Pulmonary Rehabilitation

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KEYWORDS

• Pulmonary rehabilitation • COPD • Screening • Physical activity • Exercise
• Long term management

KEY POINTS

- Pulmonary rehabilitation is an evidence-based therapy for patients with COPD that remain symptomatic despite optimal pharmacological management.
- Pulmonary rehabilitation improves exercise tolerance, symptoms and health related quality of life. It reduces health care cost, particularly in patients with exacerbations.
- Further research should focus on the strategies to ensure the long-term benefits for patients with COPD, particularly in improvements of physical activity.

OUTLINE

Definition

Pulmonary rehabilitation is now an accepted therapy for patients with respiratory diseases. Its effectiveness is supported by countless randomized controlled trials. Over the past 30 to 40 years, pulmonary rehabilitation has evolved from an "art of medicine" to evidence-based therapy. Despite the availability of an updated definition and the increased emphasis on the evidence base, the essence of definitions of pulmonary rehabilitation as an individualized and multidisciplinary treatment has existed since the very first statement on pulmonary rehabilitation of the American Thoracic Society (ATS). **Table 1** provides the history of definitions of pulmonary rehabilitation by ATS and European Respiratory Society (ERS). The most recent definition identifies the core components of a rehabilitation program.[1]

When patients remain symptomatic despite optimized pharmacotherapy, prescription of a rehabilitation program must be considered. In an initial assessment phase, a rehabilitation program aims at mapping out the modifiable nonrespiratory consequences of respiratory diseases (see below, ie, muscle weakness, depressive symptoms, poor coping with the disease, impaired engagement in physical activities, nutritional deficits). Subsequently (or in parallel) the rehabilitation program calls on the self-management of patients to engage in a healthy lifestyle in terms of physical activity, nutrition, smoking, and coping. The rehabilitation team becomes the coach of the patient. Exercise training is considered a crucial element of the rehabilitation program. More recently, the focus of research has gradually shifted toward more lifelong behavioral change. Although the science base of exercise training has reached a very high standard, the evidence base for achieving a true behavior change is less solid. Significant and important progress must be made, particularly to help maintain the benefits of an exercise training

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Table 1
Evolution of definitions of pulmonary rehabilitation by the ATS or jointly by the ATS and ERS

Date	Definition
1981 (1974)	Pulmonary rehabilitation is an art of medical practice wherein an *individually* tailored, *multidisciplinary* program is formulated, which through accurate diagnosis, therapy, emotional support, and education stabilizes or reverses both the physiology and psychology of pulmonary diseases and attempts to return the patient to the highest possible functional capacity allowed by his pulmonary handicap and overall life situation. Goals are (1) control and alleviate symptoms and complications of respiratory impairment, and (2) teach patients optimal capability to carry out activities of daily life.
1999	(No definition) The principal goals of pulmonary rehabilitation are to reduce symptoms, decrease disability, increase participation in physical and social activities, and improve the overall quality of life for individuals with chronic respiratory disease.
2006	Pulmonary rehabilitation is an evidence-based, *multidisciplinary*, and *comprehensive intervention* for patients with chronic respiratory diseases who are symptomatic and often have decreased daily life activities. Integrated into the individualized treatment of the patients, it is designed to reduce symptoms, optimize functional status, increase participation, and reduce health care costs through stabilizing or reversing systemic manifestations of the disease.
2013	Pulmonary rehabilitation is a *comprehensive intervention* based on a thorough patient assessment followed by *patient-tailored* therapies, which include, but are not limited to, exercise training, education, and behavior change, designed to improve the physical and psychological condition of people with chronic respiratory disease and to promote the long-term adherence to health-enhancing behaviors.

Definition of pulmonary rehabilitation over the past 40 years. A clear difference is the evolution from art to science. The evidence base has increased over the years but in essence pulmonary rehabilitation has always been defined as an individualized multidisciplinary treatment.

program in the long term and perhaps to have an impact on truly modifying the long-term nonrespiratory consequences of chronic obstructive pulmonary disease (COPD). In this article the different components and the setup of a rehabilitation program are reviewed. Importantly, pulmonary rehabilitation programs are often integrated in other care plans for patients with COPD, such as self-management programs, lung transplantation programs, noninvasive ventilation, or smoking cessation programs. Interaction between the different teams and experts running these care programs across lines of health care and pathologic abnormaltiy (to adequately handle comorbidity) is crucial for the overall success of the management of these patients with complex chronic diseases.

