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# Effectiveness of Pulmonary Rehabilitation in reducing mortality after acute exacerbation of chronic obstructive pulmonary disease; systematic review

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## ABSTRACT

**Background:** According to clinical guidelines, patients with COPD can benefit from pulmonary rehabilitation. Our study aim was to assess the effects of an early pulmonary rehabilitation program, initiated within 4 weeks of hospitalization for COPD acute exacerbation, vs standard therapy. **Method:** PRISMA criteria were followed in the conduct of this systematic review study. Research that compared the advantages of early PR initiated during admission or following hospital release with no early PR or standard care for patients newly admitted or previously admitted to the hospital with a COPD exacerbation were included. We performed a thorough literature search using the databases Medline, Embase, CINAHL, AND Cochrane Library, looking for publications published in the English language between January 2011 and May 2024. **Result:** It was determined that six primary RCTs qualified for this review. These studies included 394 people who had recently had COPD exacerbation. The outpatient treatment was initiated one to four weeks after the inpatient exacerbation therapy in four trials. Patients began PR as either inpatients or outpatients in one research, and they all continued as outpatients. In every study, PR encompassed managing everyday living, supervised exercise training and instruction, nutritional support, and quitting smoking. **Conclusion:** Supervised early PR is one effective way to reduce mortality following a hospital stay for COPD acute exacerbation.

**Keywords:** Pulmonary rehabilitation, chronic obstructive pulmonary disease, mortality, hospital stay

## 1. INTRODUCTION

Clinical guidelines promote pulmonary rehabilitation (PR) as an effective strategy for individuals with chronic obstructive pulmonary disease (COPD) (Celli et al., 2004; Nici et al., 2006). Meta-analyses have provided clear proof that, when compared to conventional care without rehabilitation, pulmonary rehabilitation improves exercise capacity, symptoms, and quality of life (QOL) (Lacasse et al., 2006). Moreover, a growing number of head-to-head trials are influencing clinical practice in terms of developing practical and successful physical exercise regimens for COPD patients (Beauchamp et al., 2010; Puhan et al., 2005).

Globally, individuals with COPD are referred for PR at different times: either just after an exacerbation, which is known as early referral, or later, when the patient is stable (Nici et al., 2006). According to recent data, initiating PR right away following COPD acute exacerbation may be equally, if not more, beneficial (Osthoﬀ and Leuppi, 2010). Nine randomized trials comparing standard care and rehabilitation during a COPD exacerbation were found in a recently updated Cochrane review. While the effects on exercise appeared to be greater, the meta-analyses of trials comparing rehabilitation and standard care in stable patients revealed similar effects of PR after exacerbations on QOL.

More signiﬁcantly, PR following an exacerbation was associated with a higher reduction in the risk of readmission and mortality when compared to standard care, according to meta-analyses for exacerbations and mortality (Puhan et al., 2016). The use of a window of opportunity to send COPD patients for rehabilitation while they are open to change their health behavior may be one reason for the impact of such early rehabilitation. Furthermore, individuals who are having exacerbations frequently have several modiﬁable risk factors for subsequent exacerbations and premature death that can be successfully addressed by PR (Garcia et al., 2000; Puhan et al., 2009).

However, as patients who have just experienced an exacerbation are more likely to experience another one than those who are in a stable state, it might also be simpler to identify the impact of PR on hospital admissions and deaths. One of the possible disadvantages of early PR is the possibility of subsequent exacerbations that could disrupt the treatment plan. Our goal was to compare standard therapy with a early PR program that was started within 4 weeks for patients who were hospitalized for COPD acute exacerbation. Mortality at the conclusion of PR and at the longest follow-up period was our main goal.

## 2. METHOD

This systematic review study was conducted according to PRISMA guidelines. Studies that contrasted the benefits of early PR started at the time of admission or after hospital discharge with no early PR or standard treatment for patients admitted or previously admitted to the hospital with a COPD exacerbation were deemed acceptable. The PR was primarily defined by supervised Exercise training (ET), but it may also include nutrition counseling, management of daily living tasks, education, and physio-social support. If rehabilitation continued after discharge or if a thorough PR could be demonstrated, studies offering inpatient PR with ET were included. Research that were not randomized were disqualified.

