

Challenges in pulmonary rehabilitation: COVID-19 and beyond

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ABSTRACT

Pulmonary rehabilitation is a comprehensive multidisciplinary intervention requiring a team involving an expert chest physician, an exercise training specialist, a nutritional expert, a psychologist, a social worker, and an occupational therapist, who together aim at improving respiratory functional capacity in patients with chronic obstructive pulmonary disease (COPD). We aimed at evaluating the effectiveness of pulmonary rehabilitation in a large number of trials, systematic reviews, and meta-analyses in pre-COVID-19 conditions, and the impact of pulmonary rehabilitation during the COVID-19 pandemic was estimated based on results of abundant available studies. As many as 34 studies were selected to assess the global results of pulmonary rehabilitation in COPD patients before the pandemic, and 40 studies were selected from the literature concerning pulmonary rehabilitation during the COVID-19 pandemic. A large number of systematic reviews and meta-analyses reported on the efficacy of rehabilitation in COPD patients, based on the improvement in inspiratory muscle strength, exercise capacity, dyspnea, and quality of life. The response to rehabilitation in patients with COVID-19 is also satisfactory. The effectiveness of pulmonary rehabilitation in COPD patients shows an evolving need for health care professionals to design an individually tailored pulmonary rehabilitation program for patients with COVID-19 to alleviate the chronic symptoms and reduce complications.

Introduction With its estimated worldwide prevalence of 10%, the mortality rate of 3.2 million deaths in 2017, and the expected toll of 4.4 million fatalities annually by 2240, chronic obstructive pulmonary disease (COPD) is a critically important condition.^{1,2} For a long time, pharmacological therapy of COPD has been based on inhaled or systemic corticosteroids, anticholinergics, β -agonists, methylxanthines, and combinations of 2 or more drugs used when symptom control was insufficient.³ The drug choice depended on the severity of symptoms, frequency of exacerbations, and respiratory functional measurements. In severe diseases causing loss in respiratory function, decrease in the quality of life, and psychological impairments, nonpharmacological treatments, including long-term oxygen therapy, surgery, noninvasive positive pressure ventilation, caring nutrition, and pulmonary rehabilitation are used.⁴ The notion of pulmonary rehabilitation

was derived from both long-standing and modern concepts, and particularly from pivotal importance of exercise training raised in the mid-1990s.⁵ Nowadays, pulmonary rehabilitation is generally defined as a comprehensive multidisciplinary intervention that requires a team involving an expert chest physician, an exercise training specialist, a nutritional expert, a psychologist, a social worker, and an occupational therapist.⁶

The achievements of pulmonary rehabilitation

The most reliable demonstration of the medical treatment efficacy is presented in systematic reviews and meta-analyses. Numerous analyses are available for pulmonary rehabilitation of patients with COPD. Limiting the examination of positive outcomes to an example, Beaumont et al⁷ included in their systematic review and meta-analysis of 43 studies, providing evidence that using threshold devices improves inspiratory

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muscle strength, exercise capacity, dyspnea, and the quality of life.⁷ A meta-analysis using a Cochrane Collaboration tool to assess the risk of bias for each included study found that breathing exercises had a significant effect on inspiratory muscle strength but not on the quality of life.⁸ Conversely, another meta-analysis of a large number of studies has found that rehabilitation may be beneficial in improving the quality of life of COPD patients.⁹ A further Cochrane meta-analysis by Lacasse et al,¹⁰ including 23 randomized controlled trials, found that rehabilitation reduces dyspnea and fatigue, and improves emotional functions and patients' feeling of control over their disease. These improvements were moderate to large but nonetheless clinically meaningful. The authors concluded that rehabilitation is an important component of COPD management.¹⁰ In a Cochrane meta-analysis¹¹ addressing an assorted range of interventions, mainly from single center studies, improvements in physical activity were not steadily demonstrated for any particular intervention, resulting in limited evidence of betterment following exercise training, physical activity counselling, and drug treatment, and not providing clear guidance on optimal timing, components, duration, and models for interventions in patients with COPD. Systematic reviews and meta-analyses were also performed to evaluate particular treatments. Zang et al¹² recently assessed both efficacy and safety of early (<3 days since hospital discharge) pulmonary rehabilitation in 829 patients hospitalized for acute COPD exacerbation. Significant improvement was found in the 6-minute walk distance, and in the subgroup analysis, the exercise-training group showed a marked improvement, with only 1 serious adverse event. The authors concluded that even though 3 days of hospitalization may increase exercise capacity and improve the quality of life, further investigation is still needed. In the same year, a protocol for systematic review and meta-analysis¹³ compared the efficacy of pulmonary rehabilitation in home-based unsupervised patients vs outpatient rehabilitation programs for COPD patients. The authors hypothesized that the 2 methods are likely to provide similar therapeutic benefits, but this outcome also needs to be confirmed. A further topic of Cochrane analysis was rehabilitation after COPD exacerbation. The results from 9 small studies of moderate quality suggested that pulmonary rehabilitation is effective and safe in reducing hospital admissions and mortality and improving the quality of life in COPD patients recently suffering from an exacerbation.¹⁴

