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Impact of Resistance Training in Subjects With COPD: A Systematic Review and Meta-Analysis

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BACKGROUND: The goal of this study was to evaluate the effects of resistance training on subjects with COPD. METHODS: We performed a systematic search in MEDLINE, PubMed, Embase, CINAHL, Elsevier ScienceDirect, EBM Reviews, Cochrane Central Register of Controlled Trials, and ClinicalTrials.gov and also of leading respiratory journals for randomized controlled trials on COPD treatment for ≥ 4 weeks with resistance training compared with non-exercise control or with combined resistance and endurance training compared with endurance training alone. Data from these studies were pooled to calculate odds ratio and weighted mean differences (WMDs) with 95% CI. RESULTS: Eighteen trials with 750 subjects with advanced COPD met the inclusion criteria. There were 2 primary and 5 secondary outcomes. Compared with non-exercise control, resistance training led to significant improvements in the dyspnea domain of the Chronic Respiratory Disease Questionnaire (WMD of 0.59, 95% CI 0.26–0.93, $I^2 = 0\%$, $P < .001$), skeletal muscle strength, and percent-of-predicted FEV_1 (WMD of 6.88%, 95% CI 0.41–13.35%, $I^2 = 0\%$, $P = .04$). The combination of resistance and endurance training significantly improved the St George Respiratory Questionnaire total score (WMD of −7.44, 95% CI −12.62 to −2.25, $I^2 = 0\%$, $P = .005$), each domain score, and skeletal muscle strength. There were no significant differences in 6-min walk distance, 6-min pegboard and ring test, maximum exercise work load, and maximum oxygen consumption between the 2 groups. There were no reports of adverse events related to resistance-training intervention. CONCLUSIONS: Resistance training can be successfully performed alone or in conjunction with endurance training without increased adverse events during pulmonary rehabilitation in COPD. *Key words: chronic obstructive pulmonary disease; resistance training; meta-analysis.* [Respir Care 0;0(0):1–•. © 0 Daedalus Enterprises]

Introduction

COPD is a major cause of chronic morbidity and mortality throughout the world and is projected to be the third most common cause of death by 2020.[1] Exercise intolerance is a cardinal complaint of patients with COPD. Skeletal muscle dysfunction is a common extrapulmonary manifestation of COPD.[2] Studies suggest that skeletal muscle dysfunction is associated with exercise limitation and health-care utilization.[3,4] Skeletal muscle dysfunction is

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also an independent predictor of morbidity and mortality in COPD,[5] irrespective of the degree of air-flow limitation. Muscle changes observed in patients with COPD include reductions in type I fibers, atrophy of type I and II fibers, reduced capillarity, and altered metabolic enzyme levels.[6] The pathogenic mechanisms of skeletal muscle dysfunction are considered to be related to multiple factors, including nutritional abnormalities, muscle disuse, systemic inflammation, medical use of corticosteroids, tissue hypoxia, and hypercapnia.[6,7]

Progressive resistance training provides a training modality for increasing peripheral muscle strength in COPD. Ortega et al[8] reported that the increase in muscle strength obtained after resistance training is higher than that obtained after endurance training. In addition, resistance training evokes less dyspnea during exercise,[9] thereby making this strategy easier to tolerate than endurance training.[10,11] A combination of resistance and endurance training in COPD has demonstrated a greater improvement in peripheral muscle function compared with endurance training alone.[12]

In the past few years, there have been several systematic reviews on the efficacy of resistance training.[13-16] However, previous meta-analyses focused on whether resistance training is effective in improving skeletal muscle strength and lung function, whereas little data are so far available on other clinically relevant outcomes, such as quality of life, dyspnea, and exercise capacity. Moreover, previous analyses[13-15] included both randomized controlled trials (RCTs) and case-control trials, which potentially introduced bias because the real-world outcomes of pulmonary rehabilitation can be affected by a number of social and cultural factors. Finally, many RCTs have been published since the previous meta-analysis conducted by O'Shea et al[14], offering input for more extensive analysis.[17-23] The aim of this meta-analysis was to investigate the effects of resistance training alone or combined with endurance training on clinically relevant rehabilitation outcomes in advanced COPD, including quality of life, dyspnea, functional exercise capacity, maximum exercise capacity, skeletal muscle function, lung function, and adverse events.

QUICK LOOK

Current knowledge

COPD is a major cause of chronic morbidity and mortality throughout the world and is projected to be the third most common cause of death by 2020. Skeletal muscle dysfunction is associated with exercise limitation and increased health-care utilization. The impact of respiratory muscle training in COPD has met with conflicting results.

What this paper contributes to our knowledge

A meta-analysis showed that dyspnea scale scores, skeletal muscle strength, and lung function improved following resistance training. Although skeletal muscle strength and quality of life improved following combined resistance and endurance training, this failed to translate into improved exercise capacity. The data suggest that resistance training can be successfully performed alone or in conjunction with endurance training without increasing adverse events during pulmonary rehabilitation.

Methods

Data Sources

We searched MEDLINE, PubMed, Embase, CINAHL, Elsevier ScienceDirect, EBM Reviews, Cochrane Central Register of Controlled Trials, ClinicalTrials.gov and leading respiratory journals and conference abstracts from January 1980 to October 2013 to identify related articles. We also searched the Science Citation Index database (Web of Science) and PubMed using the related-articles function by entering all included studies. Reference lists from original and review articles were also reviewed to identify additional relevant studies. All publications and abstracts in English were considered. Moreover, an additional search in May 2014 was performed to identify additional trials that fulfilled our search criteria.

The search terms were as follows: COPD, chronic obstructive pulmonary disease, chronic obstructive lung disease, chronic airways limitation, chronic airways obstruction, chronic bronchitis, and pulmonary emphysema. These terms were used in various combinations with strength training, strength exercise, resistance training, resistance exercise, weight training, weight lifting, aerobic training, aerobic exercise, endurance training, endurance exercise, exercise training, and pulmonary rehabilitation.

Study Selection

The inclusion criteria were: (1) subjects with stable moderate-to-very-severe COPD without other lung diseases; (2) RCTs comparing resistance training with non-exercise control or combined resistance and endurance training with endurance training alone; (3) exercise duration of at least 4 weeks; (4) outcomes including health-related quality of life, dyspnea scale, functional exercise capacity, maximum exercise capacity, skeletal muscle function, and pulmonary function; (5) human studies; and (6) English language.

Quality Assessment

The methodological quality of each study was assessed by the modified Jadad scale,[24] which scores trials according to randomization, concealment of allocation, double blinding, withdrawals, and dropouts.

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Data Extraction

Data extraction was based on reported statistics (means, SD, and SE). Two reviewers (WL and JC) independently extracted data from the selected studies. If a disagreement arose, all authors conferred until a consensus was achieved. Authors of a publication were contacted if only the abstract was available or data were missing. Supplemental data for included studies were reviewed to minimize selective reporting of secondary end points in published manuscripts. Primary outcomes were changes from baseline in health-related quality of life and dyspnea scale. Secondary outcomes included changes from baseline in skeletal muscle function, functional exercise capacity, maximum exercise capacity, FEV_1, and adverse events.

Statistical Analysis

RevMan 5.2 (The Nordic Cochrane Centre, The Cochrane Collaboration, Copenhagen, Denmark) was used to analyze all collected data. Fixed-effects odds ratios for dichotomous outcomes and weighted mean differences (WMDs) for continuous outcomes, with corresponding 95% CI, were calculated for individual trials. The trials were pooled using fixed-effects odds ratios or WMDs as appropriate. I^2 was calculated to efficiently test heterogeneity, with values of 25, 50 and 75% considered to represent low, moderate, and high heterogeneity, respectively. The differences between resistance-training groups and non-exercise control groups or resistance-and-endurance-training groups and endurance-training-alone groups were pooled using a fixed-effects model when there was no evidence of significant heterogeneity in the analysis. If significant heterogeneity was found, a random-effects model was used.[25]

Results

Search Results

The process used for searching and selecting trials is presented in Figure 1. Of the 3,562 English articles screened, we excluded 3,544 that were not relevant, had incomplete or duplicate data, or were not RCTs. Eighteen parallel RCTs involving 750 subjects met the inclusion criteria and were selected for analysis. Thirteen of the 18 included trials compared resistance training with non-exercise control, and 4 trials compared combined resistance and endurance training with endurance training alone. One trial compared resistance training, endurance training, combined resistance and endurance training, and non-exercise control. The main characteristics of these trials are listed in Tables 1 and 2. All data adopted in this study were published openly in various journals.

Quality Assessment

The methodological quality of the included studies is provided in Table 2. There were 8 studies with Jadad scores of ≥ 3 points. Ten trials scored poorly according to the modified Jadad scale. Eight trials reported blinding methods. Of these, 6 trials reported blinding of the investigators or outcome assessors, and 2 trials reported blinding of both outcome assessors and subjects with COPD. Per-protocol analysis was used in 16 trials, and intention-to-treat analysis was used in 2 trials.