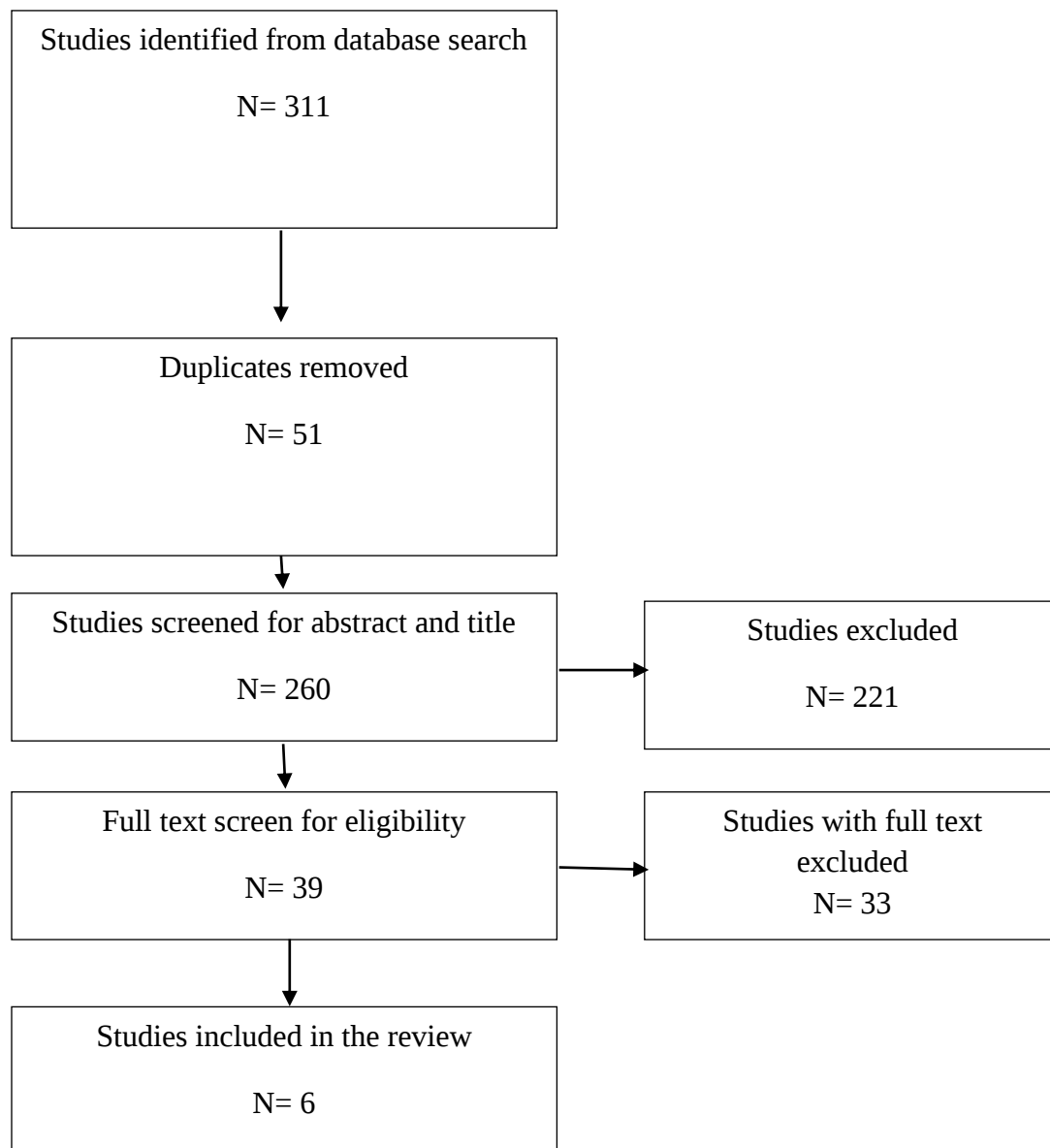
Our main goal was mortality; secondary goals were length of stay, number of readmissions due to COPD, walking tests, Qol, daily living activities, and dropout rates. Using the databases Medline, Embase, CINAHL, AND Cochrane Library, we conducted a comprehensive literature search, for articles published in English language in the period from January 2011 and May 2024. Two separate authors assessed the articles found in the first database search, and disagreements were settled by consensus. Based on the predetermined criteria, two authors independently assessed the entire text of all suitable articles found in the second search and determined which research to include or omit. Our initial search included 311 articles, following screening of abstract and title and duplication removal 39 remained which were assessed in full text and 6 articles were included in the review.

