Evidence-Based Outcomes from Pulmonary Rehabilitation in the Chronic Obstructive Pulmonary Disease Patient

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KEYWORDS

• Chronic obstructive pulmonary disease • Pulmonary rehabilitation • Quality of life
• Self-management • Quality of evidence

KEY POINTS

- Pulmonary rehabilitation consists of exercise, education, and support in self-management behaviors.
- The quality of evidence is high for patient-centered outcomes such as health-related quality of life and exercise capacity in stable patients.
- Pulmonary rehabilitation after an exacerbation has strong effects, and the evidence for most outcomes at this time demonstrates moderate to high quality of evidence.

INTRODUCTION

Pulmonary rehabilitation consists of exercise, education, and support in self-management behaviors. Those completing pulmonary rehabilitation have shown measureable improvement in quality of life, symptoms, exercise performance, depression and anxiety, and health care utilization. Although it is obvious why an exercise program would improve the individual's exercise capacity, the reasons why improvement occurs in other outcome areas are not as clear.[1] The purpose of this article however, is not to provide details on the reasons for these improvements, but to describe the strength of the evidence demonstrating these changes in outcomes.

Historically, attempts were made to link rehabilitation outcomes with improvements in lung function, a common goal in many trials, in particular pharmaceutical trials. However, lung function has only occasionally been found to improve following pulmonary rehabilitation, suggesting that other changes resulting from pulmonary rehabilitation may underlie these beneficial effects. Any improvements in lung function, such as prolonged time to hyperinflation with exercise, is likely due to multiple factors, including physical deconditioning and reduction in anxiety related to dyspnea. However, given the body of evidence, one is able to make some conclusions about changes in outcomes based on the quality of evidence currently available.

Outcomes that will be the focus of this article include quality of life, symptoms, exercise capacity, hospitalizations, exacerbations, and mortality. Quality-of-life outcomes that have been consistently shown to improve have usually been measured with 2 common chronic obstructive pulmonary disease (COPD) instruments, the Chronic

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Clin Chest Med 35 (2014) 295–301
http://dx.doi.org/10.1016/j.ccm.2014.02.001

Respiratory Disease Questionnaire (CRQ)[2] and the Saint George's Respiratory Questionnaire (SGRQ).[3] Several symptoms have also been shown to improve with rehabilitation, with dyspnea, fatigue, depression, and anxiety being the most common and relevant to patients, and therefore most frequently measured and reported. Dyspnea and fatigue were among the earliest symptoms measured as outcomes in the rehabilitation setting, having been demonstrated to improve using the dyspnea and fatigue subscales on the CRQ. Symptoms relating to mood have also been responsive to rehabilitation, as measured by depression and anxiety scales such as the Hospital Anxiety and Depression Score (HADS),[4] the Center for Epidemiological Studies Depressions Scale (CES-D),[5] and the Revised Symptom Checklist (SCL-90-R).[6] Improvements in exercise capacity have been measured with field tests (the 6-minute walk distance [6MWD][7] and shuttle walk test [SWT])[8] or tests of maximal exercise capacity by either treadmill or bicycle. The latter tests of exercise capacity can determine peak exercise capacity or endurance exercise capacity. Although there are other measures that have been used to evaluate quality of life and symptoms, those noted were most frequently used in meta-analysis.[9] In the last decade, the capacity to expand areas of study has occurred, and more programs are delving into assessing other outcomes of rehabilitation. Consequently, outcome researchers now also assess the effects of pulmonary rehabilitation on exacerbations,[10] hospital utilization, and mortality.

The aim of this article is to systematically appraise the quality of evidence reported for important outcomes in pulmonary rehabilitation using the approach of the Grading of Recommendations Assessment, Development and Evaluation (GRADE) Working Group. This appraisal was carried out by identifying Cochrane systematic reviews and systematic reviews that have been subsequently reported since the last Cochrane report. The focus of this appraisal was to determine the effectiveness of pulmonary rehabilitation programs versus control therapy (usually otherwise standard care) in COPD patients. This analysis did not evaluate other aspects of the pulmonary rehabilitation intervention, such as which programs provided the most benefit (eg, inpatient vs outpatient) or how long the programs should be held (program duration).

METHODS

The approach of the GRADE Working Group[11,12] is one of several approaches to evaluate the quality of evidence in a systematic way. This approach has been adopted by over 70 organizations, including the World Health Organization (WHO), the Cochrane Collaboration, the National Institute of Health and Clinical Excellence in the UK (NICE), the American College of Physicians, and UpToDate. In brief, the GRADE approach evaluates the confidence in the estimates of effects for each outcome of interest as a function of the quality of the evidence. The result is the GRADE rating from high to low that can be used to gauge how well the estimates can be trusted. A rating of high means one can be confident that: (1) the true effect (eg, odds ratio for hospitalization in treated vs untreated patients or the difference in quality of life between treatment groups) lies close to the estimates from the available evidence, and (2) that additional evidence is unlikely to change the estimate. Very low means one should have very little confidence in the effect estimate and that the true effect estimate is likely to be substantially different when more data become available. Rating of the confidence in the effect estimates (if based on randomized trials) begins at the highest level and is rated down (if there are reasons to lose confidence in the effect estimates). For example, if there are serious concerns regarding risk of bias[13] (eg, failure to conceal random allocation or blind participants to the study intervention), then the quality of evidence is rated down from high to moderate. Other criteria that may lead to a downrating are inconsistency[14] of effect estimates across studies and indirectness[15] in cases where surrogate outcomes (such as inflammatory biomarkers) are used instead of patient-important outcomes (such as exacerbations). Another example is if patients are recruited from an intensive care setting, there is a good chance that the estimates of effect are unlikely to apply to a broader COPD population. Also, imprecision[16] (a wide confidence interval) may lead to down rating in that it makes decision making challenging. Other biases that may lead to a downgrading are publication bias[17] or outcome reporting bias, if, for example, only positive results were presented when clearly there must have been negative findings.

RESULTS

Health-Related Quality of Life

Health-related quality of life as measured by the SGRQ and the CRQ in stable COPD patients following pulmonary rehabilitation is shown in **Tables 1** and **2**. These tables identify

- The subscales and total scores
- The minimal important difference (MID) (defined as "the smallest difference in score in the