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Early Pulmonary Rehabilitation in Acute Exacerbation of Chronic Obstructive Pulmonary Disease: A Meta-Analysis of Randomized Controlled Trials

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ABSTRACT

Pulmonary rehabilitation (PR) is an essential method for Acute exacerbation in chronic obstructive pulmonary disease (AECOPD) recovery. We perform a meta-analysis to compare early PR with usual care. A literature search was performed through these databases: PubMed, MEDLINE database, Google Scholar, Cochrane, Embase from inception to July 2021. Eligible trials were clinical randomized controlled trials comparing the effects of early PR and usual care in AECOPD patients. The primary endpoint of this meta-analysis was FEV1% predicted, 6-min walk test (6MWD), modified Medical Research Council (mMRC) and George Respiratory Questionnaire-total (SGRQ-total). The secondary outcomes were borg dyspnea score, short-form 36 health survey questionnaire physical (SF-36 physical) and SF-36 mental. We included 13 RCTs with a total of 866 patients. There were no significant effects of the PR group on measures of FEV1% predicted (MD = 0.50, 95%CI −1.43 to 2.44, $Z=0.51$, $p=0.61$), borg dyspnea score (MD = −0.88, 95%CI −1.89 to 0.13, $Z=1.71$, $p=0.09$) and SF-36 mental (MD = 4.34, 95%CI −1.64 to 10.32, $Z=1.42$, $p=0.16$) compared with usual care. PR group achieved better 6MWD (MD = 97.58, 95%CI 17.21 to 177.96, $Z=2.38$, $p=0.02$), mMRC (MD = −0.36, 95%CI −0.52 to −0.21, $Z=4.56$, $p < 0.00001$), SGRQ-total (MD= −9.67, 95%CI −16.23 to −3.11, $Z=2.89$, $p=0.004$) and SF-36 physical (MD = 4.98, 95%CI 0.60 to 9.35, $Z=2.23$, $p=0.03$) compared with usual care group. Early PR in AECOPD patients would lead to better 6MWD, mMRC, SGRQ-total and SF-36 physical. But there were no significant effects of the PR group on measures of FEV1% predicted, borg dyspnea score and SF-36 mental.

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KEYWORDS
Pulmonary rehabilitation; acute exacerbation; chronic obstructive pulmonary disease; early rehabilitation

Introduction

For the high rates of smoking and air pollution worldwide, Chronic obstructive pulmonary disease (COPD) is still a challenge for clinicians today [1]. COPD patients sometimes experience an acute worsening of symptoms like sputum color changes or an increase in dyspnea and leading to a change in medication. This event is defined as an Acute exacerbation in chronic obstructive pulmonary disease (AECOPD) [2]. AECOPD is the most common result in hospital admission and higher mortality [3]. Hospitalization is accompanied by a rapid decline in lung function and other adverse outcomes like endotracheal intubation [4]. AECOPD is associated with a delay in the recovery of lung function. There is a risk of another exacerbation during this period [5]. Repeated acute exacerbation will cause low exercise capacity, which is related to a high risk of mortality [6].

Pulmonary rehabilitation (PR) because of its beneficial effects on maximal exercise capacity and health-related quality of life has been suggested in AECOPD [7]. Exercise training is an essential part of PR in COPD patients [8]. A meta-analysis demonstrates the effectiveness of an early supervised PR following AECOPD can reduce mortality, the number of readmissions, and the number of days in hospital [9]. The increase in exercise capacity was associated with oxygen uptake increases. Many research found that the ability to achieve the anaerobic threshold predicts more extensive improvements after PR [10]. Some research found PR following AECOPD could improve skeletal muscle function [11].

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PR has been shown to be an essential method for AECOPD recovery. However, the meta-analysis of PR study before compared early PR to delay PR [9]. Whether early PR can improve lung function, release dyspnea and improve quality of life is still need more study. We perform a meta-analysis to compare early PR with usual care.

Methods

Search strategies

We searched electronic literature databases for randomized controlled trials (RCTs) comparing early PR with usual care in AECOPD patients. A literature search was performed through these databases: PubMed, MEDLINE database, Google Scholar, Cochrane, Embase from inception to March 2021. The following search terms were used: pulmonary rehabilitation, acute exacerbation of the chronic obstructive pulmonary disease, early rehabilitation, randomized controlled trial.

Data extraction

Two reviewers independently evaluated the included studies and extracted data into RevMan 5.3 (Review Manager: Cochran handbook for systematic reviews). Any disagreement about whether the trials meet the inclusion or exclusion criteria between the two reviewers was resolved by discussing with a third reviewer. If still more data was required, communication through E-mail would be carried out with the authors.

Study selection

We included RCTs comparing early PR with usual care in AECOPD patients. The inclusion criteria included: (1) human studies, (2) randomized control trials (RCT), (3) the comparison between early PR with usual care in AECOPD patients was performed in the study, (4) all participants were adults, (5) if more than one eligible study from the same center using the same protocol, the study with the longest follow-up was used. The exclusion criteria were:(1) studies reported none of these outcomes: 6-min walk test (6MWD), modified Medical Research Council (mMRC), borg dyspnea score, short-form 36 health survey questionnaire (SF-36) physical, SF-36 mental, George Respiratory Questionnaire-total (SGRQ-total), FEV1% predicted. (2) The studies compared the effect of PR initiated after 4 weeks of hospital discharge with early supervised PR initiated during admission or within 4 weeks of hospital discharge.

