50% PImax and PEmax	Exercise capacity↑ Respiratory muscle strength↑
	Cavalheri et al 2017[134]	3 times/week	8 weeks	Equipment and free weights	Varies with each person	Exercise capacity↑
	Vanderbyl et al 2017[122]	2 times /week	6 weeks	Equipment and free weights	60–70% HRmax or 2–4 METs	Feelings of weakness↓ Walking capacity↑ Well-being↑ Sleep↑
	Quist et al 2015[135]	2 times /week	6 weeks	Equipment	70–90% 1RM	Physical capacity↑ Anxiety↓ Well-being↑
Aerobic exercises	Machado et al 2023[130]	3 times/week	2–6 weeks	Walking	RPE Borg CR-10 (3–5)	HRQoL↑ Lower limb functional strength↑ Fatigue↓
	Mikkelsen et al 2022[131]	2 times/week	12 weeks	Home-based walking		Physical function↑ Lower body muscle strength↑ Psychological well-being↑ Lean body mass↑
	Lei et al 2022[136]	5 times/week	8 weeks	Baduanjin	Moderate intensity	QoL↑ Depression↓ Anxiety↓
	Scott et al 2021[132]	3 times/week	16 weeks	Cycle ergometry	55%–>95% VO2 Max	Cardiorespiratory fitness↑
	Messaggi-Sartor et al 2019[133]	3 times/week	8 weeks	Ergometric bicycle	60% Wpeak (increasing 5 watt weekly)	Exercise capacity↑ Respiratory muscle strength↑
	Bhatia & Kayser 2019[137]	3 times/week	2–3 weeks	HIIT	30%–100%Wpeak	Cardio-respiratory fitness↑ Walking capacity↑
	Cavalheri et al 2017[134]	3 times/week	8 weeks	Walking Cycling	60% Wmax	Exercise capacity↑
	Vanderbyl et al 2017[122]	2 times/week	6 weeks	Walking	Varies with each person	Feelings of weakness↓ Walking capacity↑ Well-being↑ Sleep↑
	Quist et al 2015[135]	2 times/week	6 weeks	Stationary cycle ergometer	60–90% HRmax	Physical capacity↑ Anxiety↓ Well-being↑

Abbreviations: RPE, rate of perceived exertion; Wpeak, peak workload; PEmax, maximal expiratory pressure; MET, metabolic equivalent; ↑, upward arrow represents a positive improvement in function; ↓, downward pointing arrow represents symptom relief.

randomized controlled trials are required to further evaluate individualized training modalities in patients with comorbidities. More in-depth studies are needed to investigate the pathophysiological mechanisms by which different forms of exercise improve CRD and determine alternatives to pulmonary rehabilitation in patients with exercise limitations.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

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