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Review Article

Meta-analysis of the Effect of a Pulmonary Rehabilitation Program on Respiratory Muscle Strength in Patients with Chronic Obstructive Pulmonary Disease

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ABSTRACT

Purpose: Pulmonary rehabilitation (PR) programs are important in the treatment of patients with chronic obstructive pulmonary disease (COPD) but vary widely in type, duration, and efficacy. This meta-analysis investigated the effect of PR programs on respiratory muscle strength in patients with COPD.
Methods: PubMed, Embase, and CINAHL were searched. The primary outcome variables were maximal expiratory pressure (MEP) and maximal inspiratory pressure (MIP). The secondary outcome variables were the modified Borg score after the 6-min walking test, percent predicted forced expiratory volume in 1 second (FEV_1%pred), and percent FEV_1/forced volume capacity (FVC). Comprehensive Meta-Analysis, version 3.0, was used to analyze the data. The effect size was calculated using the standardized mean difference (SMD) and 95% confidence interval (CI).
Results: Twenty randomized controlled trials (with 992 participants) were included in the analysis. The PR programs had a significant effect on the MEP (SMD, 0.87; 95% CI, 0.42−1.32; $p < .001$), MIP (SMD, 0.53; 95% CI, 0.13−0.93; $p = .009$), and modified Borg score (SMD, −0.37; 95% CI, −0.52 to −0.22; $p < .001$) in patients with COPD. There was no effect on FEV_1%pred (SMD, 0.09; 95% CI, −0.12 to 0.30; $p = .406$) or FEV_1/FVC% (SMD, 0.04; 95% CI, −0.17 to 0.26; $p = .702$).
Conclusion: PR programs improve respiratory muscle strength in patients with COPD. Strategies for selecting a suitable PR program need to be developed, and future studies should evaluate the long-term effects of such programs on pulmonary function.

Introduction

Chronic obstructive pulmonary disease (COPD) is characterized by dyspnea, chronic cough, production of sputum, and decreased physical activity [1] along with a marked reduction in exercise capacity [2]. The management of COPD imposes a heavy economic burden [3], and the disease is one of the major causes of mortality throughout the world [1,4]. However, the Global Initiative for Obstructive Lung Disease (GOLD) considers COPD to be controllable if managed well and has set a goal of relieving symptoms and reducing exacerbations in these patients [1].

Movement of the diaphragm decreases in patients with COPD because of reduced airflow, which leads to a compensatory increase in the activity of the respiratory muscles in the chest wall [5]. This abnormal increase in muscle activity causes a feeling of exhaustion and increases dyspnea and exercise intolerance [6]. Respiratory muscle weakness increases the mortality risk in patients with COPD, and weakness of the expiratory muscles in particular is a risk factor for acute exacerbation, requiring readmission to hospital [7]. Therefore, it is necessary to assess respiratory muscle strength in patients with COPD and provide intervention if necessary.

Pulmonary rehabilitation (PR) is an important non-pharmacologic approach in the management of patients with COPD [8]. Respiratory muscle training (RT) is a type of PR that helps reduce dyspnea and improve respiratory muscle strength, lung function, and quality of life in patients with COPD [9–12]. Respiratory muscle dysfunction may be present even in patients whose COPD is clinically stable [7]. Therefore, in an effort to increase exercise capacity and reduce dyspnea, RT should be considered when planning a PR program [2].

Physical exercise (PE) is also a type of PR that can improve exercise tolerance, symptoms of dyspnea, and fatigue in patients with COPD [1]. The National Institute for Health and Care Excellence

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recommends that all patients with COPD should participate in a PE program [13]. Therefore, reduced exercise capacity should be detected early in patients with COPD, and systematic PE programs should be implemented to prevent exacerbations [14].

Various PR programs have been developed to improve dyspnea and pulmonary function in patients with COPD. However, the effectiveness of these programs has varied depending on the study design, the type and duration of the program used, and the severity of the disease. Therefore, there is a need to integrate the results of the individual studies. Both PE and RT are important interventions in PR programs for patients with COPD. The effect of RT on respiratory muscle strength in patients with COPD has been demonstrated in meta-analyses. However, we could not find a meta-analysis of the effects of PE on respiratory muscle strength in these patients. In this study, we confirmed the total effect size for PR as well as the effect sizes for PE and RT by subgroup analysis.

The primary outcome variables in this meta-analysis were the associations of respiratory muscle strength with mortality and readmission to hospital. The secondary outcome variables included dyspnea and lung function, which directly affect the exercise capacity, prognosis, and quality of life.

Methods

Search strategy

The PubMed, Embase, and CINAHL databases were searched using the following terms: ("chronic obstructive pulmonary disease" OR "COPD" OR "chronic obstructive lung disease" OR "chronic obstructive airway disease" OR "chronic bronchitis" OR "emphysema" OR "pulmonary emphysema") AND ("pulmonary rehabilitation" OR "program" OR "intervention" OR "training" OR "exercise" OR "activit*" OR "respirat*" OR "breath*"). Medical Subject Headings (MeSH) search terms were used. The searches were limited to English language publications in the previous 10 years (2006–2016), randomized controlled trials (RCTs) in human adults, and articles for which the full-text versions were available.

Study selection

The criteria for study selection, according to the PICO (Population–Intervention–Comparison–Outcomes) process, were as follows: (1) Population, patients with COPD; (2) Intervention, PR programs that included PE or RT; (3) Comparison, usual treatments; and (4) Outcomes, maximal expiratory pressure (MEP) and maximal inspiratory pressure (MIP) in cmH_2O (primary outcomes) and modified Borg score after the 6-min walking test (6MWT), percent predicted forced expiratory volume in 1 second (FEV_1% pred), and FEV_1/forced vital capacity (FVC) as a percentage (secondary outcomes); and (5) an RCT design.

Studies were excluded if the participants were inpatients, if pharmacologic, oxygen, ventilator, electrical stimulation, or acupuncture therapy was provided as an intervention, if the full text of the article was unavailable, if only one study of a certain type of PR program was available, and if the mean and standard deviation values for the outcome variables were not reported.

Data extraction

Two researchers extracted the following data from the included studies: first author; year of publication; the number of subjects; age of the participants; FEV_1%pred (disease severity); characteristics of the program (i.e., type, duration, frequency, time); and outcome values (i.e., MEP [cmH_2O], MIP [cmH_2O], modified Borg score after 6MWT, FEV_1%pred, and FEV_1/FVC%). Any discrepancies in data extraction between the two researchers were resolved by discussion.

Quality assessment of selected studies

Two researchers assessed the quality of the included studies by independently evaluating each of the seven items included in the "Risk of Bias" tool developed by the Cochrane Collaboration. Each of the following items was rated as "high," "low," or "unclear": "random sequence generation," "allocation concealment," "blinding of participants and personnel," "blinding of outcome assessment," "incomplete outcome data," "selective reporting," and "other bias." The two researchers performed a pilot test that included five of the studies to ensure the reliability of the quality assessment.

Data analysis

The data were analyzed using Comprehensive Meta-Analysis, version 3.0 (Biostat, Englewood, NJ, USA). For continuous outcomes, the effect size variables, including the standardized mean difference (SMD) and 95% confidence interval (CI), were calculated. A random effects model was used if the results showed heterogeneity. Heterogeneity was assessed using the Higgins I^2 test and defined as low ($I^2 \leq 25\%$), moderate ($25\% < I^2 \leq 50\%$), or high ($I^2 > 50\%$) [15]. Potential publication bias was evaluated using a funnel plot.