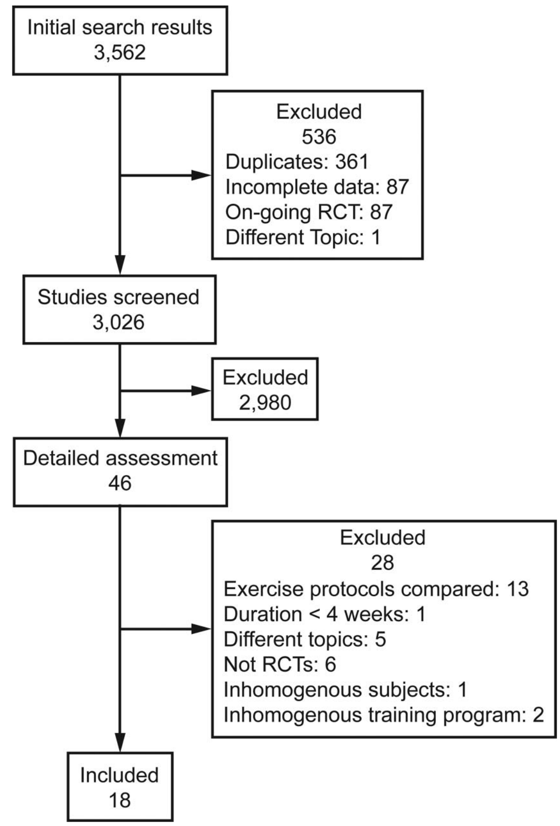

Fig. 1. Flow chart. RCT = randomized controlled trial.

Primary Outcomes

Chronic Respiratory Disease Questionnaire Score

Resistance-Training Group Versus Non-Exercise Control Group. Three studies reported dyspnea domain scores using the Chronic Respiratory Disease Questionnaire (CRQ).[18,19,32] The results of each study showed significant improvements in CRQ dyspnea domain scores in the resistance-training groups. The overall analysis showed statistically significant improvements in CRQ dyspnea domain scores in the resistance-training groups (WMD of 0.59, 95% CI 0.26–0.93, $I^2 = 0\%$, $P < .001$). The improvement in dyspnea domain scores achieved a minimum clinically important difference of 0.5 units.[37] Two included trials reported CRQ fatigue domain scores, whereas the pooled analysis showed no significant improvements in fatigue domain scores (WMD of 0.26, 95% CI −0.11 to

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Table 1. Subject Characteristics

Study	Group (n)	Age (y)*	Males (%)	BMI (kg/m^2)*	FEV_1 (% predicted)*	FEV_1/FVC*	Inclusion Criteria	Exclusion Criteria
Alexander[26]	RT: n = 10 Control: n = 10	RT: 65.0 ± 8.0 Control: 73.0 ± 9.0	Average: 70.0	RT: 24.6 ± 5.5 Control: 28.5 ± 5.0	RT: 29.8 ± 13.4 Control: 38.6 ± 14.5	RT: 0.41 ± 0.10 Control: 0.46 ± 0.12	Diagnosis of COPD, FEV_1 < 60% of normal predicted, no previous pulmonary rehabilitation	Medical, physical, or cognitive impairment that would preclude participation in evaluation and training protocols
Benton and Wagner[17]	RT: n = 10 Control: n = 9	RT: 71.0 ± 3.7 Control: 69.9 ± 6.3	RT: 40.0 Control: 11.0	RT: 28.2 ± 5.6 Control: 26.1 ± 3.9	RT: 42.0 ± 8.5 Control: 32.8 ± 15.4	RT: 0.52 ± 0.13 Control: 0.39 ± 0.10	Diagnosis of severe COPD according to GOLD, no previous rehabilitation experience	ND
Casaburi[27]	RT: n = 12 Control: n = 12	RT: 68.9 ± 9.8 Control: 67.7 ± 8.7	ND	ND	RT: 35.9 ± 9.2 Control: 38.6 ± 12.1	RT: 0.36 ± 0.07 Control: 0.41 ± 0.10	Stable COPD, 55–80 y old, FEV_1 ≤ 60% of normal predicted, FEV_1/FVC ≤ 0.60	Significant cardiovascular or orthopedic impairments; < 75% or > 130% of ideal body weight; history of benign prostatic hypertrophy, prostate cancer, or serum prostate-specific antigen > 4 μg/L; hemoglobin > 16 g/dL
Clark[28]	RT: n = 26 Control: n = 17	RT: 51.0 ± 10.0 Control: 46.0 ± 11.0	RT: 58.0 Control: 59.0	RT: 26.0 ± 4.0 Control: 26.0 ± 4.0	RT: 76.0 ± 23.0 Control: 79.0 ± 23.0	ND	Diagnosis of COPD	Hypoxemia or hypercapnia at rest or during exercise; long-term oral steroid therapy, > 65 y old, any other significant concomitant illness such as unstable ischemic heart disease or severe osteoarthritis
Covey[18]	RT: n = 43 Control: n = 21	RT: 70.4 ± 8.7 Control: 71.5 ± 7.5	RT: 79.1 Control: 85.7	RT: 28.1 ± 6.5 Control: 28.2 ± 6.4	RT: 57.6 ± 18.6 Control: 58.2 ± 16.0	ND	Diagnosis of moderate-to-severe COPD according to GOLD, ≥ 45 y old, no exacerbations in previous 2 m or recent change in medical therapy, experienced dyspnea with upper-body activity	Other major health problems
Hoff[29]	RT: n = 6 Control: n = 6	RT: 62.8 ± 3.4 Control: 60.6 ± 7.3	Average: 67.0	RT: 32.9 ± 8.1 Control: 39.5 ± 15.7	RT: 49.9 ± 11.3 Control: 45.2 ± 14.7	ND	Diagnosis of COPD according to GOLD, 40–70 y old, FEV_1/FVC < 0.70, FEV_1 < 60% of normal predicted	History of cardiovascular disease, other lung diseases, diabetes mellitus or other metabolic diseases, or malignant disease; pregnancy; steroid use in the previous 6 mo; respiratory tract infection within previous 4 wk
Janaudis-Ferreira[19]	RT: n = 13 Control: n = 18	RT: 67.0 ± 11.0 Control: 67.0 ± 11.0	RT: 53.0 Control: 63.0	RT: 27.9 ± 7.9 Control: 25.7 ± 8.2	RT: 37.8 ± 16.2 Control: 32.5 ± 14.1	ND	Diagnosis of stable COPD according to GOLD, FEV_1 < 80% of normal predicted, dyspnea or arm fatigue during at least 1 ADL requiring arm exercise	Musculoskeletal or neurologic conditions that might affect exercise performance; symptomatic cardiac disease previous lung surgery, COPD exacerbation within previous 2 mo, oral corticosteroids
Kongsgaard[30]	RT: n = 6 Control: n = 7	RT: 71.0 ± 3.9 Control: 73.0 ± 5.4	RT: 100.0 Control: 100	ND	RT: 48.0 ± 13.2 Control: 44.0 ± 7.8	RT: 0.53 ± 0.06 Control: 0.54 ± 0.09	Diagnosis of COPD, 65–80 y old, able to transport themselves to the hospital	Fractures of lower extremities within previous 6 mo, neurologic or cardiovascular diseases requiring walking devices, cognitive dysfunctions
Marrara[31]	RT: n = 8 Control: n = 6	RT: 65.0 ± 9.8 Control: 68.0 ± 10.4	RT: 100.0 Control: 100	RT: 24.0 ± 4.5 Control: 23.0 ± 3.3	RT: 45.0 ± 11.5 Control: 42.0 ± 11.6	RT: 0.50 ± 0.08 Control: 0.48 ± 0.10	Diagnosis of moderate COPD according to GOLD, FEV_1/FVC < 0.70, stable clinical condition in previous 2 mo	Smokers with exacerbated pulmonary disease; rheumatic, neuromuscular, orthopedic, or decompensated cardiovascular disease that would hinder execution of tasks; S_{pO_2} < 80% during physical effort; not able to complete 1 of the tests or predetermined protocol
McKeough[20]	RT: n = 9 Control: n = 9 ComT: n = 9 ET: n = 11	RT: 65.0 ± 9.0 Control: 65.0 ± 7.0 ComT: 66.0 ± 6.0 ET: 66.0 ± 8.0	RT: 44.0 Control: 44.0 ComT: 67.0 ET: 82.0	RT: 23.0 ± 4.0 Control: 27.0 ± 9.0 ComT: 26.0 ± 5.0 ET: 26.0 ± 5.0	RT: 60.0 ± 17.0 Control: 57.0 ± 12.0 ComT: 54.0 ± 16.0 ET: 57.0 ± 17.0	RT: 0.51 ± 0.10 Control: 0.53 ± 0.09 ComT: 0.50 ± 0.09 ET: 0.52 ± 0.11	Diagnosis of COPD according to GOLD	Musculoskeletal, cardiovascular, or neurologic condition likely to adversely affect performance during assessment or training; participation in exercise training within previous 12 mo; oxygen supplementation; cannot understand English
Nyberg[21]	RT: n = 20 Control: n = 20	RT: 69.0 ± 5.0 Control: 68.0 ± 6.0	RT: 55.0 Control: 50.0	RT: 26.0 ± 4.0 Control: 25.0 ± 5.0	RT: 59.0 ± 11.0 Control: 55.0 ± 15.0	RT: 0.47 ± 0.09 Control: 0.42 ± 0.10	Diagnosis of moderate-to-very-severe COPD according to GOLD, ex-smokers, no exacerbations or changes in medication within 4 wk preceding start of intervention, live < 60 km from exercise facilities	Musculoskeletal, rheumatic, cardiac, or neurologic disorders that could affect exercise performance in training and tests; previous lung surgery; long-term oxygen treatment; participation in regular organized exercise training within 6 mo