THE EVIDENCE BASE FOR PULMONARY REHABILITATION

Several reviews have summarized the evidence for pulmonary rehabilitation[2–4] and practice guidelines are available.[5,6] Therefore, a comprehensive review of all the evidence on the effectiveness of pulmonary rehabilitation is beyond the scope of this article.

Pulmonary rehabilitation, including exercise training, enhances exercise tolerance mainly through enhanced skeletal muscle function and reduced ventilatory requirements during exercise. Functional performance is increased through physiologic improvements, enhanced movement efficiency, and perhaps increased self-efficacy. Rehabilitation also improves patient-reported outcomes, such as symptoms and health-related quality of life. These improvements are of clear clinical significance in patients with COPD.[4]

Beyond these benefits, rehabilitation also leads to psychological improvements.[7] In patients referred to the authors' rehabilitation program, depressive symptoms were present in 42% of patients and symptoms compatible with anxiety were present in 38% of patients. Improvements of depressive symptoms and anxiety are only to be expected if patients do have these symptoms. Hence the relatively small effect size reported in the meta-analysis[7] may be induced by the dilution of the depressed patients in the larger patient pool.

As per definition, rehabilitation attempts to increase the amount of physical activity patients engage in. The systemic consequences of COPD, such as cardiovascular morbidity, muscle

weakness, and osteoporosis, originate to a large extent directly or indirectly from living an inactive lifestyle. When pulmonary rehabilitation aims at achieving a sustained effect, an inactive lifestyle after rehabilitation should be avoided. The effect of pulmonary rehabilitation programs on physical activity levels has only been studied in the past 10 years. It was commonly taken for granted that a comprehensive rehabilitation program would increase physical activity levels, but studies have reported conflicting results. Few randomized controlled trials have addressed the topic[8,9] and no long-term follow-up studies are available. Changing physical activity behavior is challenging and in general results are somewhat disappointing. Although endurance capacity virtually doubles, physical activity levels increase less than 20% across studies.[10] Changing physical activity may not simply follow the increased exercise capacity or improved skeletal muscle function. Probst and colleagues[11] showed that more increased exercise tolerance (by providing higher intense exercise programs) did not lead to further enhanced physical activity levels. Physical activity is a complex behavior that depends on physiologic capacity, but also on psychological processes. In addition, environmental, societal, and cultural factors are important and there is even a genetic component in physical activity behavior.[12] To have a major impact on physical activity, an even more comprehensive approach may be needed that reaches out to the family and social network of the patient and to the community.

In recent years, appealing new strategies have been developed that may potentially help to increase the effects of classical rehabilitation on physical activities. First, providing patients real-time feedback with pedometers on their physical activity levels may, along with setting achievable goals, enhance daily activity levels inside or outside the context of pulmonary rehabilitation.[13] Second, walking at home has been stimulated effectively using group activities such as Nordic Walking or using modern interfaces such as mobile phone technology, which included paced walking on the rhythm of music adapted to the possibilities of the patient. Even more recently, “gaming”-based or Internet-based programs have become available that may support rehabilitation programs, but must be further validated in this context.[14] Future research should focus on further strategies that may help to lead to a sustainable behavior change.

A last benefit of pulmonary rehabilitation is a decrease in the use of health care recourses. Hospital admissions are an important driver of direct costs of COPD. These health care recourses do not occur in all patients, but once they occur they tend to be repetitive[15] and are expensive. In one of the first large randomized controlled trials on pulmonary rehabilitation there was a trend for a lower number of hospital days[16]; a more recent trial showed a significant reduction in the number of hospital days.[17] Comparable findings were obtained in relatively long open studies comparing use of health care recourses before and after taking part in pulmonary rehabilitation. When trials focus on more fragile patients, such as those recently admitted to hospital and at risk for readmission, a meta-analysis showed that the risk for readmission was substantially reduced.[18]