Results

Literature search

Figure 1 shows the literature search process according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [16]. A total of 1822 potentially relevant studies were identified. After removing duplicates, reviewing the titles and abstracts, and excluding inadequate studies, 20 studies were eligible for inclusion in the meta-analysis. These 20 articles are listed in the Appendix.

Characteristics of selected studies

The characteristics of the 20 included studies (representing 25 PR programs) are shown in Table 1. There were 595 patients in the experimental group (7–60 patients per study) and 397 in the control group (6–48 patients per study). The mean patient age was 63.44 (range, 54.40–73.60) years in the experimental group and 65.32 (range, 56.40–73.60) years in the control group. The mean FEV_1%pred was 46.1% (range, 27.0–75.3%) in the experimental group and 45.9% (range, 28.0–75.31%) in the control group. Most of the patients had stage II or III COPD. Thirteen studies involved PE [A6–8,A10–12,A14–20], five involved RT [A1–2,A4–5,A13], and two involved a combination of both strategies [A3,A9] (see Appendix). The program application time was 10–90 minutes per session, and the frequency ranged from twice a week to daily. The control group usually received routine treatments.

MEP [A2,A4,A6,A14,A16,A20] and MIP [A1–2,A6,A13–14,A20] were measured in six studies (eight programs) to evaluate respiratory muscle strength. Thirteen studies (16 programs) measured the modified Borg score after the 6MWT to assess dyspnea [A1,A4–5,A7–8,A10–11,A14–19]. Pulmonary function was evaluated using the FEV_1%pred [A1,A3,A9,A12,A15,A20] and FEV_1/FVC% [A1,A3–4,A12,A15,A20] in six studies (eight programs).

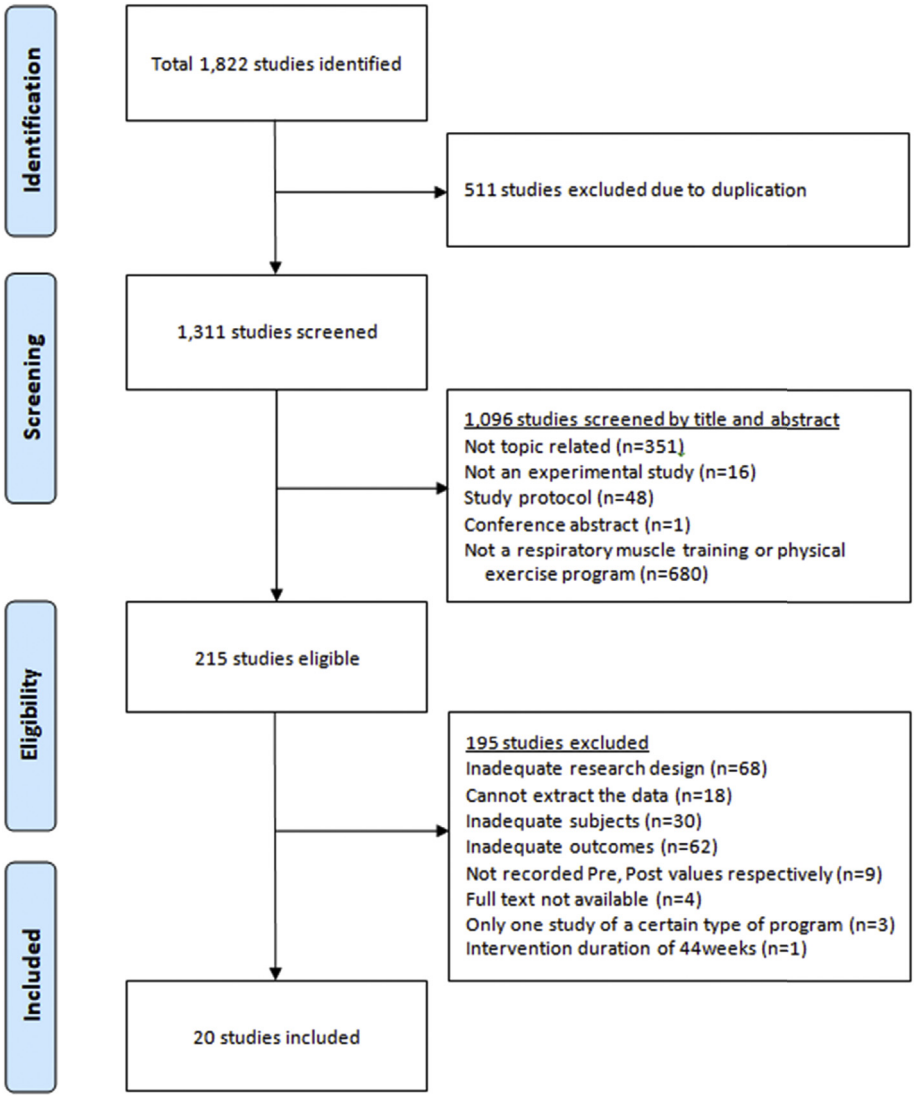


Figure 1. Flow diagram of the study selection process.

Quality of the selected studies

The methodologic quality of all the included studies was judged to be "moderate" based on the distribution for each item assessed for risk of bias. For random sequence generation, the risk of bias was low in all studies (100.0%). For allocation concealment, the risk of bias was low in 15.0% and unclear in 85.0%. For blinding of participants and personnel, there was a low risk of bias in 30.0% and a high risk in 70.0%. For blinding of outcome assessment, the risk of bias was low in 35.0%, high in 55.0%, and unclear in the remaining 10.0%. For incomplete outcome data, most studies (95.0%) had a low risk of bias. Finally, for selective reporting, the risk of bias was low in 25.0% and unclear in the remaining 75.0%. There was no mention of "other bias". The detailed results of the quality assessment for selected studies are shown in Table 1.

Effects of PR programs

The effects of the PR programs were calculated according to the primary and secondary outcome variables. The primary outcome variables were the MEP and MIP, and the secondary outcome variables were the modified Borg score after the 6MWT, FEV_1%pred, and FEV_1/FVC%. In cases in which there was heterogeneity in any of the variables, a subgroup analysis was performed according to the PR strategy used (PE vs. RT) and duration of the program (4–6 weeks vs. 8–12 weeks). The effect size in the subgroup analysis was calculated only when the number of studies was ≥2.

Effects of the PR program on expiratory muscle strength

The MEP was measured in six studies. The heterogeneity was more than moderate ($\chi^2 = 18.12$, df = 7, $p = .011$; $I^2 = 61.4\%$), so a random effects model was used (Figure 2). The overall effect size of the PR program gave an SMD of 0.87 (95% CI, 0.42–1.32), indicating a statistically significant improvement in MEP (Z = 3.81, $p < .001$).