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Table I—continued

Study	Group (n)	Age (y)*	Males (%)	BMI (kg/m^2)*	FEV_1 (% predicted)*	FEV_1/FVC*	Inclusion Criteria	Exclusion Criteria
O'Shea[32]	RT: n = 27 Control: n = 27	RT: 66.9 ± 7.0 Control: 68.4 ± 9.9	Average: 39.0	RT: 25.5 ± 5.1 Control: 27.8 ± 7.9	RT: 49.0 ± 25.0 Control: 52.0 ± 22.0	RT: 0.50 ± 0.16 Control: 0.49 ± 0.15	Diagnosis of COPD, written informed consent, no pulmonary rehabilitation in previous 12 mo	Other respiratory diseases, unstable medical conditions limiting RT
Ries[33]	RT: n = 8 Control: n = 11	ND	ND	ND	RT: 46.0 ± 20.0 Control: 31.0 ± 8.0	RT: 0.45 ± 0.14 Control: 0.38 ± 0.04	Diagnosis of stable COPD, written informed consent	ND
Simpson[34]	RT: n = 14 Control: n = 14	RT: 73.0 ± 4.8 Control: 70.0 ± 5.7	RT: 36.0 Control: 71.0	ND	RT: 39.5 ± 19.0 Control: 39.2 ± 21.4	RT: 0.49 ± 0.13 Control: 0.48 ± 0.14	Diagnosis of stable COPD, 58–80 y old, $FEV_1/FVC < 0.70$, within 30% of predicted ideal body weight, written informed consent	Other disorders likely to affect exercise training
Mador[35]	ComT: n = 11 ET: n = 13	ComT: 74.0 ± 6.6 ET: 68.0 ± 7.2	ND	ComT: 27.6 ± 1.3 ET: 27.5 ± 7.2	ComT: 44.0 ± 13.2 ET: 44.0 ± 14.4	ND	Diagnosis of COPD, no previous participation in a rehabilitation program, received inhaled β_2 agonists, successfully stopped smoking for at least 3 mo before assessment	ND
Pereira[22]	ComT: n = 25 ET: n = 25	ComT: 64.5 ± 2.5 ET: 63.0 ± 1.7	ComT: 100 ET: 100	ComT: 27.6 ± 2.6 ET: 25.4 ± 1.8	ComT: 52.4 ± 8.7 ET: 51.5 ± 7.8	ND	Diagnosis of moderate-to-severe COPD according to GOLD, no previous participation in a rehabilitation program, stopped smoking for at least 6 mo, no exacerbations and hospital admissions in previous 6 mo, no relevant cardiac or skeletomuscular pathology, not undergoing oxygen therapy	ND
Phillips[36]	ComT: n = 10 ET: n = 9	ComT: 71.0 ± 3.2 ET: 70.0 ± 6.0	ComT: 40.0 ET: 13.0	ComT: 28.5 ± 5.7 ET: 26.1 ± 3.9	ComT: 42.0 ± 10.1 ET: 32.8 ± 18.6	ComT: 0.52 ± 0.16 ET: 0.39 ± 0.12	Diagnosis of COPD, 60–81 y old, stable at the time of entry into exercise program, ability to participate in RT program, willingness to accept random group assignment	History of unstable angina and multiple inguinal hernia repairs
Vonbank[23]	ComT: n = 12 ET: n = 12	ComT: 59.2 ± 7.7 ET: 61.8 ± 5.4	ComT: 67.0 ET: 75.0	ComT: 28.2 ± 8.4 ET: 26.2 ± 4.4	ComT: 51.1 ± 20.3 ET: 58.1 ± 19.3	ComT: 0.47 ± 0.14 ET: 0.52 ± 0.14	Diagnosis of COPD according to GOLD, stable out-patients, received inhaled β_2 agonists	Other lung diseases or cardiovascular disorders, any pathology that could possibly interfere with ability to exercise

* Data are presented as mean ± SD
BMI = body mass index
RT = resistance training group
ComT = combined training group
ET = endurance training group
ND = no data
ADL = activity of daily living
GOLD = Global Initiative for Chronic Obstructive Lung Disease

Table 2. Included Studies

Study	Intervention	Study Design	Outcomes	Jadad Scale Score	Attrition Rate (%)
Alexander[26]	RT: 5 exercises, 8–10 wk, twice/wk, 1 set/12 reps, load of 50% 1RM (1st wk), increase based on successful completion of > 12 reps for 2 consecutive training sessions in 3–5-pound increments Control: non-exercise Baseline PR: identical intensity ET and low-intensity upper-extremity RT for all subjects	RT vs control	Exercise tolerance: 6MWD Muscle strength: leg and incline bench press Other outcomes: functional fitness	2	26
Benton and Wagner[17]	RT: 5 exercises, 8 wk, 1 set/8–12 reps, load of 50% 1RM for leg and chest press, with other 3 exercises set at a weight that allowed completion of 10 repetitions with good form and without undue fatigue Control: non-exercise Baseline PR: identical intensity ET and low-intensity upper-extremity RT for all subjects	RT vs control	HRQOL: SF-36 Exercise capacity: 6MWD Muscle strength: incline chest and leg press	2	0
Casaburi[27]	RT: 10 wk, 3 times/wk, 3 sets/12 reps 1st 4 wk, 4 sets/8–10 reps last 6 wk, loads of 60% 1RM (1st 4 wk) and 80% 1RM (next 6 wk) Control: non-exercise	RT vs control	Pulmonary function: FEV_1, FEV_1 % predicted, FEV_1/FVC	6	11
Clark[28]	RT: 8 exercises, 12 wk, 3 sets/10 reps, load of 70% of subject's maximum value Control: non-exercise	RT vs control	Physiologic parameters: $\dot{V}_{O_2}$, heart rate, $\dot{V}_E$, V_T, breathing frequency Dyspnea: Borg dyspnea scale Muscle strength: quadriceps	2	0
Covey[18]	RT: 8 exercises, 16 wk, twice/wk, 2 sets/8–10 reps 1st 4 wk, 3 sets/8–10 reps next 5–16 wk, load of 80% 1RM Control: sham training	RT vs control	HRQOL: CRQ Muscle strength: upper body Other outcomes: P_{Imax}, functional status, self-efficacy	7	19
Hoff[29]	RT: 8 wk, 4 sets/5 reps, load of 85–90% 1RM, increased by 2.5 kg until 5 repetitions could again be achieved Control: non-exercise	RT vs control	Physiologic parameters: $\dot{V}_{O_2}$, $\dot{V}_E$, heart rate, lactate, S_{aO_2}, maximum work capacity Muscle strength: quadriceps Other outcomes: RPE	2	0
Janaudis-Ferreira[19]	RT: 6 wk, 3 times/wk, 1 set/10–12 reps, load of loads equivalent to the 10–12-rep maximum (if completed, loads were increased) Control: sham training Baseline PR: identical intensity ET, RT, and breathing exercises for all subjects	Arm RT vs control	HRQOL: CRQ Dyspnea: dyspnea domain of CRQ Muscle strength: elbow flexion and extension, shoulder flexion and abduction Other outcomes: arm function, arm exercise capacity[16]	6	6
Kongsgaard[30]	RT: 12 wk, twice/wk, 4 sets/8 reps, load of 80% 1RM Control: non-exercise	RT vs control	Pulmonary function: FEV_1 Muscle strength: knee extension, trunk, leg extension power Other outcomes: CSA of quadriceps, normal and maximum gait speed, stair-climbing time	2	28
Marrara[31]	RT: 6 exercises, 6 wk, 3 times/wk, 3 sets/10 reps, load of 50% of 10RM (1st set), load of 75% of 10RM (2nd set), 100% of load of 10RM (3rd set) Control: non-exercise	RT vs control	Physiologic parameters: $\dot{V}_E$/MVV (%), $\dot{V}_{O_2}$/maximum $\dot{V}_{O_2}$ (%) during daily physical activities test Dyspnea: Borg dyspnea scale during daily physical activities test	1	24
McKeough[20]	Arm RT: 8 wk, 3 times/wk, 2 sets/10 reps to 3 sets/10 reps, load of 60% 1RM to 80% 1RM Arm ET: arm cranking and unsupported arm exercise, 8 wk, 3 times/wk, 60% work rate of peak arm crank test for 15 min/session and 1 level below the maximum level achieved on the unsupported arm test for 5 min/session, intensity increased according to breathlessness and perceived arm exertion Arm ComT: arm RT plus arm ET Arm control: non-exercise Baseline PR: identical intensity RT and ET of lower extremities for all subjects	Arm RT vs control Arm ComT vs arm ET	Physiologic parameters: $\dot{V}_{O_2}$, $\dot{V}_E$, $\dot{V}_{CO_2}$ HRQOL: SGRQ Dyspnea: Borg scores Other outcomes: Functional arm exercise testing	6	27
Nyberg[21]	RT: 8 exercises, 8 wk, 3 times/wk, 2 sets/25 reps, load individually determined and progressed using Borg category ratio scale Control: non-exercise	RT vs control	Physiologic parameters: $\dot{V}_{O_2}$ HRQOL: CRQ, SF-36 Exercise capacity: 6MWD, 6PBRT Muscle strength: knee extensor, shoulder flexion	4	9
O'Shea[32]	RT: 6 exercises, 12 wk, 3 times/wk, 3 sets/8–12 reps, load of maximum to complete sets/reps Control: non-exercise	RT vs control	HRQOL: CRQ Exercise capacity: 6MWD Muscle strength: knee extensor, hip abductor, shoulder horizontal flexor, shoulder flexor Other outcomes: mobility, upper-limb activity, participation restrictions	3	19