WHERE CAN PULMONARY REHABILITATION BE ORGANIZED

Pulmonary rehabilitation programs have traditionally been developed as outpatient programs. In the early 1990s, however, it was suggested that home-based programs could also be applied. Community-based settings were later proposed as an alternative. Inpatient programs are effective but very expensive and should perhaps be reserved for the most complex patients. Ideally, a center should be able to offer rehabilitation programs that are also individually tailored in terms of setting and supervision, complexity, and duration (**Fig. 1**). If not, the available program format may not be the desired program from a patient perspective or may simply be impossible to cope with. As a consequence many patients decline the invitation to take part in rehabilitation or drop out from programs. Because different forms of programs were shown to be effective, perhaps a way to increase uptake would be to offer different options to patients. Challenges obviously will remain in the funding and management of different programs at once. **Fig. 1** represents the different organizational options for pulmonary rehabilitation. For most of these evidence of efficacy is available if patients are well selected and supervision is provided. Perhaps all these options may not be offered by one rehabilitation team, but ideally links between different teams exist across lines of health care to allow that patients can be offered a program that is in line with their needs and their desires. **Fig. 1** also provides a few examples of clinical scenarios, but obviously these are not exhaustive.

A COMPREHENSIVE INTERVENTION: PROGRAM CONTENT

Exercise training is an essential component in the rehabilitation program of patients with COPD that

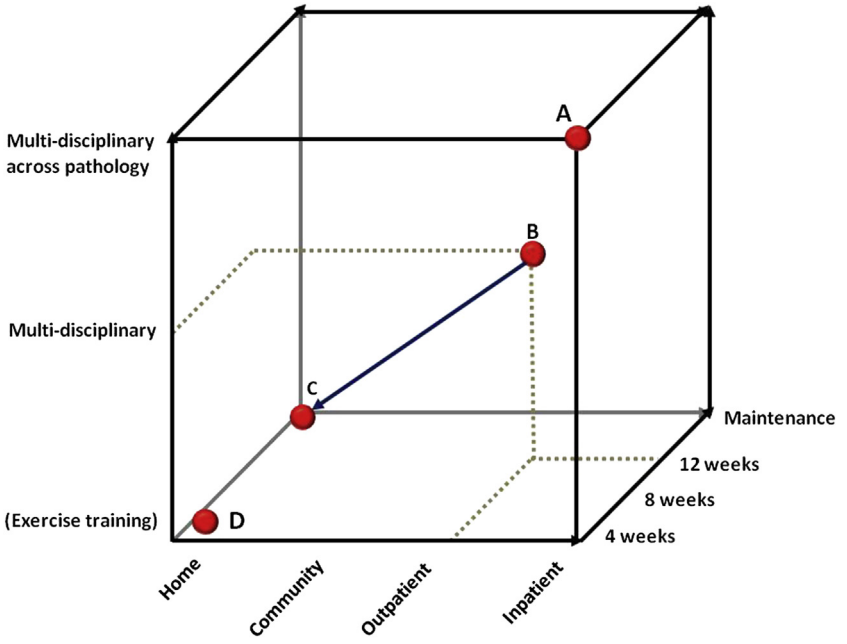

Fig. 1. Different types of rehabilitation. All of the combinations in the 3 dimensions are theoretically possible. A few examples are given. In patient A, a patient on noninvasive mechanical ventilation and with severe COPD, heart failure, and type 2 diabetes, an in-patient complex rehabilitation program is offered. Patient B is a patient with severe COPD, symptoms of depression, and a body mass index of 29 kg m^{-2}, who still drives his own car. He is enrolled in an outpatient program after which he will follow a maintenance program in primary care (a fitness facility (C)). Patient D is a patient with mild COPD who is deconditioned due to a prolonged inactive lifestyle. The patient has mild symptoms and further uncomplicated COPD. He is referred to a simple exercise training program in primary care.

suffer from deconditioning. The program must be individualized in terms of exercise modalities, specificity of the training, the training intensity, and specific inspiratory muscle training. To obtain significant physiologic improvements in skeletal muscle function, it is important to train patients at a training intensity that is "high" relative to the maximum capacity of the patients.[19] Recently, programs eliciting more significant skeletal muscle fatigue were related to better training effects in terms of functional exercise tolerance and reduction of symptoms.[20] To combine an effective training program with patient comfort, clinicians have the choice of several exercise training modalities. These exercise training modalities include endurance training, interval training, and resistance training. Further individualization of the training program can be achieved through more complex training regimens, including the use of oxygen supplements, noninvasive mechanical ventilation, single leg training, or inspiratory muscle training. More fine-tuned modulation of the training intensity and close follow-up of patients during training may also result in better training outcomes.[21] Across the world, programs of different program length have been adopted. Six-week to 6-month programs have been described. In the latest consensus statement of ATS and ERS the program length is stated as "Optimal duration for the individual can be considered the longest duration that is possible and practical, since programs longer than 12 weeks have been shown to produce greater sustainable benefits than shorter programs." In the real world, the duration often depends on funding schemes, patient's willingness to continue, waiting lists, and so on. To result in physiologic benefits, the duration of an exercise training program is generally thought to be at least 8 weeks with a minimum frequency of 3 training sessions a week. One of these sessions can be conducted outside the formally supervised setting by the patients, provided that the session is comparable in terms of duration and intensity to the supervised sessions.[22] Although the evidence for exercise training is well accepted, less evidence is available on the involvement of other disciplines. Nevertheless, there is, for almost 40 years already (see **Table 1**), consensus that other disciplines may add value to a pulmonary rehabilitation program in specific patients. Other disciplines that can be considered to intervene in selected patients are occupational