In the subgroup analysis according to the type of program (Figure 2), the effect size of the PE strategy gave an SMD of 0.87 (95% CI, 0.44–1.31), indicating that there was a significant increase in MEP ($p < .001$) after PE. However, the effect size of RT (k = 2) gave an SMD of 1.01 (95% CI, −0.95 to 2.97), meaning that RT did not significantly improve the MEP ($p = .313$). There was no

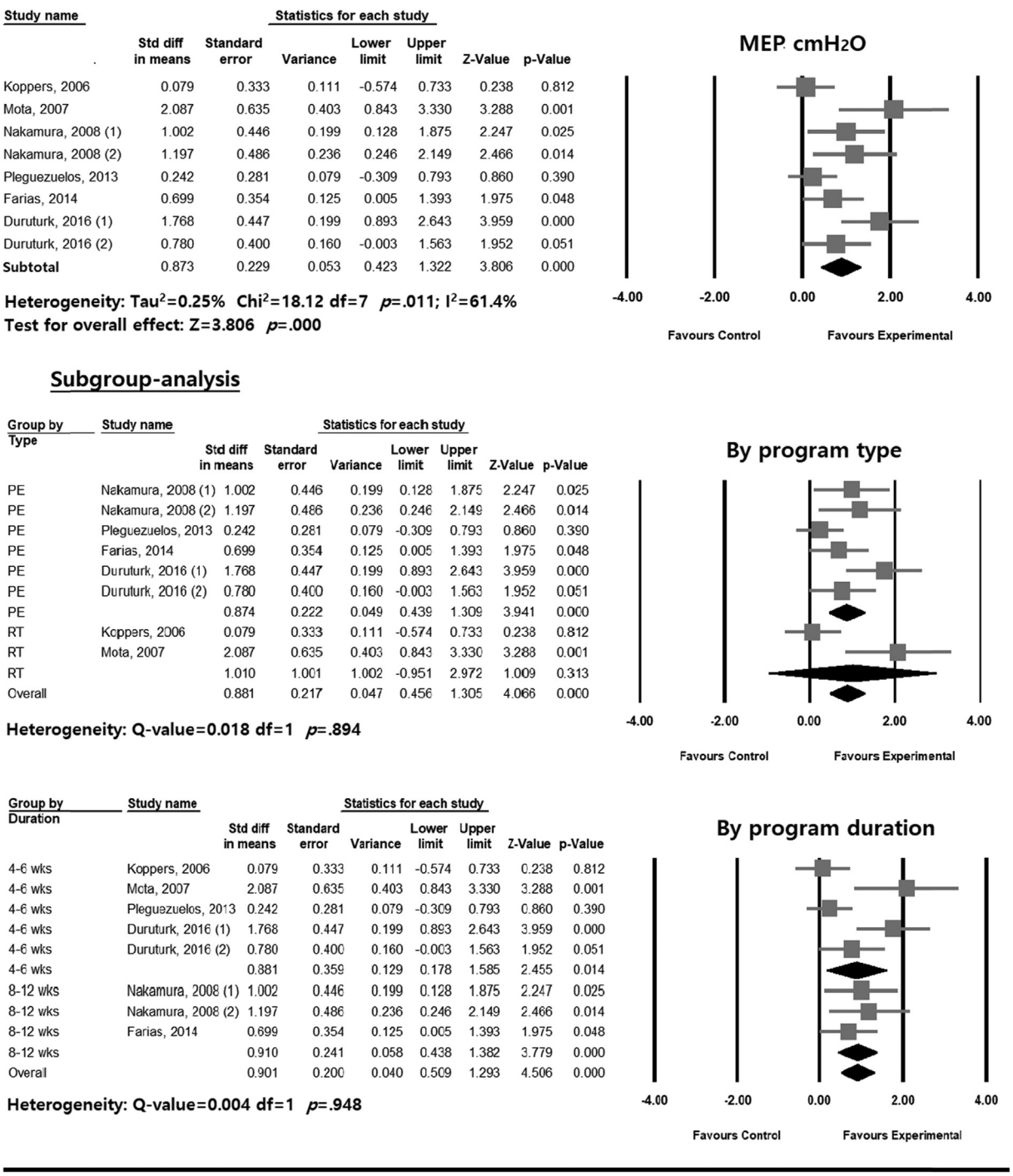


Figure 2. The effect of pulmonary rehabilitation on expiratory muscle strength.
Note. MEP = maximal expiratory pressure.

significant difference in the effect size between PE and RT (Q = 0.02, df = 1, p = .894).

In the subgroup analysis according to duration of the program (Figure 2), the effect size of a 4- to 6-week program (k = 5) gave an SMD of 0.88 (95% CI, 0.18−1.59), indicating a statistically significant improvement in MEP (p = .014). Similarly, an 8- to 12-week program (k = 3) resulted in an SMD of 0.88 (95% CI, 0.18−1.59), indicating a statistically significant improvement in MEP (p < .001). There was no significant difference in the effect size according to duration of intervention (Q = 0.00, df = 1, p = .948).

Effects of PR program on inspiratory muscle strength

The MIP was measured in six studies. The heterogeneity between studies was more than moderate ($\chi^2 = 15.61$, df = 7, p = .029; I^2 = 55.1%), so a random effects model was used for the analysis

Table 1 *Characteristics of Included Studies in the Meta-Analysis.*

Study (year)	Group	Sample size (n)	Age (yrs)	Disease- Severity ($FEV_1\%_{Pred}$)	Type of program	Program			Outcomes
						Time (min)	Freq (/wk)	Duration (wks)	
Hill (2006) [A1]	Exp	16	69	37.4	High intensity inspiratory-muscle training	20	3	8	MIP, mBorg score
	Cont	17	67	36.5	Sham training				FEV_1, FEV_1/FVC
Koppers (2006) [A2]	Exp	18	54	50.0	Respiratory muscle -endurance training	30	daily	5	MEP
	Cont	18	57	58.0	Sham training				MIP
Karapolat (2007) [A3]	Exp	26	65	54.8	Conventional PR	30	3	8	FEV_1
	Cont	19	67	55.0	Usual care				FEV_1/FVC
Mota (2007) [A4]	Exp	10	62	27.0	Expiratory muscle training	30	3	5	MEP, mBorg score
	Cont	6	66	28.0	Sham training				FEV_1/FVC
Nield (2007) [A5]	Exp1	10	62	35.0	Pursed lip breathing	10-25	daily	4	mBorg score
	Exp2	7	63	43.0	Expiratory muscle training				
	Cont	9	69	40.0	No intervention				
Nakamura (2008) [A6]	Exp1	10	69	53.2	Aerobic+Strength	60	-	12	MEP
	Exp2	13	68	52.7	Aerobic+Recreation				MIP
	Cont	10	70	48.2	No program				
Borghi-Silva (2009) [A7]	Exp	20	67	33.0	Aerobic exercise	50	3	6	mBorg score
	Cont	14	67	35.0	Usual care				
Breyer (2010) [A8]	Exp	30	62	48.1	Nordic walking	60	3	12	mBorg score
	Cont	30	59	47.1	No exercise				
Ghanem (2010) [A9]	Exp	25	57	29.4	Home-based PR	-	3-4	8	FEV_1
	Cont	14	56	23.2	Usual care				
Chan (2011) [A10]	Exp1	60	72	-	Tai-chi Qigong	60	2	12	mBorg score
	Exp2	50	74	-	Exercise				
	Cont	48	74	-	Routine activity				
Souto Araujo (2012) [A11]	Exp1	8	62	43.9	Aquatic exercise	90	3	8	mBorg score
	Exp2	13	57	39.2	Floor exercise				
	Cont	11	71	45.1	Usual care				
Liu (2012) [A12]	Exp1	51	62	74.4	Health Qigong	60	3	24	FEV_1
	Exp2	32	61	75.3	Conventional PR				FEV_1/FVC
	Cont	35	62	75.3	Usual medical treat				
Petrovic (2012) [A13]	Exp	10	59	55.9	Inspiratory muscle training	-	daily	8	MIP
	Cont	10	60	54.8	No training				
Pleguezuelos (2013) [A14]	Exp	26	68	37.1	Whole body vibration	20	3	6	MEP, MIP
	Cont	25	71	32.0	No intervention				mBorg score
Wadell (2013) [A15]	Exp	17	67	48.0	Pulmonary rehabilitation	50	3	8	mBorg score
	Cont	24	66	48.0	Usual care				FEV_1, FEV_1/FVC
Farias (2014) [A16]	Exp	18	65	56.1	Aerobic walking	40-60	5	8	MEP
	Cont	16	71	51.0	Education				mBorg score
Mkacher (2015a) [A17]	Exp	32	61	40.2	Balance training+PR	30	3	24	mBorg score
	Cont	30	64	39.3	Standard PR				
Mkacher (2015b) [A18]	Exp	35	58	39.4	Balance training+PR	30	3	24	mBorg score
	Cont	33	61	38.6	Standard PR				
Pradella (2015) [A19]	Exp	29	62	43.9	Home-based PR	15-40	3	8	mBore score
	Cont	15	65	54.0	No intervention				
Duruturk (2016) [A20]	Exp1	15	61	58.4	Cycle exercise	20-30	3	6	MEP, MIP
	Exp2	14	61	57.2	Calisthenic exercise				FEV_1
	Cont	13	64	63.6	Education				FEV_1/FVC