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Table 2. Included Studies

Study	Intervention	Study Design	Outcomes	Jadad Scale Score	Attrition Rate (%)
Ries[33]	RT: 5 exercises, 6 wk, 7 times/wk (1st wk) and 14 times/wk (2nd wk), 1–2 sets/10 reps, load of added hand weights (1–5 pounds) Control: non-exercise	RT vs control	Pulmonary function: FEV_1, FEV_1 % predicted, FVC, FEV_1/FVC, RV % predicted, TLC % predicted, RV/TLC (%) Physiologic parameters: maximum work capacity Exercise capacity: endurance time Other outcomes: RPB, RPE	2	38
Simpson[34]	RT: 3 exercises, 8 wk, 3 times/wk, 3 sets/10 reps, load increased progressively from 50% 1RM (1st wk) to 85% 1RM (final wk) Control: non-exercise	RT vs control	Pulmonary function: FEV_1 % predicted, FEV_1 Physiologic parameters: maximum $\dot{V}_{O_2}$ HRQOL: CRQ Exercise tolerance: 6MWD Dyspnea: Borg dyspnea scale Muscle strength: arm curl, knee extension, leg press Other outcomes: P_{Imax} and P_{Emax}	5	18
Mador[35]	ET: 8 wk, 3 times/wk, 50% maximum work capacity, 60 min/session, cycle ergometer RT: 4 exercises, 8 wk, 3 sets/10 reps, load of 60% 1RM, increased by 5 pounds when 3 sets could be performed without difficulty ComT: RT plus ET	ComT vs ET	Physiologic parameters: $\dot{V}_{O_2}$, $\dot{V}_E$, heart rate, maximum work capacity HRQOL: CRQ Exercise tolerance: endurance time, 6MWD Muscle strength: quadriceps, hamstrings, pectoralis major, latissimus dorsi Other outcomes: quadriceps fatigability	4	25
Pereira[22]	ET: 10 wk, 3 times/wk, 60–70% of reserve heart rate, 30–60 min/session, cycle ergometer RT: 5 exercises, 10 wk, 2 sets/6–12 reps, load of 50–70% 1RM ComT: RT plus ET	ComT vs ET	HRQOL: SGRQ, SF-36	1	No data
Phillips[36]	ET: 8 wk, twice/wk, 3 metabolic equivalents, 20–40 min/session, Monark arm ergometer and motor-driven treadmill RT: 5 exercises, 8 wk, twice/wk, load of 50% 1RM, increased by 5%–10% as tolerated when 10 repetitions of an exercise were successful completed ComT: RT plus ET	ComT vs ET	Exercise tolerance: 6MWD Muscle strength: incline chest press, leg press Other outcomes: functional fitness	2	21
Vonbank[23]	ET: 12 wk, twice/wk, 60% peak $\dot{V}_{O_2}$, 20–60 min/session, cycle ergometer RT: 8 exercises, 12 wk, twice/wk, 2–4 sets/8–15 reps, load of maximum ComT: RT plus ET	ComT vs ET	Physiologic parameters: $\dot{V}_{O_2}$max, maximum work capacity, maximum work capacity % predicted, $\dot{V}_{O_2}$ % predicted, lactate, $\dot{V}_E$, heart rate HRQOL: SGRQ Muscle strength: quadriceps femoris, pectoralis, latissimus dorsi	2	16

RT = resistance training
ET = endurance training
ComT = combined training
PR = pulmonary rehabilitation
reps= repetitions
1RM = one repetition maximum
6MWD = 6-min walk distance
HRQOL = health-related quality of life
SF-36 = Medical Outcomes Study Short Form questionnaire 36-item version
$\dot{V}_{O_2}$ = oxygen uptake * Here we do not have a detailed description of peak V_{O_2} or maximum V_{O_2}, though we analyze them separately
$\dot{V}_{CO_2}$ = carbon dioxide production
$\dot{V}_E$ = minute ventilation
V_T = tidal volume
S_{aO_2} = arterial oxygen saturation
P_{Imax} = maximum inspiratory pressure
P_{Emax} = maximum expiratory pressure
RPE = ratings of perceived exertion
RPB = ratings of perceived breathlessness
CSA = cross-sectional area
MVV = maximum voluntary ventilation
RV = residual volume
TLC = total lung capacity
CRQ = Chronic Respiratory Disease Questionnaire
SGRQ = St George Respiratory Questionnaire
6PBRT = 6-min pegboard and ring test

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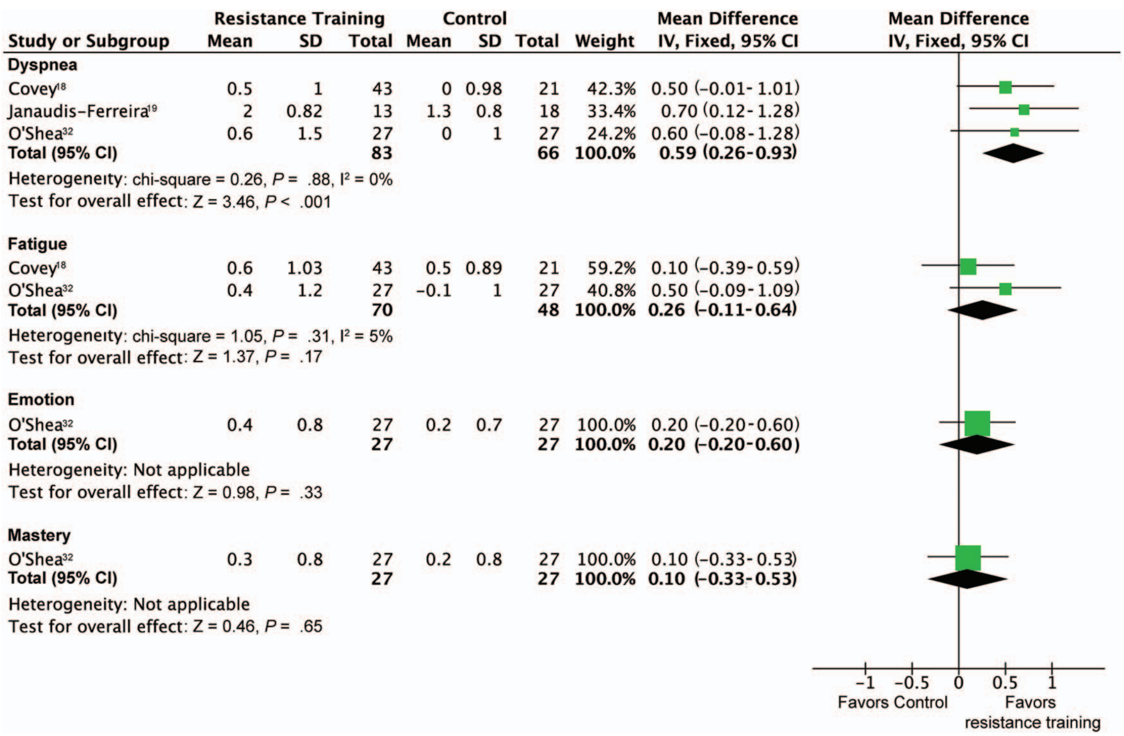

Fig. 2. Effects of resistance training vs non-exercise control on Chronic Respiratory Disease Questionnaire scores. IV = inverse variance weighting.