In recent years, development of personalized medicine paved the way for modern tools that enable diagnosis, stratification, and treatment of COPD patients according to pathobiological mechanisms. Wouters et al¹⁵ summarized current developments in personalized medicine in COPD aimed at classifying its complexity through comprehensive, individualized interventions, such as

specific treatable traits classified as endotypes.¹⁵ Barbosa et al¹⁶ recently analyzed 10 randomized studies including 9350 participants undergoing community-based pulmonary rehabilitation. The results tended to be better for health-related quality of life and symptoms than for control interventions, but they were inconsistent in outcomes, resulting in a very low certainty of evidence, which warrants further studies.

Adherence and compliance to pulmonary rehabilitation

Insufficient adherence of patients to medical therapies is a widespread problem that limits the effectiveness of any intervention.^{17,18} Pierobon et al¹⁹ studied a COPD population in a rehabilitative setting and used the Mini Mental State Examination and the Montreal Cognitive Assessment to investigate the level of anxiety, depressive symptoms, and mild cognitive impairment, in combination with self-reported pharmacological and nonpharmacological adherence. The authors suggested that the prevalence of neuropsychological impairments in COPD patients should require regular use of screening tools for evaluating mood and cognitive function, detecting psychosocial comorbidities, and personalizing the rehabilitative programs. Sørensen et al²⁰ assessed the adherence at an individual level by making before-and-after comparisons between 2 groups. The patients were randomly assigned to either a group that self-reported their perceived exertion breathing and received automatic Internet-based feedback concerning their next threshold loadings, or a group that performed inspiratory muscle training with 30% maximal inspiratory pressure and received no feedback. The results showed greater adherence in patients who self-reported their perceived breathing exertion and received automatic Internet-based feedback than in those who self-reported their training sessions without any feedback. A study²¹ of 518 patients undergoing pulmonary prerehabilitation found that patients with moderate to very severe COPD who had acute COPD exacerbation were largely affected by dropout, while patients with mild to moderate exacerbations were not affected by dropout from pulmonary rehabilitation. The authors remarked that exacerbation should not lead to discontinuation of pulmonary rehabilitation, since the response is in general not affected. Despite the mentioned studies, there are still no specific strategies to identify the risk of nonadherence in individual patients.

Impact of the COVID-19 pandemic on pulmonary rehabilitation

The pandemic caused by SARS-CoV-2, a causative agent of respiratory disease COVID-19, began in 2019 in the city of Wuhan, China, and spread worldwide.²² To date, more than 280 articles have been published on the COVID-19 pandemic. Our interest was limited to studies in COPD patients treated with pulmonary rehabilitation who were affected by COVID-19. It was soon apparent that the COVID-19 pandemic was

associated with a 5 times higher risk of a more severe viral infection course in patients with COPD,²³ and that COVID-19 commonly disturbed performance of public health systems.²⁴ The initial systemic clinical signs of COVID-19 include fatigue, fever, myalgia, and arthralgia,²⁴ while lung inflammation may present with variable symptoms, such as mild to moderate cough, breathlessness and sputum production, but also with hemoptysis and acute respiratory distress syndrome.²⁵ The disease severity and mortality rates were found to be high in COPD patients.²⁶