Note. Cont = control group; Exp = experimental group; FEV_1 = forced expiratory volume in one second; FVC = forced volume capacity; MEP = maximal expiratory pressure; MIP = maximal inspiratory pressure; mBorg score = modified Borg score; PR = pulmonary rehabilitation; wks = weeks; yrs = years.

(Figure 3). The effect size of a PR program on the MIP resulted in an SMD of 0.53 (95% CI, 0.1–0.93), indicating a statistically significant improvement ($Z = 2.60$, $p = .009$).

In the subgroup analysis according to the type of program (Figure 3), the effect size of PE ($k = 5$) on the SMD was 0.33 (95% CI, 0.00–0.65), indicating a statistically significant improvement ($p = .048$). However, the effect size of RT ($k = 3$) resulted in an SMD of 1.06 (95% CI, −0.15 to 2.28), indicating no statistically significant improvement ($p = .087$). There was no significant difference in the effect size between PE and RT ($Q = 1.31$, $df = 1$, $p = .253$).

In the subgroup analysis according to duration of the program (Figure 3), the effect size of the 4- to 6-week group ($k = 4$) resulted in an SMD of 0.34 (95% CI, −0.02 to 0.69), indicating no statistically significant improvement ($p = .064$). The effect size of the 8- to 12-week group ($k = 4$) gave an SMD of 0.86 (95% CI, −0.01 to 1.78), which was not statistically significant ($p = .054$). There was no significant difference in the effect size between the 4- to 6-week and 8- to 12-week groups ($Q = 1.18$, $df = 1$, $p = .278$).

Effects of a PR program on dyspnea (modified Borg score)

The modified Borg score after the 6MWT was measured to assess dyspnea in 13 studies. The heterogeneity of these studies was low ($\chi^2 = 17.59$, $df = 15$, $p = .285$; $I^2 = 14.7\%$), and the effect size was calculated using a fixed effects model (Figure 4). In the meta-analysis, the overall effect size gave an SMD of −0.37 (95% CI, −0.52 to −0.22), indicating that participation in a PR program significantly reduced dyspnea in patients with COPD ($Z = -4.90$, $p < .001$).

Effects of a PR program on pulmonary function ($FEV_1\%_{pred}$, FEV_1/FVC%)

Six studies that measured FEV_1%pred showed no heterogeneity ($\chi^2 = 1.62$, $df = 7$, $p = .978$; $I^2 = 0\%$), and the effect size was