0.64, $I^2 = 5\%$, $P = .17$).[18,32] Only one study reported CRQ emotion and mastery domain scores.[32] The results showed no significant difference in CRQ emotion domain scores (d = 0.20, 95% CI −0.20 to 0.60) and mastery domain scores (d = 0.10, 95% CI −0.33 to 0.53) between the 2 groups (Fig. 2).

Resistance-and-Endurance-Training Group Versus Endurance-Training-Alone Group. Only one trial reported each CRQ domain score.[35] There were no significant differences in dyspnea domain scores (d = −0.60, 95% CI −1.23 to 0.03), fatigue domain scores (d = −0.30, 95% CI −1.18 to 0.58), emotion domain scores (d = 0.00, 95% CI −0.74 to 0.74), and mastery domain scores (d = 0.10, 95% CI −0.89 to 1.09) between the 2 groups.

St George Respiratory Questionnaire

Resistance-Training Group Versus Non-Exercise Control Group. Only one included trial reported St George Respiratory Questionnaire (SGRQ) total scores and each domain score.[20] The results showed no statistically significant improvements in SGRQ total scores (d = −3, 95% CI −14 to 8), symptom domain scores (d = −7, 95% CI −23 to 9), activity domain scores (d = −0.1, 95% CI −15 to 15), and impact domain scores (d = −3, 95% CI −16 to 10) in the resistance-training group.

Resistance-and-Endurance-Training Group Versus Endurance-Training-Alone Group. Three studies reported SGRQ total scores,[20,22,23] and 2 studies reported each SGRQ domain score.[22,23] The results of 2 included studies showed significant improvements in SGRQ total scores, symptom domain scores, activity domain scores, and impact domain scores in the resistance-and-endurance-training group. The overall analysis showed statistically significant improvements in SGRQ total scores (WMD of −7.44, 95% CI −12.62 to −2.25, $I^2 = 0\%$, $P = .005$), symptom domain scores (WMD of −14.81, 95% CI −21.23 to −8.39, $I^2 = 0\%$, $P < .001$), activity domain scores (WMD of −25.27, 95% CI −31.46 to −19.08, $I^2 = 11\%$, $P < .001$), and impact domain scores (WMD of −8.23, 95% CI −15.31 to −1.15, $I^2 = 0\%$, $P = .02$), favoring the combination training (Fig. 3).

Secondary Outcomes

Skeletal Muscle Function

Resistance-Training Group Versus Non-Exercise Control Group. The cumulative analysis showed significant improvements in knee extension strength (WMD of 7.78 kg, 95% CI 5.18–10.38 kg, $I^2 = 0\%$, $P < .001$),[28,32,34] leg press strength (WMD of 16.67 kg, 95% CI 2.87–30.47 kg, $I^2 = 0\%$, $P = .02$),[17,26,27,29,34] and shoulder flexion strength (WMD of 2.88 kg, 95% CI 0.56–5.20 kg, $I^2 = 0\%$, $P = .01$)[19,32] in the

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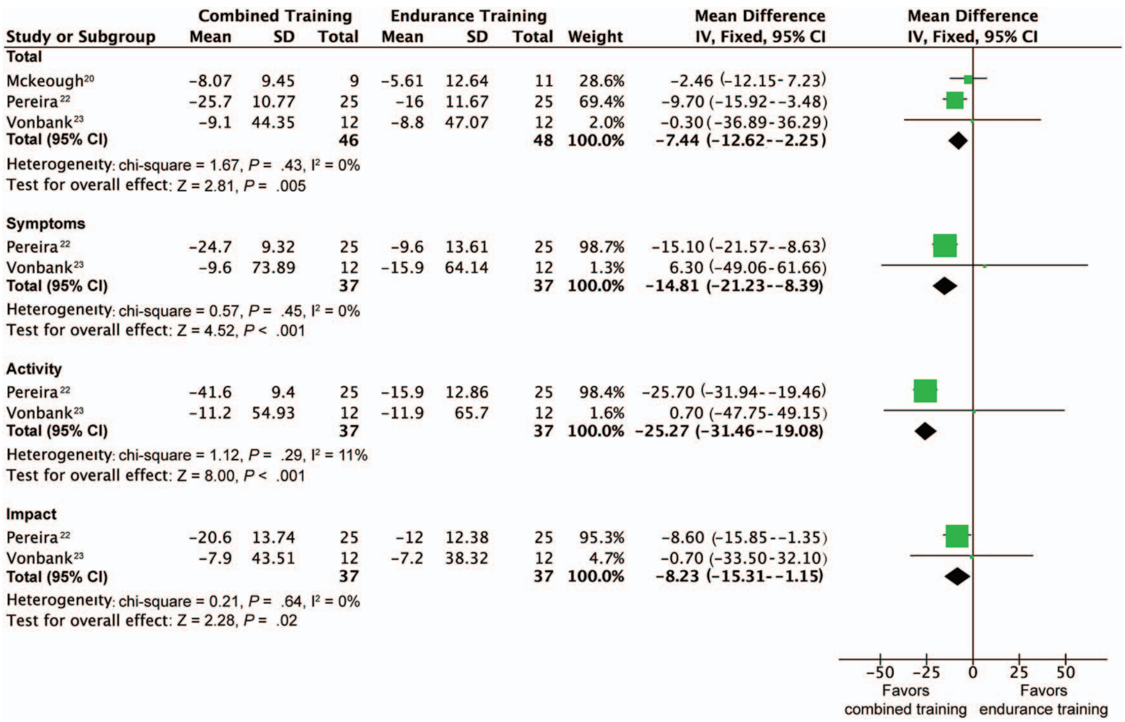

Fig. 3. Effects of combined resistance and endurance training vs endurance training alone on St George Respiratory Questionnaire scores. IV = inverse variance weighting.

resistance-training groups. However, the difference was not statistically significant in pectoral muscle strength (WMD of 2.29 kg, 95% CI −0.41 to 4.99 kg, $I^2 = 0\%$, $P = .10$) after resistance training (Fig. 4).[17,26,32] Only one study measured latissimus dorsi strength, which showed a significant improvement (d = 2.50 kg, 95% CI −0.70 to 5.70 kg) in the resistance-training group.[19]

Resistance-and-Endurance-Training Group Versus Endurance-Training-Alone Group. The cumulative analysis showed significant improvements in leg press strength (WMD of 12.34 kg, 95% CI 5.96–18.72 kg, $I^2 = 0\%$, $P < .001$)[23,36] and pectoral muscle strength (WMD of 4.48 kg, 95% CI 2.53–6.43 kg, $I^2 = 0\%$, $P < .001$)[23,35,36] in the resistance-and-endurance-training group compared with the endurance-training-along group. No significant difference in latissimus dorsi strength (WMD of 6.07 kg, 95% CI −3.22 to 15.37 kg, $I^2 = 0\%$, $P = .20$) was observed after the addition of resistance training to endurance training (Fig. 5).[23,35] Only one study measured knee extension strength (d = 10.00 kg, 95% CI −1.53 to 21.53 kg, $P < .002$).[35]

6-min Walk Distance

Resistance-Training Group Versus Non-Exercise Control Group. Five studies included the 6-min walk distance (6MWD) as an end point.[17,21,26,32,34] The results of each study and of our pooled analysis showed no significant difference in 6MWD (WMD of 1.83 m, 95% CI −15.32 to 18.97 m, $I^2 = 0\%$, $P = .83$) between the 2 groups.

Resistance-and-Endurance-Training Group Versus Endurance-Training-Alone Group. Two included trials reported 6MWD.[35,36] The results of each study showed no significant improvements in 6MWD in the resistance-and-endurance-training group. The pooled analysis showed no obvious changes in 6MWD between the 2 groups (WMD of −1.94 m, 95% CI −49.55 to 45.67 m, $I^2 = 0\%$, $P = .94$).

6-min Pegboard and Ring Test

Resistance-Training Group Versus Non-Exercise Control Group. Two included trials[19,21] reported results from the 6-min pegboard and ring test. The cumulative analysis showed no significant difference between the 2 groups (WMD of 20.52 rings, 95% CI −2.54 to 43.58 rings, $I^2 = 0\%$, $P = .08$).