Outcome measures

The primary endpoint of this meta-analysis was FEV1% predicted, 6MWD, mMRC, and SGRQ-total. The secondary outcomes were borg dyspnea score, SF-36 physical and SF-36 mental.

Quality assessment

We used the Cochran Handbook for Systematic reviews of Interventions guidelines to assess the risk of bias. Each study was evaluated for random sequence generation, concealment of allocation sequence, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome, and selective reporting. And they were classified by two authors as having a high risk of bias and unclear risk of bias, or a low risk of bias based on the Cochrane tool.

Statistical analysis

Statistical analysis of our meta-analysis was using Cochrane systematic review software RevMan 5.3. We used Mann-Whitney U-test to help us verify the hypothesis and rendered statistical significance as a p-value and Z-value < 0.05. Odds ratio (OR) and 95% confidence intervals (CI) were calculated for dichotomous outcomes, and weighted mean differences (WMD) and 95% confidence intervals (CI) were calculated for continuous outcomes in each included study. I^2 value was used to assess statistical heterogeneity. If I^2 value ≤50% was considered as having no statistical heterogeneity, a fixed-effects model was used to estimate the overall summary effect sizes. Otherwise, we used a random-effects model. And subgroup analysis or sensitivity analysis would be carried out.

Assessment of PR extensiveness

Intervention in the hospital included: PR consisted of conventional therapy including 30 min of daily breath exercises with repirologists and hospital-based training. Exercise training consisted of 6MWT and 5 self-controlled walking sessions at 75% of the treadmill walking distance of the respective. Some patients completed 16 revolutions on the "bike" with both the upper and lower. Three times a day for 5 consecutive days. Intervention after discharge included: Supervised home-based training for 6 months walking training 3/day at 125% of the best 6MVWD. Physiotherapists deliver the sessions to provide them with a functional assessment of participants. Four sessions were delivered over 2 weeks, starting within 72 h of discharge. Or consisted of 90 min supervised endurance training and resistance training. Endurance training consists of cycling, treadmill walking, and stair climbing at 60–80% of initial W_{max} during cycle ergometer/maximal walking speed. Resistance training consists of strength exercises for 5 muscle groups, 10 reps at 60% 1 repetition maximum. Others consisted of supervised exercise training including treadmill, arm cycling, arm and leg strength training at 60–70% of VO_{2max} or HR_{max}.

Result

Study selection

The search algorithm identified 169 records. We identified 143 records from electronic databases and 26 additional

records from reference lists and other sources. After deduplication 36 records were excluded. 133 records were screened. 94 records were excluded by reading the abstracts for not about early PR ($n = 16$), not about AECOPD ($n = 13$), not RCT ($n = 48$), non-human studies ($n = 7$), retrospective studies ($n = 10$). 39 full-text studies were assessed for eligibility. 13 articles were excluded for outcomes that have not met this review, 10 articles were excluded for lack of essential data, 3 articles were excluded for comparing early PR with late PR in AECOPD. Finally, 13 articles were included in the final meta-analysis [12–24] (Figure 1).

Included studies

We included a total of 866 patients. All included studies had been published (Table 1). Three trials included in and outpatients with AECOPD [12, 13, 15]. Eight trials included outpatients with AECOPD [14, 18–24]. Two trials included inpatients with AECOPD [16, 17].

Quality assessment

The risk of bias abuts the methodological quality of the included studies are elaborated and summarized respectively in (Figures 2 and 3). Quality assessment of 13 included studies indicated that blinding of participants in the PR is impossible, so the performance bias is high. Different rehabilitation training plans in included studies also caused bias in our meta-analysis.

Heterogeneity

There was no statistical heterogeneity between PR and usual care group in FEV1% predicted, mMRC, SF-36 physical and SF-36 mental. Statistical heterogeneity was found between PR and usual care in 6MWD, SGRQ-total and borg dyspnea score.

Effect of the intervention

The primary endpoint

The primary endpoint contains four outcomes: FEV1% predicted, 6MWD, mMRC, and SGRQ-total. Firstly, "FEV1% predicted" was reported in four studies. 148 patients in the PR group and 147 patients in the control group were available to compare the FEV1% predicted. There were no significant effects of the PR group on measures of FEV1% predicted compared with usual care (MD = 0.50, 95%CI −1.43 to 2.44, $Z = 0.51$, $p = 0.61$) (Figure 4).

Secondly, "6MWD" was reported in nine studies. 286 patients in the PR group and 261 patients in the control group were available to compare the 6MWD. The result showed that the 6MWD was significantly higher in the PR group (MD = 97.58, 95%CI 17.21 to 177.96, $Z = 2.38$, $p = 0.02$) (Figure 5).