therapists, psychologists, nutritional experts, physiotherapists, nurses, and social workers. Tasks of these health care providers should be discussed in a specific rehabilitation team. Indications and possible tasks are provided in Table 2. It is clear that not all patients will benefit to the same extent of the involvement of a particular health care provider. For example, a patient with a normal body mass index and body composition and healthy nutritional habits will likely not benefit from seeing a nutritional specialist. Conversely, patients with symptoms of depression may benefit from seeing a psychologist to establish the potential diagnosis of depression and if so suggest appropriate treatment.

Proper screening of patients at the moment of the intake will orient patients toward the different health care providers in a rehabilitation program.

Because many patients with COPD can be considered "frail elderly" patients, aspects of rehabilitation for this patient group can be included in the rehabilitation process. For example, because of poor proprioceptive balance control and skeletal muscle weakness, the balance of patients with COPD may be disturbed,[29] leading to increased risk of falling. Combined with osteoporosis, it is clear that falls are an important precursor of fractures. Recently the added value of a balance training program was shown in patients with COPD.[27]

PATIENT SCREENING AND SELECTION

The 2006 definition of pulmonary rehabilitation included the goals of rehabilitation: pulmonary rehabilitation is "designed to reduce symptoms,

Table 2
Health care providers and their suggested task in a rehabilitation team

Health Care Provider	Suggested Tasks
Chest physician (preferably with pulmonary rehabilitation specialty)	Medical treatment and patient referral Diagnosis and follow-up of comorbidities Setup and supervision of multidisciplinary team Referral for comorbidities
Exercise specialist (physiotherapist)	Setup and supervision of the exercise program Home exercise program (follow-up) Arrangement of maintenance training strategies
Psychologist	Management of uncertainty[23] Management of depression in depressed patients[24,a] Smoking cessation
Occupational therapist	Home energy efficiency[25] Specific training of home activities[26] Use of walking aids Pacing techniques
Nutritional experts	Management of overweight Management of cachexia Nutrient intake in line with exercise training program Nutritional supplements
Nurse specialist	Medication adherence Smoking cessation Self-management program for exacerbation management
Physiotherapist	Mucous clearance in patients with mucous hypersecretion and difficulties to clear spontaneously[5] Balance/proprioceptive training in frail patients at risk for falling[27]
Social worker	Solve transportation issues in outpatient programs Map out the social support network around a patient to anticipate on dropout[28] Implementation of social support measures provided by the health care system to alleviate financial burden

An overview of different health care providers and their tasks in a rehabilitation team. This list is not exhaustive and may be complemented by speech therapists, specific disciplines involved in the management of comorbidity, and so on. Family members as well as general practitioners are also members of the rehabilitation team around a patient.

[a] Intervention implemented by trained nurse.

optimize functional status, increase participation, and reduce health care costs through stabilizing or reversing systemic manifestations of the disease."[22] From this it followed that the ideal candidate for rehabilitation is symptomatic, has impaired functional status, participation, and high utilization of health care resources, and should suffer from the "systemic consequences of COPD" or perhaps better "the nonrespiratory consequences" of COPD. Hence the selection of patients should not be done based on lung function, but rather on the proper assessment of the extrapulmonary consequences of COPD found to be reversible with rehabilitation, symptoms, functional status, the levels of participation in daily life, and health-related quality of life. Other factors, such as age, gender, and smoking status, are not important to predict the outcome of rehabilitation. It is important that patients are screened for pulmonary rehabilitation after establishing optimal pharmacotherapy. Although being screened for rehabilitation, patients can also be considered for other programs, such as a lung transplantation or lung volume reduction program, a program of noninvasive ventilatory support, or oxygen therapy. Such programs have no exclusion criteria for pulmonary rehabilitation. On the contrary, oftentimes pulmonary rehabilitation is strongly recommended in these patients.