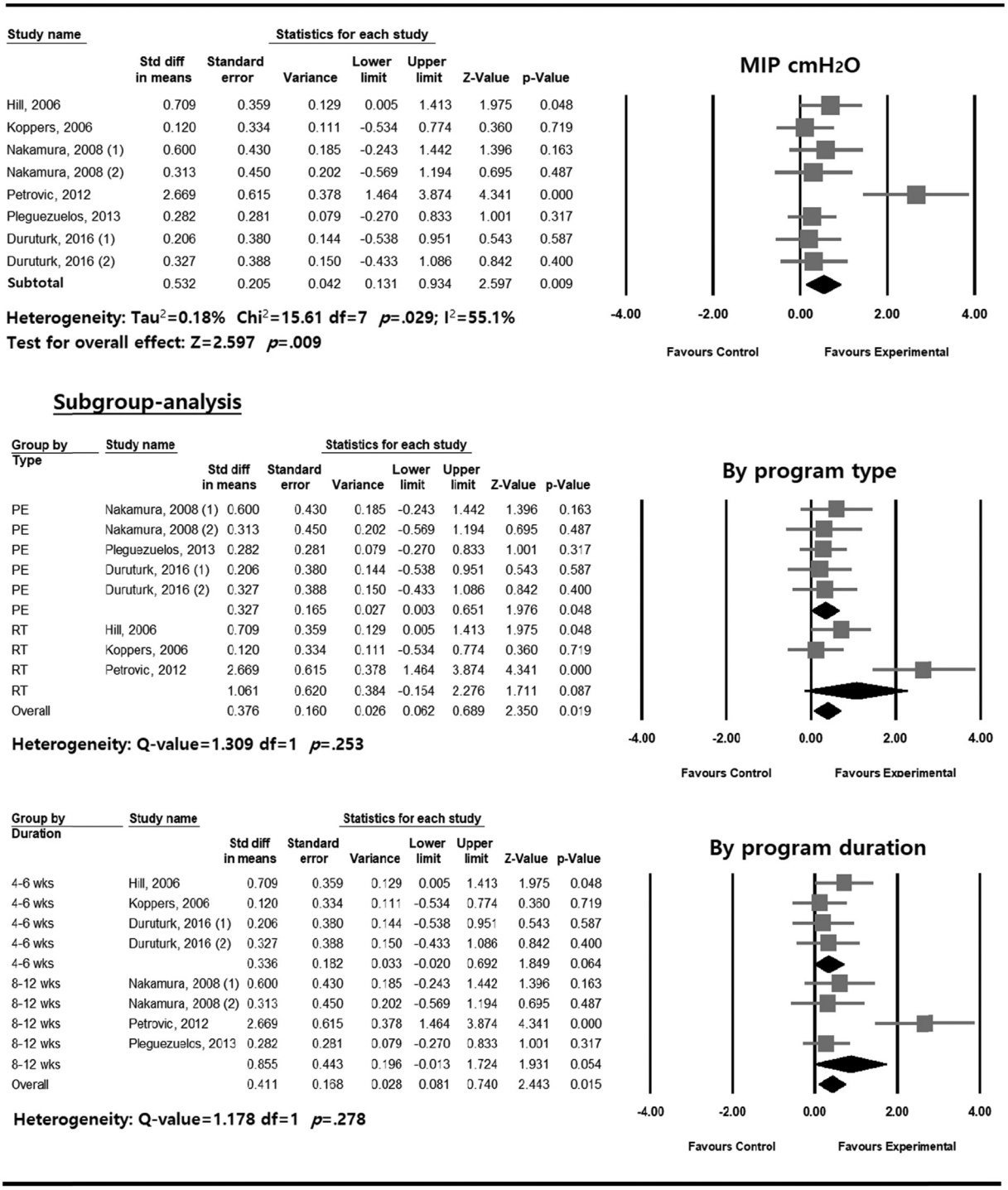


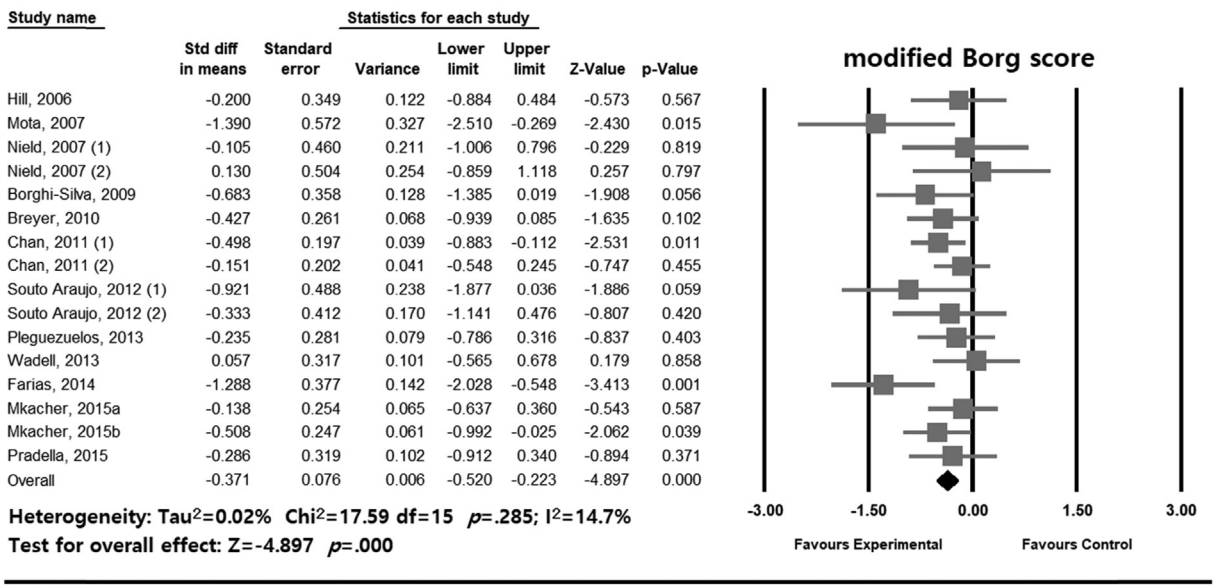
Figure 3. The effect of pulmonary rehabilitation on inspiratory muscle strength.
Note. MIP = maximal inspiratory pressure.

calculated using a fixed effects model (Figure 5). The overall effect size resulted in an SMD of 0.09 (95% CI, −0.12 to 0.30), indicating that the PR program did not significantly improve FEV_1%pred ($Z = 0.83$, $p = .406$).

The FEV_1/FVC% was measured in six studies. No heterogeneity was found between the studies ($\chi^2 = 6.11$, $df = 7$, $p = .527$; $I^2 = 0\%$), and the fixed effects model was used (Figure 5). The overall effect size resulted in an SMD of 0.04 (95% CI, −0.17 to 0.26), indicating that PR programs did not significantly improve the FEV_1/FVC% ($Z = 0.38$, $p = .702$).

Publication bias

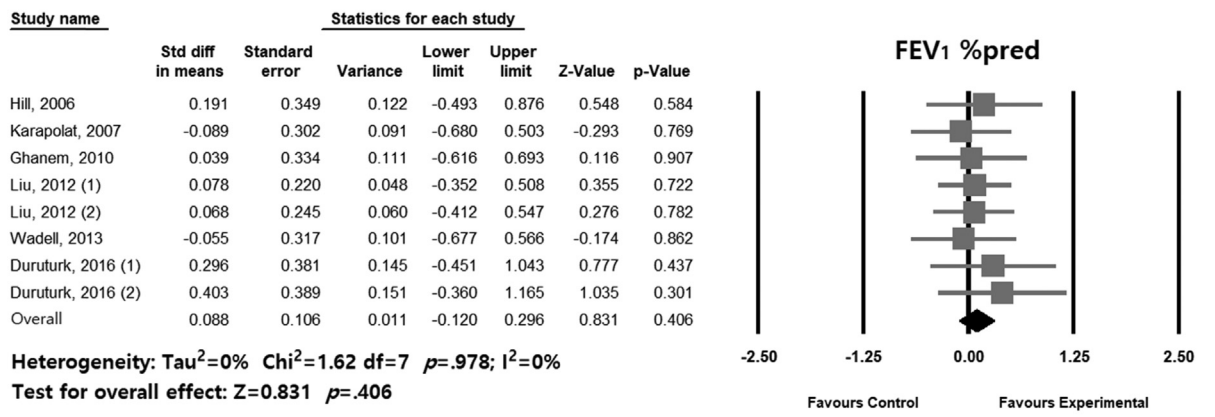
The effect size of the PR program revealed statistically significant changes in the MEP, MIP, and modified Borg score. Therefore, we examined the publication bias of the studies that included these



Study name	Std diff in means	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Hill, 2006	-0.200	0.349	0.122	-0.884	0.484	-0.573	0.567
Mota, 2007	-1.390	0.572	0.327	-2.510	-0.269	-2.430	0.015
Nield, 2007 (1)	-0.105	0.460	0.211	-1.006	0.796	-0.229	0.819
Nield, 2007 (2)	0.130	0.504	0.254	-0.859	1.118	0.257	0.797
Borghi-Silva, 2009	-0.683	0.358	0.128	-1.385	0.019	-1.908	0.056
Breyer, 2010	-0.427	0.261	0.068	-0.939	0.085	-1.635	0.102
Chan, 2011 (1)	-0.498	0.197	0.039	-0.883	-0.112	-2.531	0.011
Chan, 2011 (2)	-0.151	0.202	0.041	-0.548	0.245	-0.747	0.455
Souto Araujo, 2012 (1)	-0.921	0.488	0.238	-1.877	0.036	-1.886	0.059
Souto Araujo, 2012 (2)	-0.333	0.412	0.170	-1.141	0.476	-0.807	0.420
Pleguezuelos, 2013	-0.235	0.281	0.079	-0.786	0.316	-0.837	0.403
Wadell, 2013	0.057	0.317	0.101	-0.565	0.678	0.179	0.858
Farias, 2014	-1.288	0.377	0.142	-2.028	-0.548	-3.413	0.001
Mkacher, 2015a	-0.138	0.254	0.065	-0.637	0.360	-0.543	0.587
Mkacher, 2015b	-0.508	0.247	0.061	-0.992	-0.025	-2.062	0.039
Pradella, 2015	-0.286	0.319	0.102	-0.912	0.340	-0.894	0.371
Overall	-0.371	0.076	0.006	-0.520	-0.223	-4.897	0.000

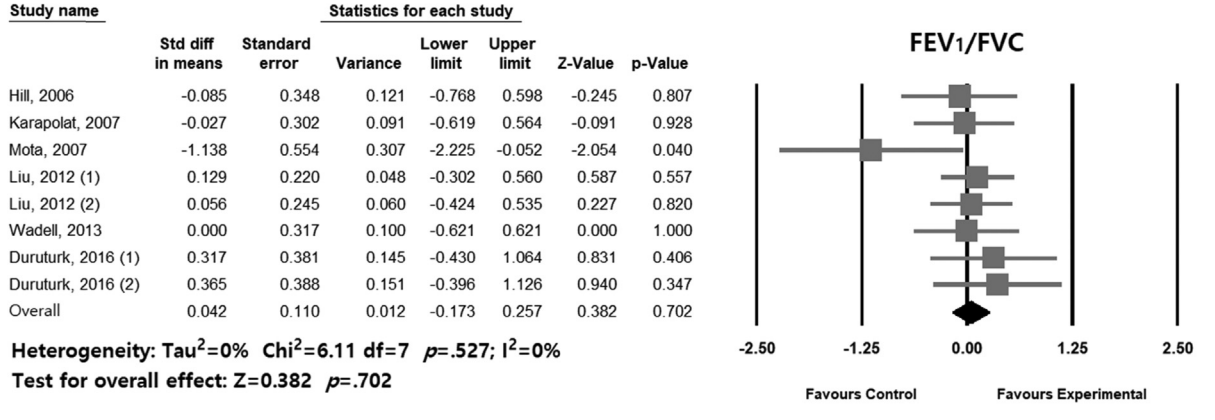
Heterogeneity: Tau^2=0.02% Chi^2=17.59 df=15 p=.285; I^2=14.7%
Test for overall effect: Z=-4.897 p=.000

Figure 4. The effect of pulmonary rehabilitation on dyspnea.