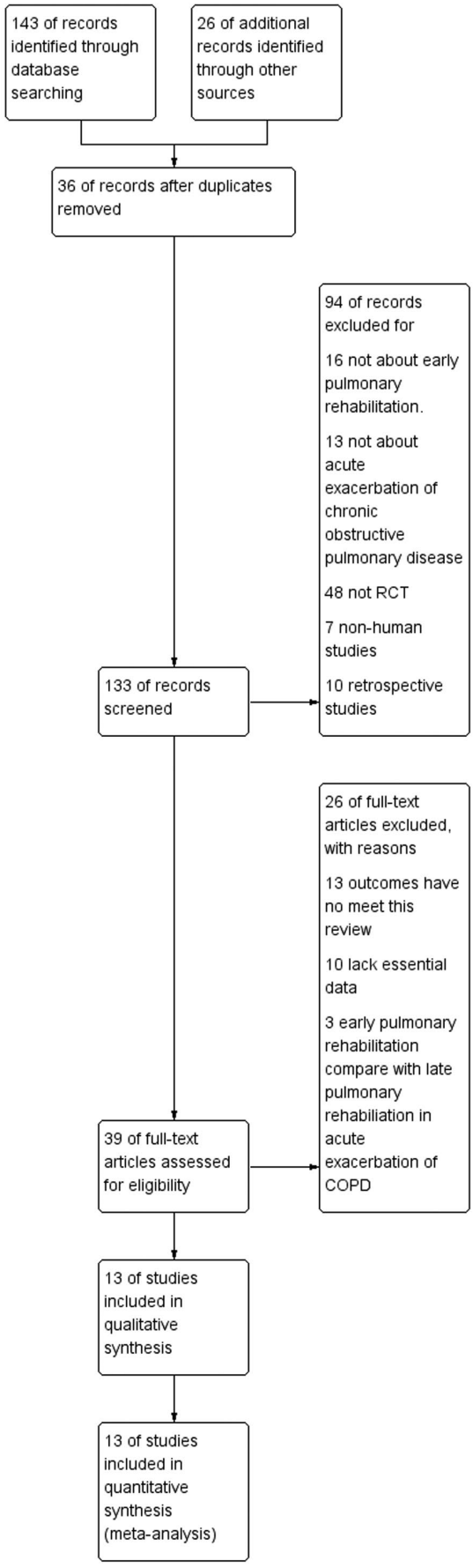

Figure 1. The graph shows a flow diagram of the details search and exclusion criteria.

Table 1. Characteristics of the Thirteen Randomized Controlled Trials included in the Meta-analysis.

Reference	Country	Study design	Setting	Duration and frequency	Frequency	n	participants	Lung function	Comorbidities	Age	Intervention	Intervention after discharge	Usual care	Outcomes
Behnke 2000	Germany	RCT	In and outpatient	Hospital-based 10 days, home-based 6 months	7/week	60	Admitted patients with AECOPD, FEV1 36% predicted	FEV1 36% of predicted	Not specified	Mean age:64-68 years	PR consisted of conventional therapy including 30 min of daily breath exercises with respirologists and hospital-based training. Exercise training consisted of daily 6MWT and 5 self-controlled walking sessions at 75% of the treadmill walking distance of the respective day	Supervised home-based training for 6 months, walking training 3/day at 125% of the best 6MVWD, health check every 2 weeks (months 0-3) followed by phone calls from month 3-6	Standard inpatient care and community care with respirologists(30min of daily breathin exercises but without exercise training	Mortality, Walking test, COPD related hospital readmission, Dropout
Cox 2018	UK	RCT	In and outpatient	Starting within 72 hours of discharge, and participants were considered to be stable 4-6 weeks post discharge.	4/2weeks	16	Admitted patients with AECOPD	FEV1 46.1% of predicted	Ischemic, stroke, vascular, diabetes	Mean age:67.8(11.12)	A workload was set at the first session and at the two subsequent daily sessions. Patients completed 16 revolutions on the "bike" with both the upper and lower. Three times a day for 5 consecutive days	The 6MWD data were made available to the physiotherapists delivering the sessions to provide them with a functional assessment of participants. Four sessions were delivered over 2 weeks, starting within 72 hours of discharge	Best available alternative management strategy	6MWD, London Chest Activity of Daily Living scale (LCADL), EuroQol-5 dimensions five-level version (EQ-5D-5L), COPD Assessment Test (CAT), MRC Dyspnea Scale, Activity monitor, Written activity diary, Health and social care resource use, Perceived Necessity and Concerns questionnair, Exacerbation, Readmission
Deepak 2014	India	RCT	outpatient	12 weeks		56	Admitted patients with AECOPD	FEV1 47-53% of predicted	Not specified	Mean age: 59 years	PR consisted of patient assessment, exercise testing, exercise training (mixture of limb strengthening and aerobic activities, tailored to individual baseline function), education, nutrition and psycho-social rehabilitation	Outpatient PR	Conventional treatment without PR	HRQoL Walking diatance