## 3. RESULT

Six primary RCTs were found to be eligible for this review (Figure 1). A total of 394 individuals who had just experienced a COPD exacerbation were included in these studies (Table 1). In four trials, the outpatient program was started one to four weeks following the inpatient exacerbation therapy. In one study, patients started PR as either inpatients or outpatients and all continued as outpatients. PR included managing activities of dietary support, daily living, supervised exercise training and instruction and smoking cessation, in all

of the studies. The PR programs varied in duration, incorporating 30-minute to 90-minute exercises and training intervals of two to seven days per week.

In four of the trials that were included, the participants followed a comprehensive PR program. The PR extensiveness was judged to be undescribed or very modestly comprehensive in the final two studies. The control group was given standard care, which included the best possible medical attention. All of the examined studies did not report any variations in the patients' baseline characteristics across groups. According to Revitt et al., (2018) study the PR group demonstrated more risk of readmissions at 12month when compared to conventional care group. In Daabis et al., (2017) study, both training modalities resulted in significant improvements in the degree of dyspnea, the QOL and the functional exercise (Table 2).



**Figure 1** PRISMA consort chart of studies selection

**Table 1** Characteristics of the included studies

| Citation            | Study duration and setting                        | Intervention                                                                                                                                                                                  | Participants                                       | Standard care                                                                                                          | Intervention after discharge                                                                                                       | Outcome                                 |
|---------------------|---------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------|------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------|
| Daabis et al., 2017 | Duration: 8 weeks<br>Setting: outpatient          | ET, patient education on disease self-management, nutrition, and lifestyle issues, and patient assessment comprised PR. Walking for 30 minutes followed an exercise regimen consisting of ET. | 30 admitted patients with acute exacerbation COPD  | Medical treatment                                                                                                      | Outpatient PR                                                                                                                      | Walking distance and QoL                |
| Deepak et al., 2014 | Duration: 12 weeks<br>Setting: outpatient         | PR included education, training, diet, psycho-social rehabilitation, patient assessment, and exercise testing,                                                                                | 60 admitted patients with COPD acute exacerbation  | Conventional treatment without PR                                                                                      | Outpatient PR                                                                                                                      | Walking distance and QoL                |
| Ko et al., 2017     | Duration: 8 weeks<br>Setting: outpatient          | PR included instruction and a personalized physical training regimen to be completed at home or over a brief period of time as an outpatient.                                                 | 180 admitted patients with COPD acute exacerbation | Medical treatment                                                                                                      | Supervised exercise training 3/week, if declining they are offered instructions for self-training, education, and telephone calls. | Hospital stay duration and walking test |
| Revitt et al., 2018 | Duration: 6 weeks<br>Setting: inpatient           | Early PR after four weeks of release. PR included personalized resistance and aerobic training along with instruction on energy saving and chest clearing.                                    | 28 admitted patients with COPD acute exacerbation  | Late PR initiated 7 weeks after discharge including exercise and education.                                            | Hospital-based PR                                                                                                                  | Dropout                                 |
| Puhan et al., 2012  | Duration: 12 weeks<br>Setting: out- and inpatient | Exercise training included calisthenics, strength, and endurance training in addition to instruction throughout the early inpatient period, which ended two weeks following the exacerbation. | 36 admitted patients with COPD acute exacerbation  | Late PR starting 6 mo. after exacerbation, exercise training included endurance, strength and calisthenics training in | Outpatient PR, exercise training included endurance, strength and calisthenics training in addition with education.                | Dropout and mortality                   |