Screening for the Extrapulmonary Consequences of COPD

In the context of exercise training the most important "systemic consequence" of COPD is skeletal muscle dysfunction. In clinical practice this can be assessed by skeletal muscle force or local skeletal muscle endurance, which is often even more affected. Roughly 70% of patients referred to an outpatient COPD clinic suffer from skeletal muscle weakness and skeletal muscle force is acutely further reduced during acute exacerbations. In patients with less severe, newly detected Global Initiative for Chronic Obstructive Lung Disease 2, COPD, about 30% of patients may suffer from muscle weakness. In these patients quadriceps force was related to exercise capacity as was shown previously in more severe patients. In milder patients (forced expiratory volume in 1 second >80% of the predicted normal value) muscle weakness was a predictor of physical inactivity levels.[30] Reversal of skeletal muscle dysfunction is an important goal of the exercise training component of a rehabilitation program and hence patients suffering from skeletal muscle weakness are particularly good candidates for exercise training.[31] Improving skeletal muscle strength can be done particularly effectively by including resistance training exercises in the exercise training sessions. When successful muscle force does increase, muscle oxidative capacity is enhanced.

Pharmacologic support with anabolic drugs can be considered in combination with exercise training to increase the effectiveness, but altogether research has focused on the average patient referred for rehabilitation rather than on targeted patient populations (for review, see ref.[32]). One study that did specifically target hypogonadal men and provided them with testosterone supplements in combination with resistance training did show benefits of the pharmacologic intervention to increase muscle strength.[33]

Impaired exercise tolerance and functional exercise capacity are the result of the pulmonary and systemic consequences of COPD. In the context of pulmonary rehabilitation the exercise tolerance is best formally assessed before the program using an incremental exercise test, which will help guide the exercise training program in terms of its intensity, the training modalities, and safety. The functional exercise capacity is best assessed using field tests such as the 6-minute walking test. For this test reference values exist and benchmark improvements for program quality[3] and clinical and statistical importance have been reported. When a patient's exercise tolerance is normal, the indication for exercise training is questionable.

Another important extrapulmonary consequence of COPD is the derangement of the body composition. Both obesity, as a consequence of an inactive lifestyle and poor nutritional hygiene, and cachexia, as observed in other chronic inflammatory disorders are important to pickup and treat in pulmonary rehabilitation programs. Obesity (defined as an increased body mass index greater than 30 kg m^{-2}) will limit the functional abilities of patients with limited ventilatory capacity as it increases the ventilatory needs for exercises against gravity. Cachexia, an involuntary loss of fat free mass, leads inevitably to skeletal muscle weakness. It is a complex problem and its origin is not yet fully understood. Energy imbalance, disuse atrophy, hormonal imbalance, chronic hypoxia, accelerated aging, and systemic inflammation have been discussed as potential factors contributing to cachexia. When present, the treatment of cachexia is an important goal of rehabilitation in patients with COPD and requires individualized interventions by nutritional specialists. To appropriately assess this aspect, body composition should be assessed using Dual-energy X-ray Absorptiometry (DXA)-scan or bio-electrical impedance measures.

Symptoms

The most disabling symptom in COPD is clearly shortness of breath. Patients report dyspnea, particularly during exercise or activity, as a significant burden. Another important symptom is fatigue.[34] Symptoms can be assessed during exercise using Borg symptom scores or during activities of daily living using specific questionnaires.[35] Dyspnea with activity (or exercise) is substantially improved with exercise training. The mechanism through which such large effects are observed is not entirely clear. Certainly there is less required pulmonary ventilation at iso-work and at iso-VO_2, leading to improved (ie, less) dynamic hyperinflation. In addition, the way the dyspnea experience is processed by the patient may improve, due to the repetitive exposure to this threatening stimulus under well-controlled circumstances (ie, in the exercise training setting). Whether genetic factors also play a role is an attractive hypothesis, but this surely requires further study.