Eaton 2009	New Zealand	RCT	In- and outpatient	8 weeks	2/week	64	Admitted patients with AECOPD	FEV1 35-36% of predicted	Measured with Charlson index (PR group:3.1; PR control: 3.2)	Mean age: 70 years	PR consisted of a daily 30-min structured supervised exercise regimen that included walking and upper and lower limb strengthening exercises	Hospital-based outpatient program consisting of 1-h sessions of supervised exercise training and educational sessions	Usual care standardized in according with the ATS/ERS COPD guidelines and standardized advises on the benefits of exercise and maintaining daily activities	Walking diatance COPD related hospital readmissions Dropout
He 2015	China	RCT	inpatient	From the second day of admission until discharge	2/day	94	Admitted patients with AECOPD	FEV1 38-39% of predicted	Not specified	Mean age: 69.2-73.9 years	Patients received 30-minute exercise twice-daily. Exercise training included stretches, endurance, and strength training		Usual care with optimal medical treatment	6MWD, the ADL-D score, mMRC, the BODE,
Kirsten 1998	Germany	RCT	inpatient	10 days	7/week	29	Admitted patients with AECOPD	FEV1 34-38% of predicted	Not specified	Mean age: 62-66 years	PR consisted of 6MWT each day and additional 5 walking sessions per day at ≥ 75% of the respective walking distance		Usual care with optimal medical treatment	Walking test
KO 2011	China Hong Kong	RCT	outpatient	8 weeks	3/week	60	Admitted patients with AECOPD	FEV1 41-46% of predicted	Coronary artery disease, cardiac arrhythmic, heart failure, hypertension, diabetes	Mean age: 73-74 years	Education on proper breathing techniques and how to cope with daily activities	PR consisted of supervised exercise training including treadmill, arm cycling, arm and leg strength training at 60-70% of VO_{2max} or HR_{max} and were advised to perform at least 20 min home exercises a day	Usual care with instructions to perform regular exercise at home (walking and muscle stretching exercise)	HRQoL[b] Mortality[a,b] Walking test[b] Dropout[a,b]
KO 2017	China Hong Kong	RCT	Outpatient	8 weeks	3/week	180	Admitted patients with AECOPD	FEV1 42-47% of predicted	Hypertention, type 2 diabetes, hyperlipidemia, ischemic heart disease, heart failure, old pulmonary tuberculosis	Mean age: 75 years	PR consisted of education (smoking cessation, technique of using medications, nutrition, dyspnea management, self-management, psychological distress, exercise benefits and strategies, breathing and sputum-removal techniques) and individual physical training program to perform at home or a short course of outpatient PR	Patients are offered supervised exercise training 3/week declining they are offered instructions for self-training, education, and telephone calls.	Usual care with medical treatment	HRQoL[b] Mortality[a] Walking test[b] Dropout[a,b] Days in hospital[a]

(*Continued*)

Table 1. (*Continued*).

Reference	Country	Study design	Setting	Duration and frequency	Frequency	n	participants	Lung function	Comorbidities	Age	Intervention	Intervention after discharge	Usual care	Outcomes
KO 2020	China, Hong Kong	RCT	Outpatient	4-8 weeks	1-2/week	136	patients with AECOPD	FEV1 46-49% of predicted	Not specified	Mean age: 74-76years	Patients also received COPD education from our respiratory nurses on the mechanisms and pathogenesis of COPD, and the importance of smoking cessation, medication compliance and inhaler techniques	Patients had training as outpatients in the physiotherapy department for 4-8 sessions, 2h each time, 1-2times weekly. Each subject in the intervention arm would have at least 4-8 weeks of supervised training by a trained physiotherapist.	The control group received neither physiotherapy training nor phone calls from the case manager for reinforcement of home exercise.	Readmission, AECOPD, mortality, COPD assessment Test (CAT), modified Medical Research Council (mMRC) Dyspnea Scale, 6MWT, St George's Respiratory Questionnaire (SGRQ)
Man 2004	England	RCT	Out patient	8 weeks	2/week	34	patients with AECOPD	FEV1 37-42% of predicted	Not specified	Mean age: 70 years	Supervised multidisciplinary PR, 1-h of exercise (aerobic walking and cycling, strength training for the upper and lower limb) and 1-h of education (with an emphasis on self-management of the disease, nutrition and lifestyle issues)	Supervised multidisciplinary PR	Usual care with optimal medical treatment	HRQoL[b] Motality[b] walking test[b] COPD related hospital readmissions[b] Dropout[a]
Murphy 2005	Ireland	RCT	Outpatient home-based	6 weeks	2/week	26	patients with AECOPD	FEV1 38-42% of predicted	Not specified	Mean age: 65-67 years	PR consisted of 30-40 min supervised home-based exercise program, aerobic exercises including stepping to stand from a chair, upper limb strength exercises with low-impactelastic band at 3-5 on the Borg breathlessness score	Supervised home-based exercise program	Standard medical treatment without any form of PR exercises or lifestyle changes advice	Walking test[a] COPD related hospital readmissions[b] Dropout[a]
Seymour 2010	United Kingdom	RCT	Outpatient Hospital-led	8 weeks	2/week	49	admitted patients with AECOPD	FEV1 52% of predicted	Hypertention, type 2 diabetes, ischemic heart disease	Mean age:65-67 years	PR consisted of supervised exercise training including a mixture of limb strengthening and aerobic activities tailored to individual baseline function and educations session (lasting 2h)	Hospital-led supervised exercise training	Usual care with optimal medical treatment	HRQoF[b] Walking test[a] hopital readmiddion[b] Dropout[b]

Troosters 2000	Belgium	RCT	Outpatient	6 months (18 months follow-up)	2-3/week	62	AECOPD referred to outpatient clinic	FEV1 41-43% of predicted	Not specified	Mean age:60-63 years	PR consisted of 90-min supervised endurance training and resistance training. Endurance training consisting of cycling, treadmill walking, and stair climbing at 60-80% of initial W_{max} during cycle ergometer/ maximal walking speed. Resistance training consisting of strenth exercises for 5 muscle groups, 10 reps at 60% 1 repetition maximum	Supervised outpatient exercise training.	Usual medical care consisting of standard community care with respirologist	Mortality[a] walking test[a] dropout[ab]

6MWT (6-min walk test), CAT (COPD assessment test), ADL-D scale (Daily Living Dyspnea scale), mMRC (Modified Medical Research Council), HAD (Hospital Anxiety and Depression score), ESAS (Edmonton Symptom Assessmint).