Maximum Exercise Work Load

Resistance-Training Group Versus Non-Exercise Control Group. Two included trials reported the maximum exercise work load.[27,29] The results of each study

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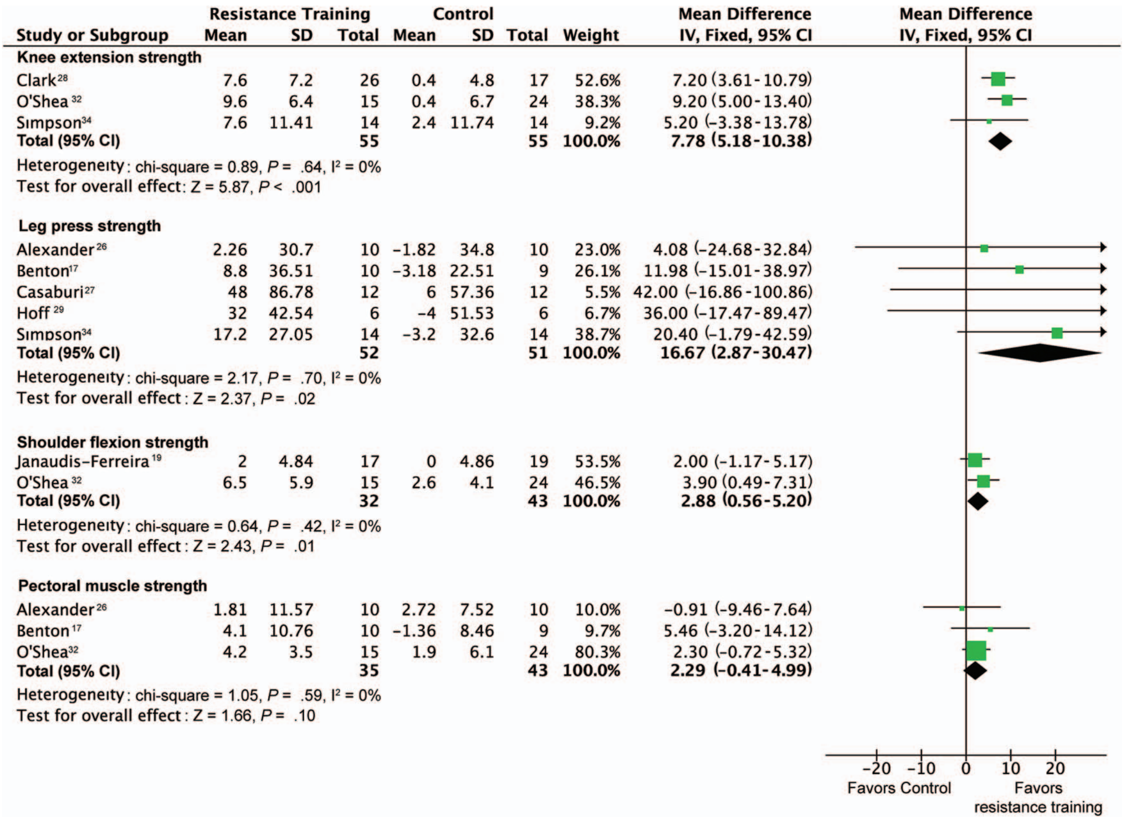

Fig. 4. Effects of resistance training vs non-exercise control on skeletal muscle strength. IV = inverse variance weighting.

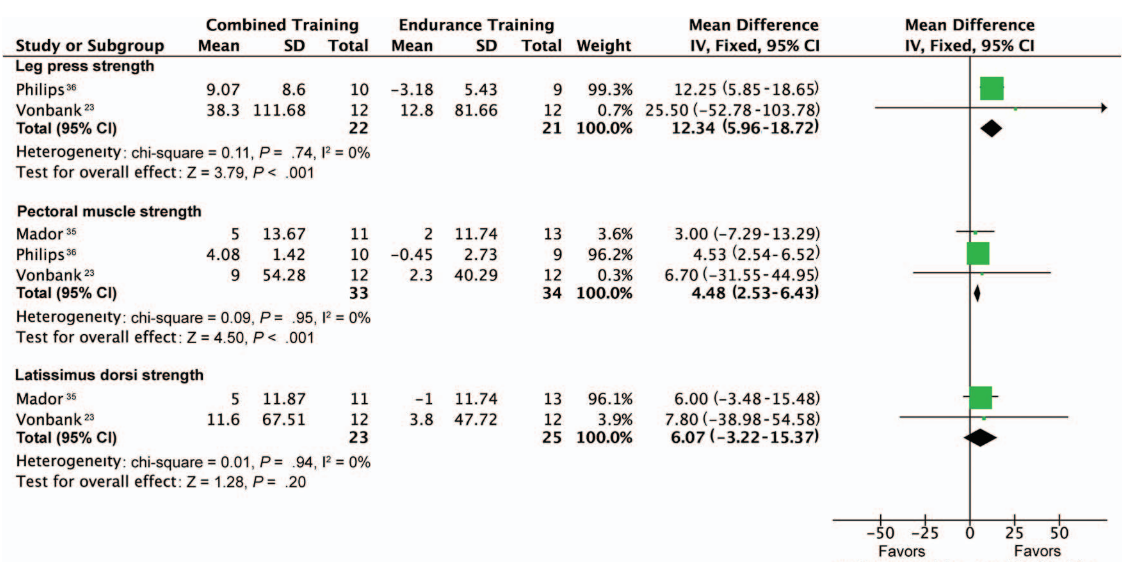

Fig. 5. Effects of combined resistance and endurance training vs endurance training alone on skeletal muscle strength. IV = inverse variance weighting.

showed no significant difference, and the overall analysis also showed no significant difference between the 2 groups (WMD of 3.46 W, 95% CI −16.75 to 23.67 W, $I^2 = 0\%$, $P = .74$).

Resistance-and-Endurance-Training Group Versus Endurance-Training-Alone Group. Two included trials reported the maximum exercise work load.[23,35] The results of each study showed no significant difference, and

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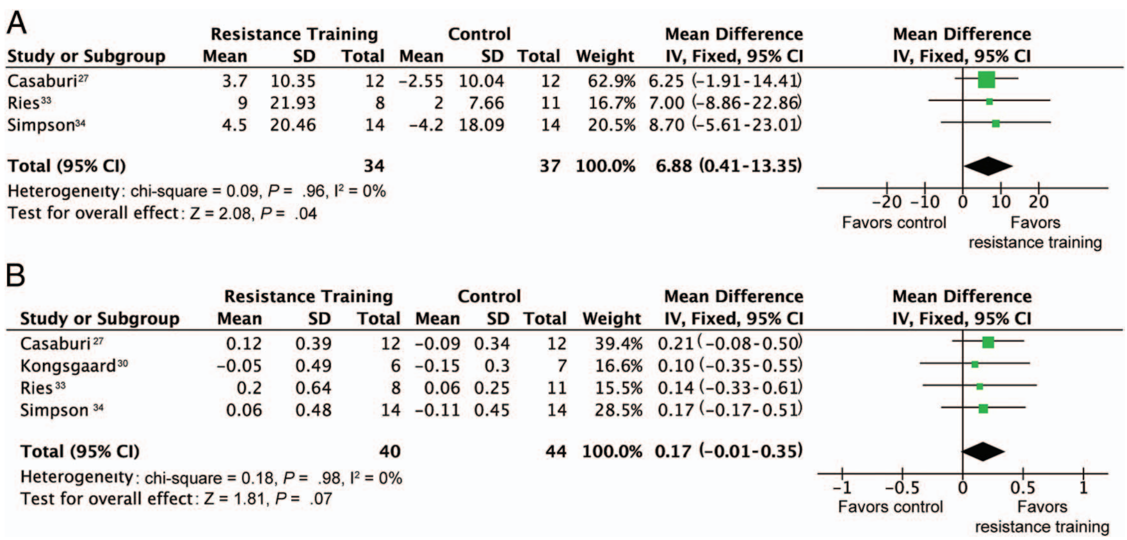

Fig. 6. Effects of resistance training vs non-exercise control on FEV_1. A: Percent-of-predicted FEV_1. B: Absolute FEV_1. IV = inverse variance weighting.

the overall analysis also showed no significant difference between the 2 groups (WMD of 2.91 W, 95% CI −18.03 to 23.85 W, $I^2 = 0\%$, $P = .79$).

Maximum Oxygen Consumption

Resistance-Training Group Versus Non-Exercise Control Group. Three included trials reported maximum oxygen consumption.[20,27,29] The results of each study showed no significant difference, and the pooled analysis also showed no significant difference between the 2 groups (WMD of 0.04 L/min, 95% CI −0.13 to 0.21 L/min, $I^2 = 0\%$, $P = .61$).

Resistance-and-Endurance-Training Group Versus Endurance-Training-Alone Group. Two studies reported maximum oxygen consumption.[20,35] The results of each study showed no significant difference, and the pooled analysis also showed no significant difference between the 2 groups (WMD of 0.02 L/min, 95% CI −0.16 to 0.21 L/min, $I^2 = 0\%$, $P = .79$).