Study name	Std diff in means	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Hill, 2006	0.191	0.349	0.122	-0.493	0.876	0.548	0.584
Karapolat, 2007	-0.089	0.302	0.091	-0.680	0.503	-0.293	0.769
Ghanem, 2010	0.039	0.334	0.111	-0.616	0.693	0.116	0.907
Liu, 2012 (1)	0.078	0.220	0.048	-0.352	0.508	0.355	0.722
Liu, 2012 (2)	0.068	0.245	0.060	-0.412	0.547	0.276	0.782
Wadell, 2013	-0.055	0.317	0.101	-0.677	0.566	-0.174	0.862
Durutürk, 2016 (1)	0.296	0.381	0.145	-0.451	1.043	0.777	0.437
Durutürk, 2016 (2)	0.403	0.389	0.151	-0.360	1.165	1.035	0.301
Overall	0.088	0.106	0.011	-0.120	0.296	0.831	0.406

Heterogeneity: Tau^2=0% Chi^2=1.62 df=7 p=.978; I^2=0%
Test for overall effect: Z=0.831 p=.406



Study name	Std diff in means	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Hill, 2006	-0.085	0.348	0.121	-0.768	0.598	-0.245	0.807
Karapolat, 2007	-0.027	0.302	0.091	-0.619	0.564	-0.091	0.928
Mota, 2007	-1.138	0.554	0.307	-2.225	-0.052	-2.054	0.040
Liu, 2012 (1)	0.129	0.220	0.048	-0.302	0.560	0.587	0.557
Liu, 2012 (2)	0.056	0.245	0.060	-0.424	0.535	0.227	0.820
Wadell, 2013	0.000	0.317	0.100	-0.621	0.621	0.000	1.000
Durutürk, 2016 (1)	0.317	0.381	0.145	-0.430	1.064	0.831	0.406
Durutürk, 2016 (2)	0.365	0.388	0.151	-0.396	1.126	0.940	0.347
Overall	0.042	0.110	0.012	-0.173	0.257	0.382	0.702

Heterogeneity: Tau^2=0% Chi^2=6.11 df=7 p=.527; I^2=0%
Test for overall effect: Z=0.382 p=.702

Figure 5. The effect of pulmonary rehabilitation on pulmonary function.
Note. FEV_1 = forced expiratory volume in one second; FVC = forced volume capacity.

three variables. After assessing the degree of symmetry using a funnel plot, Egger's regression test was performed to evaluate whether the asymmetry was statistically significant. The studies that included the modified Borg score showed no publication bias ($p = .307$), but those that included MEP and MIP did show publication bias ($p = .034$).

Discussion

In this meta-analysis, we evaluated the ability of a PR program to improve respiratory muscle strength in patients with COPD. We found a significant improvement in inspiratory and expiratory muscle strength as well as in perceived dyspnea but no significant improvement in pulmonary function. Furthermore, there was no significant difference between PE and RT in the subgroup analysis of the RCTs included in this meta-analysis, suggesting that both PE and RT are effective for symptom relief in patients with COPD.

We analyzed the effect of PR on expiratory muscle strength and found that MEP had a high effect size. Programs with a more-than-moderate effect size included aerobic exercise [A6, A16], cycling and callisthenic exercise [A20], and expiratory muscle training [A4]. In these results, PE and RT programs could be performed to improve respiratory muscle movement and expiratory muscle weakness in patients with COPD. Expiratory muscle strength is essential for coughing and clearance of the airway; however, increased airway resistance and decreased elastic recoil in patients with COPD lead to a vicious cycle of constant overload of the expiratory muscles [17]. Therefore, increasing expiratory muscle strength would reduce expiratory muscle overload, allowing the patient to breathe more comfortably and facilitating effective clearance of the airway. Our results are consistent with those of another meta-analysis that found RT to be effective in increasing the MEP in patients with COPD [11].

The overall effect size of MIP was moderate. Programs that included RT [A1, A13] and aerobic exercise [A6] showed a higher effect size. Aerobic exercise helps to strengthen not only the expiratory muscles, as mentioned previously, but also the inspiratory muscles. Aerobic exercise also improves the patient's oxidative capacity, resulting in less alveolar ventilation during exercise [18], which may reduce hyperinflation of the lungs and improve respiratory muscle strength. Increased inspiratory muscle strength is associated with improvements in exercise capacity, quality of life, and dyspnea. Most patients with COPD have weakened inspiratory muscles [12], so it is important to include inspiratory muscle strengthening program in a PR program. Meanwhile, according to one meta-analysis of studies of respiratory muscle training, the effect on MIP depended on the training method used (strength vs. endurance) [19]. Therefore, applying this strategy in practice would require selection of a program suitable for the individual patient.

Dyspnea was measured by assessment of the modified Borg score after the 6MWT. The reason for choosing the 6MWT for measurement of the modified Borg score is that it correlates with pulmonary function and can reflect changes therein in patients with COPD [20,21]. A meta-analysis of publications that included the Borg score showed that a PR program significantly improved dyspnea in patients with COPD. Programs that had an above-moderate effect size included aerobic exercise [A7,A16], tai-chi qigong [A10], aquatic exercise [A11], balance training [A18], and expiratory muscle training [A4], all of which were performed as a single strategy. Another meta-analysis of PR found that a single strategy, such as RT [22] or upper extremity exercise [23], improved dyspnea, which is similar to the findings of the present study. Therefore, even a single strategy can help improve dyspnea in patients with COPD.

The effect size of a PR program on FEV_1%pred was very low. The FEV_1 is the volume expired in the first second of maximal expiration after a maximal inspiration and measures how rapidly the lungs can be emptied, whereas the FEV_1%pred is used to compare an FEV_1 recording for a given patient against the average value for healthy people of the same age [1] and is an indicator of the severity of COPD; thus, a lower value indicates a worse prognosis. An interval of at least 12 months is recommended for follow-up of FEV_1 [1]. However, the duration of the studies included in our meta-analysis ranged from 6 to 24 weeks, which is far less than the follow-up interval recommended by the GOLD; therefore, it appears that the programs in our meta-analysis had no significant effect on FEV_1.

The FEV_1/FVC% is another indicator of pulmonary function; this is FEV_1 expressed as a proportion of the FVC and provides a clinically useful index of airflow limitation [1]. In this study, the overall effect size was very low. However, the studies included in our meta-analysis were performed in patients with more-than-moderate disease severity (stage II) and with program duration of 5–24 weeks, so it might have been difficult to improve pulmonary function in the short term. Mota et al [17] found that a 5-week RT program did not result in a significant increase in FEV_1/FVC% when compared with the control group, but lung hyperinflation tended to be somewhat reduced in the experimental group. This resulted in improvement of the air-trapping (abnormal air retention) phenomenon characteristic of patients with COPD. The participants in that study [15] had stage IV COPD, and the duration of the program was less than the 6 weeks recommended by the GOLD, which suggests that pulmonary function could be improved by continuous long-term RT.