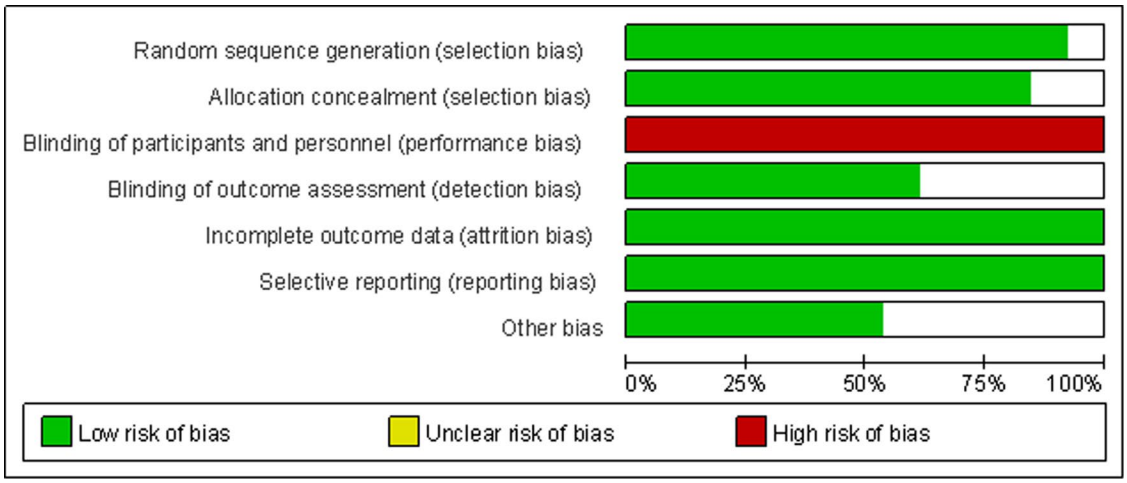

Figure 2. The graph shows the risk of bias graph.

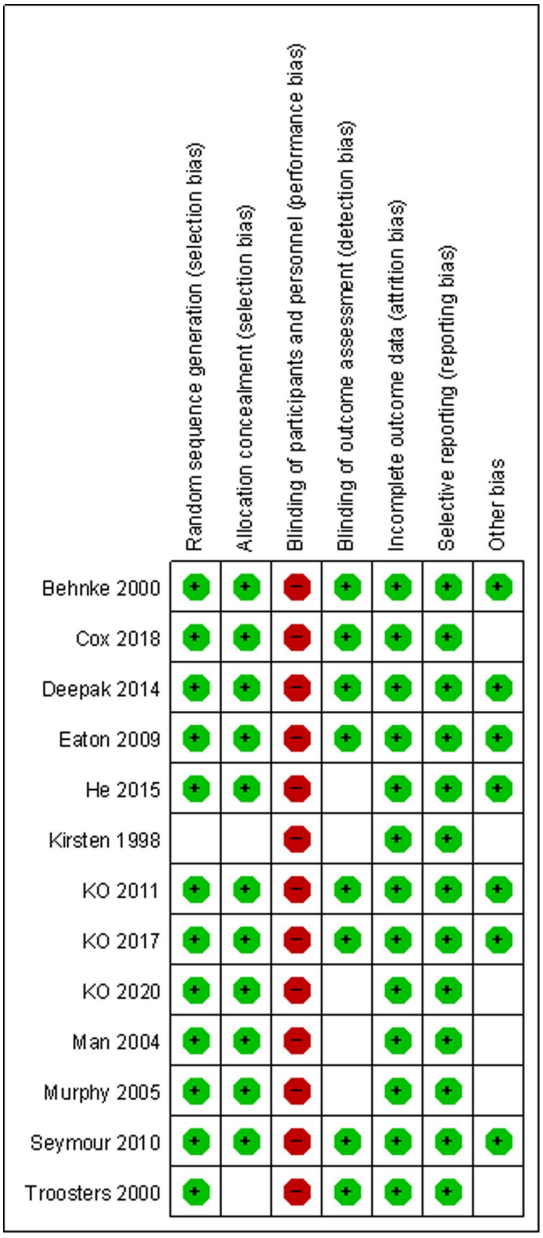

Figure 3. The graph shows the risk of bias summary.

Thirdly, mMRC was reported in six studies. 208 patients in the PR group and 197 patients in the control group were available to compare the mMRC. The result showed that the mMRC was significantly lower in the PR group (MD = −0.36, 95%CI −0.52 to −0.21, $Z = 4.56$, $p < 0.00001$) (Figure 6). It means PR group achieved better mMRC.