The first studies aimed at adapting rehabilitation methods in patients undergoing respiratory rehabilitation were conducted in 2020. Zha et al²⁷ found that rehabilitation via specifically modified exercise designed for rehabilitation of COVID-19 patients at home improved remission rate in respiratory symptoms.²⁷ Polastri et al²⁸ suggested that a rehabilitation program for post-COVID-19 patients should mirror the algorithm of pulmonary rehabilitation for patients with chronic respiratory disease as an evidence-based, widely accepted and available option. Houchen-Wolloff et al²⁹ stated that the long-term impact of the COVID-19 pandemic in patients with chronic respiratory disease is undefined but could be significant, suggesting that it is possible to carefully prescribe exercises for a longer time to these patients. Most of the studies have been performed in 2022. We have focused our attention on the articles that evaluated different model approaches to rehabilitation, and avoided examining papers that dealt with the same aspects. In a prospective observational cohort study, Gloeckl et al³⁰ found that pulmonary rehabilitation was feasible, safe, and effective in patients with COVID-19 regardless of the disease severity. Since most COVID-19 patients are elderly and suffer from comorbidities, they are often advised to stay at home. Tsutsui et al³¹ highlighted the importance of telerehabilitation of post-COVID-19 patients with COPD and discussed different strategies for its clinical implementation. Chen et al³² performed a systematic review and meta-analysis of the effect of pulmonary rehabilitation after COVID-19, and observed that the rehabilitation could improve exercise capacity measured by 6-minute walk test in patients with mild to moderate lung impairment after COVID-19. The authors recommended careful interpretation of the rehabilitation effects on lung function, dyspnea, and quality of life due to conflicting data reported in other studies. Zampogna et al³³ studied 140 patients after rehabilitation, who showed improvements in short physical performance battery, as demonstrated by a significant percentage ($P < 0.05$) of patients who progressed from inability to stand to rise from a chair and walk. The authors suggested that this finding may be useful in guiding clinicians in their care of patients surviving COVID-19. Gore et al³⁴ highlighted that the abundant evidence of multisystem involvement in

post-COVID-19 condition requires integrated delivery models addressing the health care needs of the patient. This is in agreement with World Health Organization recommendations that emphasized critical gaps in providing adequate level of integrative care required to address the multisystem needs of this population in current health care delivery models.³⁴

Tarigan et al³⁵ addressed the effectiveness of upper limb exercises and breathing exercises in stable COPD patients during the COVID-19 pandemic. After 4 weeks, they found a significant improvement in muscle mass, lung function capacity, severity of symptoms, exertion scale, and quality of life in the patients who adhered to home training with 2 sessions per week.

Williamson et al³⁶ evaluated the ability of virtual pulmonary rehabilitation by subjective telephone assessments including a lung information needs questionnaire, a COPD assessment tool, a chronic respiratory questionnaire, and a subjective medical assessment. The authors felt that although virtual rehabilitation would not replace the commonly used methods, it would be useful in patients who are confident with technology. Barradell et al³⁷ compared medical center- and home-based programs to explore the decision-making needs of patients with COPD in whom pulmonary rehabilitation is considered, highlighting that unsatisfactory knowledge of the programs would limit their perceived practicability and acceptability. Specific conditions in some countries have made respiratory rehabilitation in patients with COVID-19 more difficult. For example, in India difficulties in reaching the recommended duration of the rehabilitation result in problems and disabilities associated with prolonged intensive care unit stay, as well as consequences of severe respiratory illness.³⁸ The authors of this review focused on the indispensable role of early and interdisciplinary rehabilitation to restore functioning and to improve the quality of life in COVID-19 survivors. They outlined how to expand rehabilitation services in a resource-limited country, such as India, and listed existing limitations that prevent uniform implementation of the rehabilitation services in India.³⁸ In New Zealand, known for its huge distances between different parts of the country, Candy et al³⁹ performed a cross-sectional observational study based on 2 sequential online surveys before and after COVID-19 lockdowns. They showed that pulmonary rehabilitation programs that followed best practice guidelines were homogenous in content and structure, but that COVID-19 restrictions highlighted the need for various options of the service delivery. The authors suggested that the services developed in the future should focus on providing a range of options increasing the access to rehabilitation, tailoring the therapy to meet individual needs, and improving the intervention to optimize participation.³⁹ Apart from COVID-19, there are other numerous pandemics, both new, such as

monkeypox, and already known, such as avian influenza, Ebola, or SARS mutations, making the future of pulmonary rehabilitation very challenging and requiring maximum effort.⁴⁰

Conclusions Pulmonary rehabilitation has been progressively recognized as an effective and well-tolerated treatment of COPD patients. Its components, to be used as per characteristics of individual patients, consist of the oxygen titration therapy at rest, during exercise, and during sleep, clearance of the proximal and distal airways, exercise reconditioning, adaptation and weaning from noninvasive and invasive mechanical ventilation, monitoring and treatment of sleep disorders, nursing and weaning of the tracheostomy tube, education on the correct management of aids, and correct intake of inhalation and aerosol therapy. COVID-19, after an acute phase of the disease, is associated with prolonged persistence of disabling symptoms affecting musculoskeletal and respiratory systems, which, when long-lasting, greatly reduce the chances of rapid functional recovery. An appropriate rehabilitation program, both physical and psychological, aimed at progressively re-educating patients to resume their usual lifestyle, is often followed by functional recovery that allows the patients to return to a state close to normal, or in some cases to regain complete functionality.

ARTICLE INFORMATION

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