|                 |                                          |                                                                                                                                                                                                                                                 |                                                   |                                                                                                            |                                          |                                          |
|-----------------|------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------|------------------------------------------------------------------------------------------------------------|------------------------------------------|------------------------------------------|
|                 |                                          |                                                                                                                                                                                                                                                 |                                                   | addition with education                                                                                    |                                          |                                          |
| Ko et al., 2011 | Duration: 8 weeks<br>Setting: outpatient | PR included arm cycling, treadmill use, arm and leg strength training, and instruction on how to complete at least 20 minutes of at-home workouts per day. instruction on healthy breathing methods and coping strategies for day-to-day tasks. | 60 admitted patients with COPD acute exacerbation | Usual care with instructions to perform regular exercise at home (walking and muscle stretching exercise). | Supervised outpatient exercise training. | Mortality, Qol, dropout and walking test |

**Table 2** Main findings of the included studies

| Citation            | Main findings                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | Conclusion                                                                                                                                                                                                                                                                                 |
|---------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Daabis et al., 2017 | Significant gains were made in the functional exercise, QOL, and dyspnea severity using both training modalities. Additional gains in peripheral muscular strength were linked to the PR without requiring longer training sessions.                                                                                                                                                                                                                                                                                 | PR is a useful technique for managing COPD patients' exacerbations. Significant improvements are seen in QOL, functional exercise capacity, and dyspnea. Strength training adds benefits to an ET program in terms of muscle force, but not in terms of total exercise capacity or health. |
| Deepak et al., 2014 | It was discovered that the two groups' baseline attributes were comparable. When comparing the PR group to the conventional management group, there was a statistically significant increase in the six-minute walk distance and a significant decrease in the overall Scale and St. George's Respiratory Questionnaire (SGRQ) score.                                                                                                                                                                                | Patients with COPD acute exacerbation benefit greatly from early PR in terms of their activity ability and Qol.                                                                                                                                                                            |
| Ko et al., 2017     | After a year, the PR group's adjusted relative risk of readmission was 0.668, lower than that of the traditional management group. Compared to the standard management group, the PR experienced a shorter length of stay (LOS), and higher improvement in the SGRQ score, at 12 months.                                                                                                                                                                                                                             | A thorough COPD program can improve patients' Qol and decrease hospital readmissions for COPD and LOS while also easing symptoms.                                                                                                                                                          |
| Revitt et al., 2018 | At twelve months, the PR and conventional care groups showed a 53.3% and 43.3% probability of readmissions, respectively. For both groups, the incidence of COPD acute exacerbation and ER visits were comparable. In the RP group, the SGRQ total score was lower. At various time points, there were no statistically significant differences between the RP and conventional management groups in the FEV (1) % predicted, dyspnea score, 6-minute walk test, or maximal oxygen consumption during exercise test. | After an COPD acute exacerbation, an early rehabilitation program improved Qol for six months, but after one year, it had little effect on health-care utilization.                                                                                                                        |
| Puhan et al., 2012  | The mean number of exacerbations that required systemic corticosteroids or antibiotics was less in individuals with early rehabilitation versus late rehabilitation. Patients with delayed                                                                                                                                                                                                                                                                                                                           | There were no changes between the early and late PR that were statistically significant. Rehabilitating patients as soon                                                                                                                                                                   |

|                 |                                                                                                                                                                                                                               |                                                                                                                                                                          |
|-----------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                 | rehabilitation had higher episodes of dyspnea during the course of the 18-month period, but neither these variations nor any other variation in QOL dimensions attained statistical significance.                             | as possible after an exacerbation may result in a quicker return to a stable state than waiting until later.                                                             |
| Ko et al., 2011 | Both walking tests showed statistically significant gains for early PR, and there was no evidence of a spontaneous recovery. However, because of the small sample size in delayed PR, it was challenging to make conclusions. | Strong evidence exists to support the advantages of early PR. However, early PR has a low referral rate, and only a small percentage of patients are benefiting from it. |