Fourth, SGRQ-total was reported in six studies. 164 patients in the PR group and 166 patients in the control group were available to compare the SGRQ-total. The result showed that the SGRQ-total was significantly lower in the PR group (MD = −9.67, 95%CI −16.23 to −3.11, $Z = 2.89$, $p = 0.004$) (Figure 7). It means PR group achieved a better SGRQ-total.

The second endpoint

The second endpoint contains three outcomes: borg dyspnea score, SF-36 physical and SF-36 mental. Firstly, "borg dyspnea score" was reported in six studies. 158 patients in the PR group and 130 patients in the control group were available to compare the borg dyspnea score. There were no significant effects of the PR group on measures of borg dyspnea score compared with usual care (MD = −0.88, 95%CI −1.89 to 0.13, $Z = 1.71$, $p = 0.09$) (Figure 8).

Secondly, SF-36 physical was reported in three studies. 67 patients in the PR group and 91 patients in the control group were available to compare the SF-36 physical. The result showed that the SF-36 physical was significantly higher in the PR group compared with the usual care group. (MD = 4.98, 95%CI 0.60 to 9.35, $Z = 2.23$, $p = 0.03$) (Figure 9). It means PR group achieved better SF-36 physical.

Thirdly, SF-36 mental was reported in three studies. 67 patients in the PR group and 91 patients in the control group were available to compare the SF-36 mental. The result showed that there was no significant difference between the PR group and control group (MD = 4.34, 95%CI −1.64 to 10.32, $Z = 1.42$, $p = 0.16$) (Figure 10).

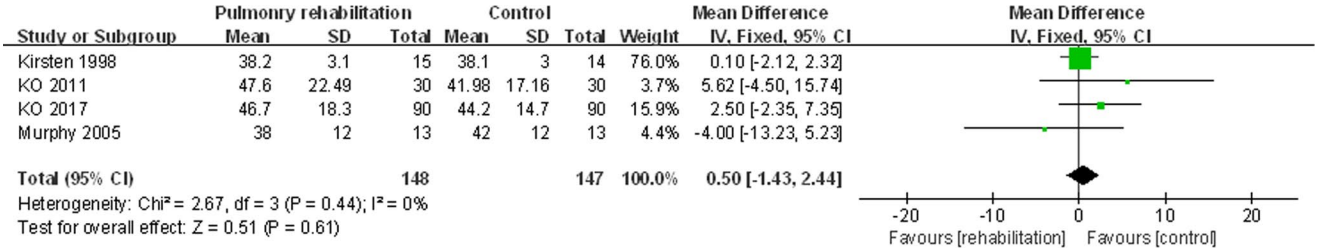

Figure 4. The graph shows a forest plot of standardized mean difference with a confidence interval for the FEV1% predicted.

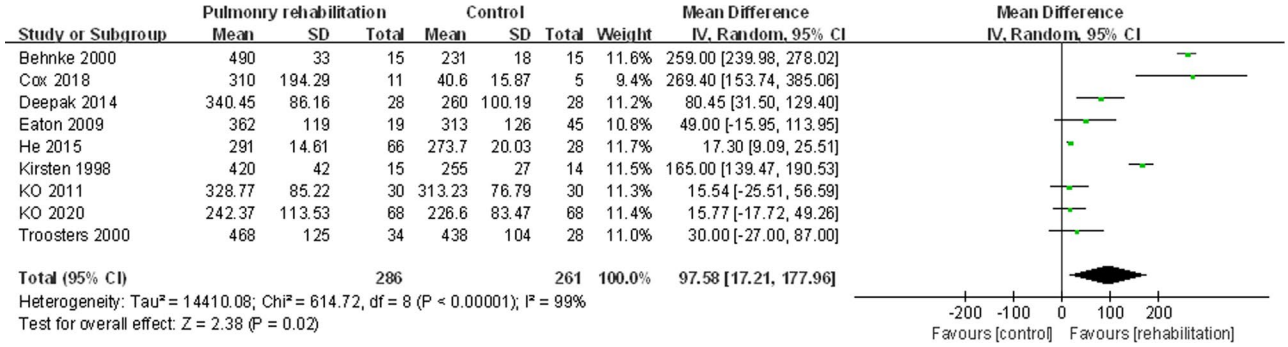

Figure 5. The graph shows a forest plot of standardized mean difference with a confidence interval for the 6MWD.

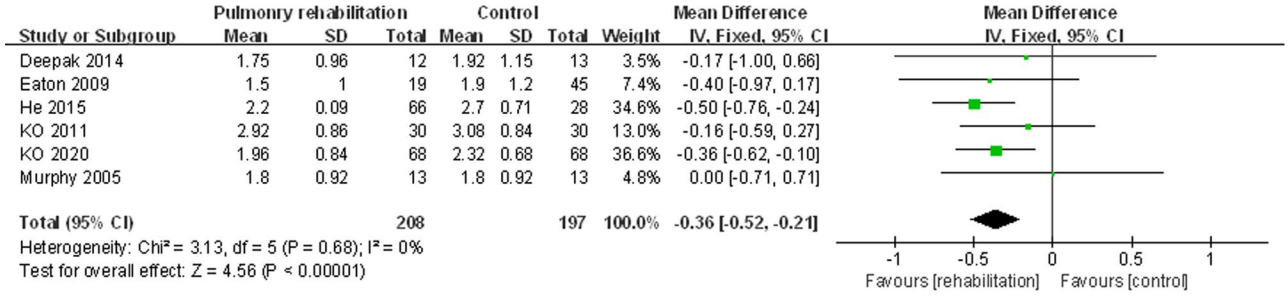

Figure 6. The graph shows a forest plot of standardized mean difference with a confidence interval for the mMRC.