To summarize, PE and RT programs increased respiratory muscle strength and reduced dyspnea in patients with COPD but did not improve pulmonary function. However, considering that the goal of treatment for COPD is to alleviate symptoms and prevent worsening [1], PE and RT are both effective programs for improvement of dyspnea, which is a major symptom in patients with COPD. In our meta-analysis, although there was no statistically significant effect on pulmonary function, use of PR programs improved exercise tolerance, which would be expected to lead to improved exercise capacity. The GOLD has suggested that even single-type PR programs are beneficial for patients with COPD [1], and our meta-analysis also showed that single PE or RT programs are valuable in patients with the disease. These results will help us to select appropriate programs tailored to the needs of the individual and the facilities available. The effectiveness of a PR program decreases between 6 and 12 months after its completion [24], so it is important that the PR program be implemented lifelong, irrespective of what the program entails. In addition, PR programs should be selectively tailored to the severity of the patient's disease, be easily accessible, and be able to be performed by the patients themselves.

The main strength of this study is that it analyzed the effectiveness of different types of PR programs. Comparing the effects of various types of programs can help to develop and implement programs according to the needs of patients and type of institution. This study is also the first to analyze the effects of PE programs on respiratory muscle strength, so it would be expected to be the basis for development of PR programs to improve respiratory muscle strength in patients with COPD. In nursing practice, we suggest that PE or RT be included to increase the effectiveness of a rehabilitation program for patients with COPD.

However, this research also has some limitations. First, the search was restricted to a period of 10 years. This was because our rapidly evolving medical environment may affect patient's health outcomes. Moreover, we only included studies that were published

in English. Finally, there was considerable variation in the severity of disease, type and duration of intervention, and methodologic quality of the studies included, so caution is needed when interpreting our study findings.

Conclusion

The findings of this meta-analysis show that PR programs help to improve respiratory muscle strength and subjective symptoms of dyspnea in patients with COPD. Strategies need to be developed to select suitable PR programs for these patients, and future studies should evaluate the long-term effects of such programs on pulmonary function.

Conflicts of interest

There are no conflicts of interest to declare.

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Appendix. References for Studies included in Table 1

A1. Hill K, Jenkins SC, Philippe DL, Cecins N, Shepherd KL, Green DJ, et al. High-intensity inspiratory muscle training in COPD. Eur Respir J. 2006;27(6):1119–28. https://doi.org/10.1183/09031936.06.00105205

A2. Koppers RJ, Vos PJ, Boot CR, Folgering HT. Exercise performance improves in patients with COPD due to respiratory muscle endurance training. Chest. 2006;129(4):886–92. https://doi.org/10.1378/chest.129.4.886

A3. Karapolat H, Atasever A, Atamaz F, Kirazlı Y, Elmas F, Erdinç E. Do the benefits gained using a short-term pulmonary rehabilitation program remain in COPD patients after participation? Lung. 2007;185(4):221–5. https://doi.org/10.1007/s00408-007-9011-4

A4. Mota S, Güell R, Barreiro E, Solanes I, Ramírez-Sarmiento A, Orozco-Levi M, et al. Clinical outcomes of expiratory muscle training in severe COPD patients. Respir Med. 2007;101(3):516–24. https://doi.org/10.1016/j.rmed.2006.06.024

A5. Nield MA, Soo Hoo GW, Roper JM, Santiago S. Efficacy of pursed-lips breathing: a breathing pattern retraining strategy for dyspnea reduction. J Cardiopulm Rehabil Prev. 2007;27(4):237–44. https://doi.org/10.1097/01.HCR.0000281770.82652.cb

A6. Nakamura Y, Tanaka K, Shigematsu R, Nakagaichi M, Inoue M, Homma T. Effects of aerobic training and recreational activities in patients with chronic obstructive pulmonary disease. Int J Rehabil Res. 2008;31(4):275–83. https://doi.org/10.1097/MRR.0b013e3282fc0f81

A7. Borghi-Silva A, Arena R, Castello V, Simões RP, Martins LE, Catai AM, et al. Aerobic exercise training improves autonomic nervous control in patients with COPD. Respir Med. 2009;103(10):1503–10. https://doi.org/10.1016/j.rmed.2009.04.015

A8. Breyer MK, Breyer-Kohansal R, Funk GC, Dornhofer N, Spruit MA, Wouters EF, et al. Nordic walking improves daily physical activities in COPD: a randomised controlled trial. Respir Res. 2010;11:112. https://doi.org/10.1186/1465-9921-11-112

A9. Ghanem M, Elaal EA, Mehany M, Tolba K. Home-based pulmonary rehabilitation program: Effect on exercise tolerance and quality of life in chronic obstructive pulmonary disease patients. Ann Thorac Med. 2010;5(1):18–25. https://doi.org/10.4103/1817-1737.58955

A10. Chan AW, Lee A, Suen LK, Tam WW. Tai chi Qigong improves lung functions and activity tolerance in COPD clients: a single blind, randomized controlled trial. Complement Ther Med. 2011;19(1):3–11. https://doi.org/10.1016/j.ctim.2010.12.007

A11. de Souto Araujo ZT, de Miranda Silva Nogueira PA, Cabral EE, de Paula Dos Santos L, da Silva IS, Ferreira GM. Effectiveness of low-intensity aquatic exercise on COPD: a randomized clinical trial. Respir Med. 2012;106(11):1535–43. https://doi.org/10.1016/j.rmed.2012.06.022

A12. Liu XD, Jin HZ, Ng BH, Gu YH, Wu YC, Lu G. Therapeutic effects of qigong in patients with COPD: A randomized controlled trial. Hong Kong J Occup Ther. 2012;22(1):38–46. https://doi.org/10.1016/j.hkjot.2012.06.002

A13. Petrovic M, Reiter M, Zipko H, Pohl W, Wanke T. Effects of inspiratory muscle training on dynamic hyperinflation in patients with COPD. Int J Chron Obstruct Pulmon Dis. 2012;7:797–805. https://doi.org/10.2147/COPD.S23784

A14. Pleguezuelos E, Pérez ME, Guirao L, Samitier B, Costea M, Ortega P, et al. Effects of whole body vibration training in patients with severe chronic obstructive pulmonary disease. Respirology. 2013;18(6):1028–34. https://doi.org/10.1111/resp.12122

A15. Wadell K, Webb KA, Preston ME, Amornputtisathaporn N, Samis L, Patelli J, et al. Impact of pulmonary rehabilitation on the major dimensions of dyspnea in COPD. COPD. 2013;10(4):425–35. https://doi.org/10.3109/15412555.2012.758696

A16. Farias CC, Resqueti V, Dias FA, Borghi-Silva A, Arena R, Fregonezi GA. Costs and benefits of pulmonary rehabilitation in chronic obstructive pulmonary disease: a randomized controlled trial. Braz J Phys Ther. 2014;18(2):165–73. https://doi.org/10.1590/S1413-35552012005000151

A17. Mkacher W, Mekki M, Chaieb F, Tabka Z, Trabelsi Y. Balance training in pulmonary rehabilitation: effects on psychosocial outcomes. J Cardiopulm Rehabil Prev. 2015;35(4):278–85. https://doi.org/10.1097/HCR.0000000000000122

A18. Mkacher W, Mekki M, Tabka Z, Trabelsi Y. Effect of 6 months of balance training during pulmonary rehabilitation in patients with COPD. J Cardiopulm Rehabil Prev. 2015;35(3):207–13. https://doi.org/10.1097/HCR.0000000000000109