4. DISCUSSION

When compared to standard therapy, we discovered that supervised early PR decreased the probability of death in individuals with COPD exacerbations. Because of methodological problems in the included studies and the relatively small number of participants, this finding was based on moderate quality evidence. Although systematic reviews have previously revealed similar conclusions, the results of a recent RCT by Greening et al., (2014) questioned the favorable effects by reporting a greater mortality in the early PR group (Puhan et al., 2011). The authors of Puhan et al., (2011) study included patients who had exacerbations of COPD at the time of admission and gave the intervention group instructions to increase their physical activity levels over the course of the following three months, with the help of technological gadgets.

The findings of this review deviate from those of a prior review conducted by Puhan et al., (2016), which found no statistically significant impact of early PR on mortality. Despite the severity of the underlying pulmonary condition, Daabis et al., (2017) observed that the combination of aerobic and strength training was safe and well tolerated, and it was linked to incremental peripheral muscle strength improvements without lengthening the training sessions. Daabis et al., (2017) did not discover a statistically significant gain in muscular strength in the ET group, in contrast to earlier research Bernard et al., (1999), Ortega et al., (2002) that demonstrated enhanced peripheral muscle strength in COPD patients with endurance training alone.

Comparing the effects of strength training alone or in combination with endurance training to isolated endurance training in patients with COPD, other studies Dourado et al., (2009), Mador et al., (2004) found no change in peripheral muscle strength following endurance training alone, which is similar to the findings of (Daabis et al., 2017). These disparities in training techniques and intensity may be the cause of these discrepancies. According to Puhan et al., (2012), there is no correlation between the exacerbation rates of patients with severe COPD and the time of pulmonary rehabilitation.

Nonetheless, over the course of the 18-month follow-up, patients who underwent early rehabilitation continuously benefited more in terms of their symptoms and QOL, even though the differences with patients who underwent late rehabilitation did not achieve statistical significance. According to a study by Ko et al., (2017) patients who had just been admitted to the hospital could experience shorter hospital stays and a lower likelihood of readmissions when they followed up with a thorough, personalized care plan as opposed to receiving standard treatment. In addition, both the individuals' overall SGRQ score and their Qol increased at 12 months. At the longest follow-up, supervised early PR considerably reduced the incidence of hospital readmissions attributable to COPD.

Furthermore, there was a decrease in the duration of hospital stays. According to earlier research by Puhan et al., (2016), PR dramatically decreased the mean annual number of hospital admissions per participant from 1.6 to 0.9 in the year that followed an acute exacerbation hospital hospitalization. There are several theories as to why PR has such a strong impact on hospital readmission. The primary cause is most likely the substantial decrease in activity level that occurs after being admitted to the hospital due to an COPD acute exacerbation (Pitta et al., 2006).

5. CONCLUSION

One successful strategy for lowering mortality after a hospital stay for a severe COPD exacerbation is supervised early PR. Our study demonstrates that supervised physical rehabilitation during an COPD acute exacerbation improves walking distance, Qol, and prognosis more than standard care. We draw the conclusion that supervised early PR leads to significant and clinically meaningful

increases in QoL and walking distance while lowering the risk of death, COPD-related hospital readmissions, and the number of hospital days based on evidence of moderate to low quality.

#### Ethical approval

Not applicable.

#### Informed consent

Not applicable.

#### Funding

This study has not received any external funding.

#### Conflict of interest

The authors declare that there is no conflict of interests.

#### Data and materials availability

All data sets collected during this study are available upon reasonable request from the corresponding author.

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