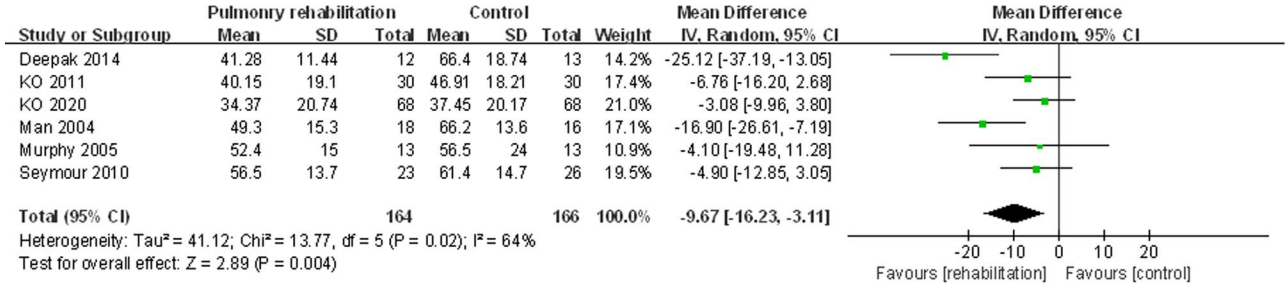

Figure 7. The graph shows a forest plot of standardized mean difference with a confidence interval for the SGRQ-total.

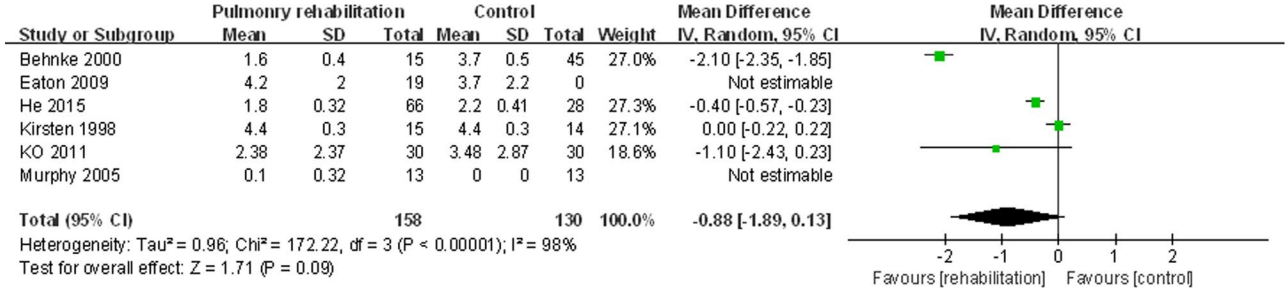

Figure 8. The graph shows a forest plot of standardized mean difference with a confidence interval for the borg dyspnea score.

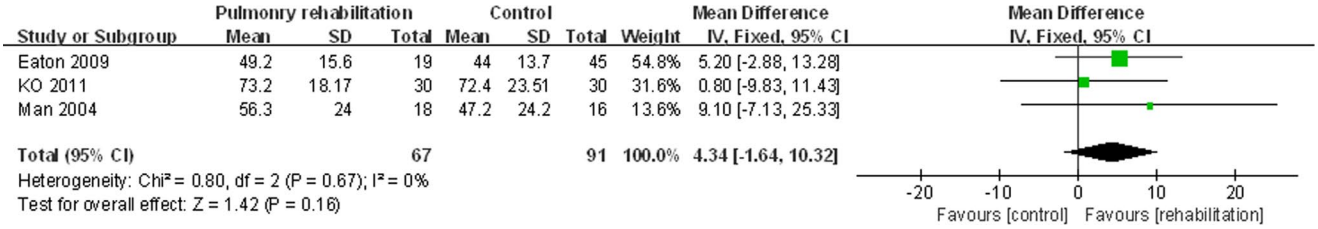

Figure 10. The graph shows a forest plot of standardized mean difference with a confidence interval for theSF-36 mental.

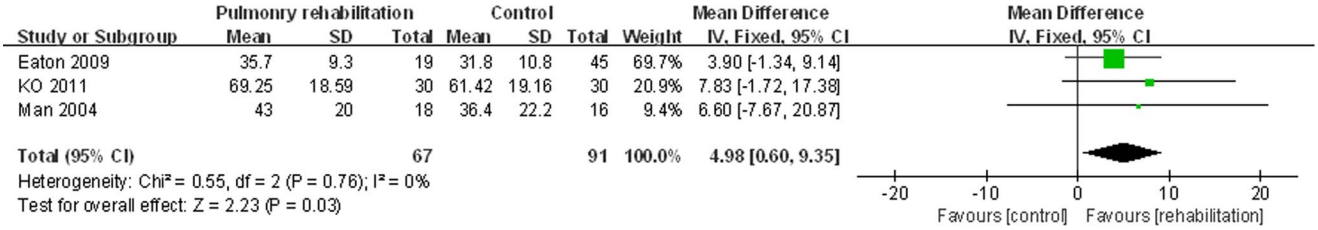

Figure 9. The graph shows a forest plot of standardized mean difference with a confidence interval for the SF-36 physical.