Physical Activity

The methodology to assess physical activity was reviewed elsewhere and is beyond the scope of the present review. Several questionnaires have been used, but increasingly activity monitors find their way to the clinical arena and validation studies of several monitors are available.[36] Validation studies, conducted under the umbrella of the PROactive (www.PROactivecopd.com) IMI-JU project, have identified 3 monitors that are valid for use in COPD. In the future it is likely that benchmark values for physical activity will become available for patients with COPD. Patients not meeting current guidelines on physical healthy physical activity (30 minutes of moderate intense exercise on 5 days of the week) can be considered candidates for pulmonary rehabilitation whereby the focus lies on improving the physical activity lifestyle of the patient.

Severe Exacerbations

Patients with COPD who have been hospitalized with an acute exacerbation are particularly good candidates to be enrolled in pulmonary rehabilitation programs. Recent systematic[37] reviews exist on the topic. Patients suffering from exacerbations have lost muscle force, functional exercise tolerance, and health-related quality of life acutely as the result of an exacerbation. Physical activity levels are also dramatically low during the hospital admission and at least up to a month afterward. That observation prompted investigators to look at the effects of muscle activation during the hospitalization phase by means of resistance training or neuromuscular electrical stimulation, which proved to be effective to maintain muscle function during this acute phase. In addition, it is well known that patients who had a hospital admission for COPD are very likely to face new hospital admissions in the year following the previous admission, imposing a high burden on health care cost.

In these frail patients, the rehabilitation program may need significant modification. The emphasis should be on acquiring appropriate self-management skills to prevent subsequent admissions[38] and the exercise training program may need to be adapted to the more severe ventilatory and/or skeletal muscle limitation, using resistance training or interval training at high intensities. A recent meta-analysis of a handful of studies, however, showed that patients who suffered from exacerbations are very good candidates for pulmonary rehabilitation.[39] Clearly these patients may impose a higher burden on the rehabilitation team and recruitment in programs and dropout from the program is a particularly important problem.[40] Although in a recent European audit 42% of eligible patients were reported to have received rehabilitation,[41] a prospective survey in the United Kingdom of close to 500 subsequent admissions found that 31% of eligible patients (63% of the population was found to be eligible) were referred to rehabilitation but only 15% of the eligible patients completed the rehabilitation program.[42] There is clearly margin for improvement by providing more tailored rehabilitation solutions (see **Fig. 1**) to these patients by integrating community- or home-based approaches with appropriate involvement of experts. Future avenues involving tele-health solutions may offer attractive novel ways of interacting across lines of care, to the benefit of these frail patients.

MAINTAINING THE EFFECTS OF PULMONARY REHABILITATION

Our current understanding of the development of systemic consequences of COPD may help to design successful longer-term strategies to maintain the effects of pulmonary rehabilitation. First, all efforts should be made to change the physical activity behavior in patients. Physical inactivity is likely to be the most important modifiable contributor to the development of systemic consequences in COPD. Providing patients direct feedback on their physical activity levels or using structured behavioral interventions may prove to yield results more rapidly. Second, exercise at home should be facilitated and can be done using

feedback on home exercises, or incentives. Such exercises must be individually tailored to achieve effective intensity to provide a continued training stimulus. Ideally the exercises are regularly supervised. In patients with moderate COPD there is no evidence that continued outpatient rehabilitation (once per week) has better outcomes than a well-prescribed home-based training program. Tele-coaching interventions, where a coaching interface is available in the home of the patients, may be a promising future direction. Last, specific attention should go to patients who suffer from exacerbations. Prevention of such events can be done in patients at risk by implementing self-management strategies and the implementation of a case manager.[38] Although it seems intuitively useful, there is currently little evidence for a short "booster" program after a hospital admission to maintain the benefits of rehabilitation. If these repeated programs are preplanned, they seem to contribute little to the overall long-term success of programs.[43]

SUMMARY

Nowadays, pulmonary rehabilitation is an evidence-based intervention for patients with COPD. Programs are individually tailored to the needs of patients in terms of the program structure and its components. According to the definition of pulmonary rehabilitation, the aim of the rehabilitation program is to lead to long-term change in physical activity and self-management behavior. Although the short-term effects of rehabilitation are well known, the long-term effects are not always guaranteed. Further research should focus on the strategies to ensure the long-term benefits for patients with COPD. Further knowledge of the processes underlying an endurable shift in lifestyle, as well as better understanding of the pathophysiologic mechanisms leading to the systemic consequences of COPD and its treatments, may lead to major advances in the future.

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