Pulmonary Function

Change in FEV_1

Resistance-Training Group Versus Non-Exercise Control Group. Three trials reported percent-of-predicted FEV_1,[27,33,34] and 4 trials reported absolute FEV_1.[27,30,33,34] The pooled analysis showed significant improvements in percent-of-predicted FEV_1 (WMD of 6.88%, 95% CI 0.41–13.35%, $I^2 = 0\%$, $P = .04$) in the resistance-training groups compared with the non-exercise control groups. For absolute FEV_1, the difference between the 2 groups was not statistically significant (WMD of 0.17 L, 95% CI −0.01 to 0.35 L, $I^2 = 0\%$, $P = .07$) (Fig. 6).

Only one trial reported absolute FVC.[33] The results showed significant improvements in the resistance-training group (d = 0.11 L, 95% CI −0.62 to 0.84 L, $P < .05$).

Attrition Rate and Adverse Events

The attrition rate was reported in 17 included studies. The mean attrition rate was 16.9%, ranging from 0 to 38.0%. The main reasons for withdrawal included COPD exacerbations (17/119), failure to complete the program (21/119), non-protocol-related or non-COPD-related health problems (34/119), personal reasons (34/119), refusal of post-rehabilitation measurements (5/119), musculoskeletal problems (4/119), treatment changes (3/119), and generalized weakness (1/119). The pooled analysis showed that the attrition rate was higher in the resistance-training group compared with the non-exercise control group (odds ratio of 1.79, 95% CI 1.04–3.08, $I^2 = 0\%$, $P = .03$) (Fig. 7). No significant difference in the attrition rate between the resistance-and-endurance-training and endurance-training-alone groups (odds ratio of 1.15, 95% CI 0.32–4.15, $I^2 = 0\%$, $P = .83$) was observed (Fig. 8). No significant changes were observed in reasons for withdrawal between the resistance-training and non-exercise control groups (Fig. 9). There were no reports of adverse events related to resistance-training intervention. The overall analysis showed no obvious difference in reasons for withdrawal between the resistance-and-endurance-training and endurance-training-alone groups (Fig. 10).

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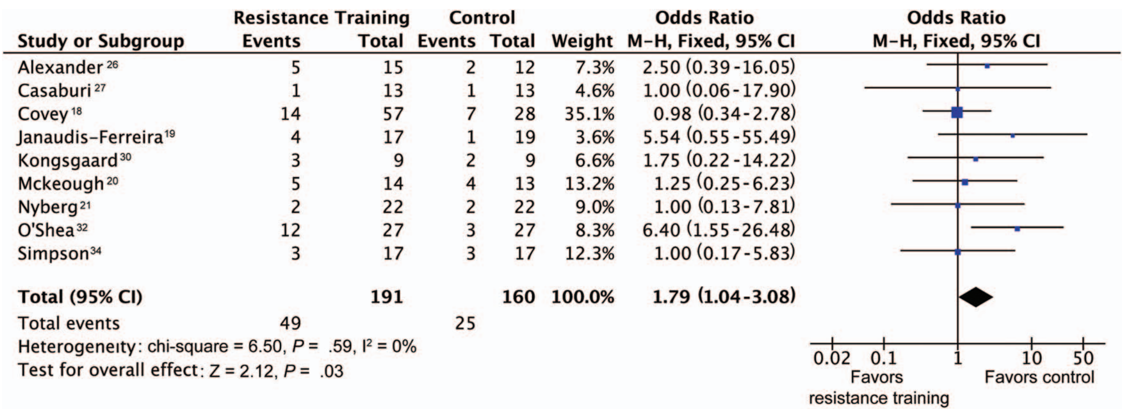

Fig. 7. Effects of resistance training vs non-exercise control on attrition rates. M-H = Mantal-Haenszel statistics.

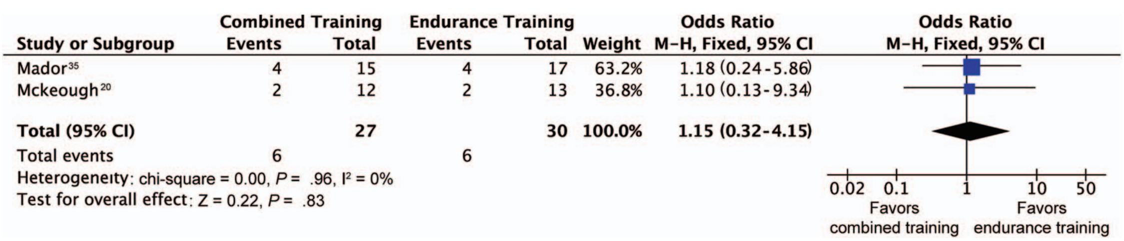

Fig. 8. Effects of combined resistance and endurance training vs endurance training alone on attrition rates. M-H = Mantal-Haenszel statistics.

Discussion

Exercise training provides an effective therapy for exercise limitation in patients with COPD. The conventional modalities of exercise training include mainly endurance and resistance training. Endurance training is recommended by various guidelines as the cornerstone of successful pulmonary rehabilitation.[38-40] Although increases in muscle strength after resistance training were demonstrated in subjects with COPD,[41] the effect of resistance training and combined resistance and endurance training on clinically relevant outcomes in patients with COPD remains controversial. This meta-analysis incorporated 18 RCTs and included data from 750 subjects with advanced COPD. The effects of resistance training and combined resistance and endurance training were evaluated by their impact on quality of life, dyspnea, functional exercise capacity, maximum exercise capacity, skeletal muscle function, lung function, and adverse events. To our knowledge, this is the largest analysis to date of the efficacy of resistance training on clinically relevant outcomes in subjects with COPD.

This meta-analysis clearly showed the beneficial effects of resistance training on skeletal muscle strength in subjects with COPD. The results support previous findings.[13,14,16] O'Shea et al[14] reported that there were obvious increases in knee extension strength, leg press strength, and latissimus dorsi strength following resistance training versus no exercise (control). We did not perform cumulative analysis of latissimus dorsi strength because there was only one suitable study. O'Shea et al[14] included some non-RCTs. In addition, they included all studies with resistance training, including resistance training versus non-exercise control, resistance training versus endurance training, resistance training versus resistance plus endurance training, resistance plus endurance training versus non-exercise control, and resistance plus endurance training versus endurance training. Thus, there may be a higher risk of heterogeneity in their analysis. Actually, O'Shea et al[14] did not report the effect of resistance training on pectoral muscle strength because statistical heterogeneity between trials prevented the use of meta-analysis. More importantly, they reported the percentage increase in skeletal muscle strength, and we reported the absolute value of skeletal muscle strength. Other important findings of our study include the beneficial effects of resistance training on shoulder flexion strength and CRQ dyspnea domain scores. The improvement in CRQ dyspnea domain scores achieved a minimum clinically important difference of 0.5 units. Despite the positive effects of resistance training on skeletal muscle strength and CRQ dyspnea domain scores, there were no significant differences between the 2 groups in functional exercise capacity (including 6MWD and 6-min pegboard and ring test scores) and maximum exercise capacity (including maximum exercise work load

Study or Subgroup	Resistance Training Events	Resistance Training Total	Control Events	Control Total	Weight	Odds Ratio M-H, Fixed, 95% CI
Exacerbation of COPD						
Janaudis-Ferreira[19]	1	17	0	19	20.1%	3.55 (0.14-93.01)
Nyberg[21]	2	22	1	22	42.1%	2.10 (0.18-25.01)
O'Shea[32]	5	27	1	27	37.8%	5.91 (0.64-54.45)
Total (95% CI)		**66**		**68**	**100.0%**	**3.83 (0.90-16.34)**
Total events	8		2			
Heterogeneity: chi-square = 0.37, *P* = .83, I^2 = 0%						
Test for overall effect: Z = 1.81, *P* = .07						
Non-protocol-related or COPD-related health problems						
Casaburi[27]	1	13	1	13	16.8%	1.00 (0.06-17.90)
Covey[18]	4	57	2	28	45.5%	0.98 (0.17-5.71)
Janaudis-Ferreira[19]	2	17	1	19	15.2%	2.40 (0.20-29.13)
O'Shea[32]	6	27	1	27	14.2%	7.43 (0.83-66.62)
Simpson[34]	1	17	0	17	8.4%	3.18 (0.12-83.76)
Total (95% CI)		**131**		**104**	**100.0%**	**2.30 (0.84-6.28)**
Total events	14		5			
Heterogeneity: chi-square = 2.35, *P* = .67, I^2 = 0%						
Test for overall effect: Z = 1.62, *P* = .11						
Change in treatment						
O'Shea[32]	1	27	0	27	52.4%	3.11 (0.12-79.87)
Simpson[34]	2	17	0	17	47.6%	5.65 (0.25-126.87)
Total (95% CI)		**44**		**44**	**100.0%**	**4.32 (0.46-40.26)**
Total events	3		0			
Heterogeneity: chi-square = 0.07, *P* = .79, I^2 = 0%						
Test for overall effect: Z = 1.28, *P* = .20						
Personal reasons						
Covey[18]	6	57	5	28	38.6%	0.54 (0.15-1.96)
Janaudis-Ferreira[19]	1	17	0	19	2.8%	3.55 (0.14-93.01)
Kongsgaard[30]	3	9	2	9	8.6%	1.75 (0.22-14.22)
Nyberg[21]	0	22	1	22	9.5%	0.32 (0.01-8.25)
O'Shea[32]	1	27	3	27	18.6%	0.31 (0.03-3.16)
Simpson[34]	0	17	3	17	21.9%	0.12 (0.01-2.48)
Total (95% CI)		**149**		**122**	**100.0%**	**0.57 (0.25-1.29)**
Total events	11		14			
Heterogeneity: chi-square = 3.72, *P* = .59, I^2 = 0%						
Test for overall effect: Z = 1.35, *P* = .18						