Discussion

Our meta-analysis found that an early PR in AECOPD patients during recovery did not alter FEV1% predicted, borg dyspnea score and SF-36 mental, but did improve mMRC, 6MWD, SGRQ-total and SF-36 physical when compared with usual care in the early PR group.

Some other research only includes stable COPD patients, usually meaning for at least two months no exacerbation. However, our meta-analysis just included patients who had just experienced an episode of AECOPD. And found early RP improved mobility and prevented muscle atrophy. The results of this preliminary meta-analysis suggest that starting rehabilitation of COPD patients as soon as possible after an exacerbation is useful.

6MWD may have been the favored walking distance that was chosen as the outcome measure. And changes of more than 54 m have been stated to be clinically relevant [25]. Both retrospective and prospective studies have used walking distance as the endpoint. Many results reported that early PR is associated with improvement in 6MWD. Initial 6MWD was predictive of survival in severe COPD patients. Patients with low initial 6MWD achieved poor overall survival at three years [26]. Our meta-analysis showed that the 6MWD was significantly higher in the PR group. Other RCT showed that early PR with AECOPD patients could effectively counterbalance the loss of skeletal muscle function in the hospitalization period. And found that balance and lower limb strength can improve with an early PR in AECOPD patients [27].

Our meta-analysis found that PR could improve breathlessness as measured by scores of mMRC. This is consistent with skeletal muscle dysfunction leads to activity reduction in COPD patients. PR improves exercise tolerance and health-related quality of life, alleviates fatigue and dyspnea, and reduces mortality and hospital readmission [28]. Some PR included therapist-assisted stretching of the respiratory muscles before starting PR to relieve dyspnea. Stretching the respiratory muscles can decrease the chest wall stiffness and expand expiratory flow. And reduce hyperinflation of the lungs at rest. This effect improves the mobility of the diaphragm and consequently greater the exercise capacity [29]. So PR can lead to less dyspnea as measured by mMRC.

The PR group reported a more remarkable improvement in the SGRQ-total. This may be due to the exercise making them more self-sufficient and helping the patients to break the deterioration of functional capacity, which causes heavier dyspnea.

We found that Moderate-to-high-intensity exercise with a compromised respiratory function may be inappropriate for AECOPD. Low-intensity activity has been found to benefit acutely ill patients. It was feasible and safe for COPD patients admitted with an exacerbation to have early inpatient-outpatient rehabilitation. After the hospital-based training in acutely ill patients, overall dyspnea assessed by mMRC was significantly reduced. But the improvement was reached in about ten days. Even a low regular exercise can lead to a persistent reduction in dyspnea. So a home-based training could be maintained after discharge. And early inpatient-outpatient rehabilitation reduced COPD related readmissions, length of hospital stays, and mortality [9]. A randomized controlled trial found that early pulmonary rehabilitation after AECOPD led to a better improvement in the incremental shuttle walk test compare to rehabilitation initiated two months after discharge [30]. A period of low-level chest physiotherapy and breathing retraining may have beneficial effects on SF-36 physical and SGRQ-total. Less strenuous exercise performed with minimal facilities provide improvement in SF-36 physical and SGRQ-total. The SF-36 mental remained unchanged in both groups. But patients can undertake a more intensive exercise to achieve the greatest benefit.

Our study observed that quadriceps muscle strength was increased by PR and may underlie the observed increase in exercise capacity. And we found that physiological or psychological changes brought about by the PR were responsible for improving healthcare utilization. An increase in quadriceps strength following PR is usually achieved by increased

volitional drive. The maximum isometric voluntary contraction force was associated with the twitch response to femoral nerve stimulation. Whole-body muscle mass was similar, so competing could involve a change in muscle fiber orientation [31].

Some study has shown that tiotropium could provide benefit with sustained improvement in health status and lung function, reduced exacerbations and hospitalizations [32, 33]. But patients in our meta-analysis were used the same drugs at the baseline between the two groups. The improvement in mMRC and 6MWD suggests the possibility that patients may have been suboptimally treated with bronchodilators before beginning rehabilitation. We carefully adjusted every included RCT and found patients in both treatment and control groups stayed on the same medications throughout the study. The FEV1% predicted and borg dyspnea score remained unchanged in both groups.

Limitations

Our meta-analysis found it impossible to bind participants and personnel. Patients who participate in PR will feel better psychologically and perform better on the test. So the risk of bias for binding participants was high in our meta-analysis. The rehabilitation interventions varied in types of exercise, frequency of sessions and duration. So statistical heterogeneity could be found between PR and usual care in 6MWD, SGRQ-total and borg dyspnea score.

Conclusion

Our meta-analysis found early PR in AECOPD patients would lead to better 6MWD, mMRC, SGRQ-total and SF-36 physical. But there were no significant effects of the PR group on measures of FEV1% predicted, borg dyspnea score and SF-36 mental compared with the usual care group.

Declaration of interest

All authors declare no conflict of interest.

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