A19. Pradella CO, Belmonte GM, Maia MN, Delgado CS, Luise AP, Nascimento OA, et al. Home-based pulmonary rehabilitation for subjects with COPD: a randomized study. Respir Care. 2015;60(4):526–32. https://doi.org/10.4187/respcare.02994

A20. Duruturk N, Arıkan H, Ulubay G, Tekindal MA. A comparison of calisthenic and cycle exercise training in chronic obstructive pulmonary disease patients: a randomized controlled trial. Expert Rev Respir Med. 2016;10(1):99–108. https://doi.org/10.1586/17476348.2015.1126419

References

1. Global Initiative for Chronic Obstructive Lung Disease (GOLD). Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease[Internet]. 2016 [Cited 2016 Nov 23]. Available from: http://www.goldcopd.org/
2. Spruit MA, Singh SJ, Garvey C, ZuWallack R, Nici L, Rochester C, et al. An official American Thoracic Society/European Respiratory Society statement: key concepts and advances in pulmonary rehabilitation. Am J Respir Crit Care Med. 2013;188(8):e13–64. https://doi.org/10.1164/rccm.201309-1634ST
3. Lisspers K, Larsson K, Johansson G, Janson C, Costa-Scharplatz M, Gruenberger JB, et al. Economic burden of COPD in a Swedish cohort: the

ARCTIC study. Int J Chronic Obstr Pulm Dis. 2018;13:275-85. https://doi.org/10.2147/COPD.S149633
4. Haraguchi M, Nakamura H, Sasaki M, Miyazaki M, Chubachi S, Takahashi S, et al. Determinants of chronic obstructive pulmonary disease severity in the late-elderly differ from those in younger patients. BMC Res Notes. 2016;9:7. https://doi.org/10.1186/s13104-015-1810-8
5. de Andrade AD, Silva TN, Vasconcelos H, Marcelino M, Rodrigues-Machado MG, Filho VC, et al. Inspiratory muscular activation during threshold therapy in elderly healthy and patients with COPD. J Electromyogr Kinesiol. 2005;15(6):631–9. https://doi.org/10.1016/j.jelekin.2005.06.002
6. Paulin E, Yamaguti WP, Chammas MC, Shibao S, Stelmach R, Cukier A, et al. Influence of diaphragmatic mobility on exercise tolerance and dyspnea in patients with COPD. Respir Med. 2007;101(10):2113–8. https://doi.org/10.1016/j.rmed.2007.05.024
7. Vilaró J, Ramirez-Sarmiento A, Martínez-Llorens JM, Mendoza T, Alvarez M, Sánchez-Cayado N, et al. Global muscle dysfunction as a risk factor of readmission to hospital due to COPD exacerbations. Respir Med. 2010;104(12):1896–902. https://doi.org/10.1016/j.rmed.2010.05.001
8. Liu XL, Tan JY, Wang T, Zhang Q, Zhang M, Yao LQ, et al. Effectiveness of home-based pulmonary rehabilitation for patients with chronic obstructive pulmonary disease: a meta-analysis of randomized controlled trials. Rehabil Nurs. 2014;39(1):36–59. https://doi.org/10.1002/rnj.112
9. Hill K, Jenkins SC, Philippe DL, Cecins N, Shepherd KL, Green DJ, et al. High-intensity inspiratory muscle training in COPD. Eur Respir J. 2006;27(6):1119–28. https://doi.org/10.1183/09031936.06.00105205
10. Nield MA, Soo Hoo GW, Roper JM, Santiago S. Efficacy of pursed-lips breathing: a breathing pattern retraining strategy for dyspnea reduction. J Cardiopulm Rehabil Prev. 2007;27(4):237–44. https://doi.org/10.1097/01.HCR.0000281770.82652.cb
11. Neves LF, Reis MH, Plentz RD, Matte DL, Coronel CC, Sbruzzi G. Expiratory and expiratory plus inspiratory muscle training improves respiratory muscle strength in subjects with COPD: systematic review. Respir Care. 2014;59(9):1381–8. https://doi.org/10.4187/respcare.02793
12. O'Donnell DE, Elbehairy AF, Berton DC, Domnik NJ, Neder JA. Advances in the evaluation of respiratory pathophysiology during exercise in chronic lung diseases. Front Physiol. 2017;8:82. https://doi.org/10.3389/fphys.2017.00082
13. National Institute for Clinical Excellence(NICE). Chronic obstructive pulmonary disease in over 16s: diagnosis and management[Internet]. London, UK: NICE; 2010 [cited 2016 Nov 20]. Available from: https://www.nice.org.uk/guidance/cg101
14. Amin S, Abrazado M, Quinn M, Storer TW, Tseng CH, Cooper CB. A controlled study of community-based exercise training in patients with moderate COPD. BMC Pulm Med. 2014;14:125. https://doi.org/10.1186/1471-2466-14-125
15. Higgins JP, Thompson SG. Quantifying heterogeneity in a meta-analysis. Stat Med. 2002;21(11):1539–58. https://doi.org/10.1002/sim.1186
16. Liberati A, Altman DG, Tetzlaff J, Mulrow C, Gøtzsche PC, Ioannidis JP, et al. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: explanation and elaboration. Ann Intern Med. 2009;151(4):W65–94. https://doi.org/10.1371/journal.pmed.1000100
17. Mota S, Güell R, Barreiro E, Solanes I, Ramírez-Sarmiento A, Orozco-Levi M, et al. Clinical outcomes of expiratory muscle training in severe COPD patients. Respir Med. 2007;101(3):516–24. https://doi.org/10.1016/j.rmed.2006.06.024
18. Nici L, Donner C, Wouters E, Zuwallack R, Ambrosino N, Bourbeau J, et al. American Thoracic Society/European Respiratory society statement on pulmonary rehabilitation. Am J Respir Crit Care Med. 2006;173(12):1390–413. https://doi.org/10.1164/rccm.200508-1211ST
19. Gosselink R, De Vos J, van den Heuvel SP, Segers J, Decramer M, Kwakkel G. Impact of inspiratory muscle training in patients with COPD: what is the evidence? Eur Respir J. 2011;37(2):416–25. https://doi.org/10.1183/09031936.00031810
20. Polkey MI, Spruit MA, Edwards LD, Watkins ML, Pinto-Plata V, Vestbo J, et al. Six-minute-walk test in chronic obstructive pulmonary disease: minimal clinically important difference for death or hospitalization. Am J Respir Crit Care Med. 2013;187(4):382–6. https://doi.org/10.1164/rccm.201209-1596OC
21. Spruit MA, Polkey MI, Celli B, Edwards LD, Watkins ML, Pinto-Plata V, et al. Predicting outcomes from 6-minute walk distance in chronic obstructive pulmonary disease. J Am Med Dir Assoc. 2012;13(3):291–7. https://doi.org/10.1016/j.jamda.2011.06.009
22. Geddes EL, O'Brien K, Reid WD, Brooks D, Crowe J. Inspiratory muscle training in adults with chronic obstructive pulmonary disease: an update of a systematic review. Respir Med. 2008;102(12):1715–29. https://doi.org/10.1016/j.rmed.2008.07.005
23. McKeough ZJ, Velloso M, Lima VP, Alison JA. Upper limb exercise training for COPD. Cochrane Database Syst Rev. 2016;11:CD011434. https://doi.org/10.1002/14651858.CD011434.pub2
24. Egan C, Deering BM, Blake C, Fullen BM, McCormack NM, Spruit MA, et al. Short term and long term effects of pulmonary rehabilitation on physical activity in COPD. Respir Med. 2012;106(12):1671–9. https://doi.org/10.1016/j.rmed.2012.08.016