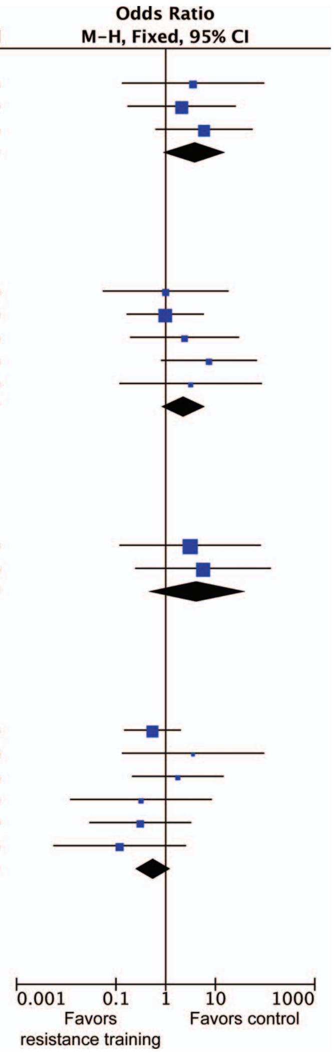

Fig. 9. Effects of resistance training vs non-exercise control on reasons for withdrawal. M-H = Mantal-Haenszel statistics.

and maximum oxygen consumption). Our results support resistance training performed in conjunction with endurance training because the combination may improve skeletal muscle strength and quality of life to a greater degree than endurance training alone in patients with COPD. However, gains in skeletal muscle strength and quality of life failed to translate into improvements in exercise capacity. The mechanisms of intrinsic muscle changes after resistance training have been scarcely studied in COPD.[41] Some authors speculated that the changes were related to the expression of muscle insulin-like growth factor-1 and myogenic regulatory factors.[42] Additional studies are required to examine the mechanisms of intrinsic muscle changes after resistance training, which should greatly improve the clinical outcomes in patients with COPD.

It has been generally accepted that pulmonary rehabilitation by itself does not improve lung function.[43,44] A meta-analysis conducted by Strasser et al[15] showed that resistance training did not increase FEV_1 but may carry potential benefits for FVC. Because of the inclusion of all studies with resistance training, there was a high heterogeneity with regard to percent-of-predicted FEV_1 (I^2 = 68.1%). Our results showed that there was an obvious improvement in percent-of-predicted FEV_1 and an increasing trend of absolute FEV_1 in the resistance-training group. Although this phenomenon had been reported previously,[15,45,46] we did not consider it to be a direct consequence of resistance training per se. We believe that it could be a result of better maintenance of lung function in a more consistent way during pulmonary rehabilitation. We did not perform a cumulative analysis of FVC due to a lack of suitable studies.

We found that the attrition rate was higher in the resistance-training group. However, there were no obvious differences between the 2 groups regarding the reasons for withdrawal. Moreover, there were no reports of adverse

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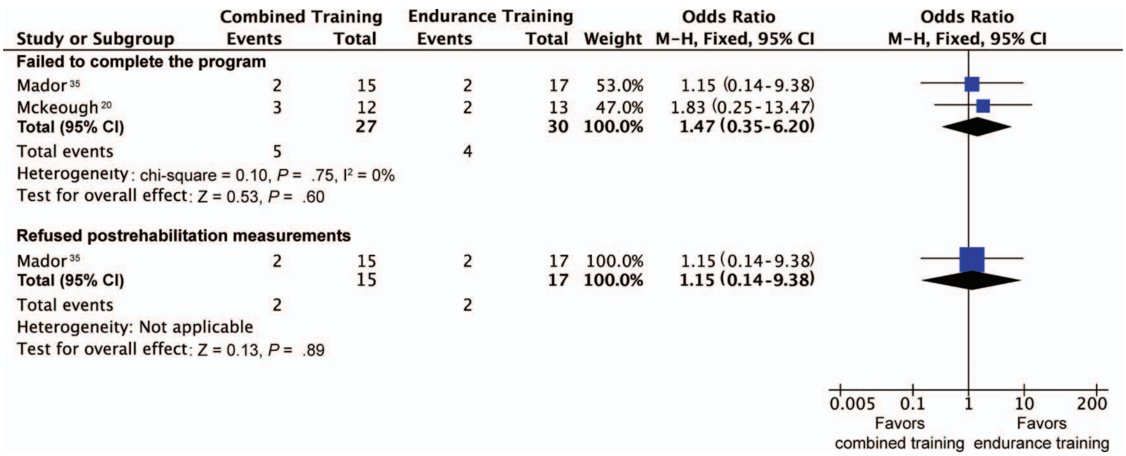

Fig. 10. Effects of combined resistance and endurance training vs endurance training alone on reasons for withdrawal. M-H = Mantal-Haenszel statistics.

events related to resistance-training intervention. Our results indicate that resistance training is a safe and tolerable modality of exercise training for patients with COPD.

The main strength of our study was inclusion of a large pool of subjects with COPD, allowing us to perform robust analysis of clinically relevant outcomes following resistance training versus no-exercise control or combined resistance and endurance training versus endurance training alone. The trials included in this analysis used almost identical designs with regard to inclusion and exclusion criteria, and the clinical characteristics of study populations were homogeneous. However, the results should be interpreted with caution because they might have been influenced by other factors. First, the duration of the resistance-training intervention in most of included trials was too short to allow adequate evaluation of the long-term efficacy and exacerbations. Additional long-term studies are anticipated to answer this question.[41] Second, the availability of outcome data suitable for meta-analysis was limited. For comparisons of resistance training versus non-exercise control or combined resistance and endurance training versus endurance training alone, there was a lack of sufficient number of studies reporting SGRQ and CRQ scores and lung function. Third, there is a potential risk of publication bias[47] because negative findings are less likely to be published. We have not analyzed this aspect here. Fourth, none of the included studies reported the sample size calculation, although we were very rigorous in a thorough search of related publications. Based on the results of the sample size calculation, many of the included trials may have lacked sufficient sample size, which might be associated with bias. Fifth, the methodological quality of the 10 included RCTs was low to moderate. The reason may be explained by the fact that a double-blind design in studies on this topic may not be achievable. Despite this, we avoided including case-control studies, unlike several other related meta-analyses. Hence, our conclusions need further validation in large-sample studies. Finally, only 2 included trials performed intention-to-treat analysis. This suggested that most subjects included in our analysis were those who were able to or wanted to complete resistance-training programs, which inevitably induced bias. The current limitations noted in many studies on the use of resistance training in patients with COPD, including ours, may encourage future improvements in the quality of related research.

Nevertheless, in our study, the clinical homogeneity of the trials resulted in statistical homogeneity for all outcome measures across the trials. Selection bias was minimized using a systematic search strategy, and we specified the inclusion and exclusion criteria. Furthermore, 2 reviewers independently evaluated the selected studies, and all authors consulted to reach consensus if necessary. Double counting of subjects from overlapping publications was avoided. Selective reporting of secondary end points in published manuscripts may also bias results. We minimized this bias by obtaining supplemental data for included studies.

Conclusions

In summary, this meta-analysis showed that dyspnea scale scores, skeletal muscle strength, and lung function improved following resistance training. Although skeletal muscle strength and quality of life improved following combined resistance and endurance training, they failed to translate into improved exercise capacity. Our results indicate that resistance training can be successfully performed alone or in conjunction with endurance training without increasing adverse events during pulmonary rehabilitation. Because of the limitations of this meta-analysis, we suggest further work to compare resistance training versus non-exercise control or combined resistance and endurance training versus endurance training alone. Larger, longer, multi-center, double-blind, parallel RCTs are needed to validate the long-term outcomes and safety of resistance-training programs for patients with COPD.

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