Effects of Breathing Exercises on Patients With Lung Cancer

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PROBLEM IDENTIFICATION: To evaluate the effects of breathing exercises on dyspnea, six-minute walk distance (6MWD), anxiety, and depression in patients with lung cancer.

LITERATURE SEARCH: A systematic literature search of the Cochrane Library, Web of Science, Embase®, PubMed®, Weipu, Wanfang, and Chinese National Knowledge Infrastructure databases was performed for publications dated prior to April 6, 2018.

DATA EVALUATION: The meta-analysis was performed using Review Manager and Stata.

SYNTHESIS: 15 randomized controlled trials with a total of 870 participants met the inclusion criteria. The findings suggest that breathing exercises have positive effects on dyspnea and 6MWD, but not on anxiety and depression. Subgroup analyses showed that breathing exercises combined with other exercises yield similar beneficial effects on dyspnea and 6MWD. In addition, breathing exercises in the surgery subgroup could significantly improve dyspnea and 6MWD. Dyspnea in the other treatment approaches subgroup was significantly improved, and 6MWD did not increase significantly.

IMPLICATIONS FOR NURSING: Breathing exercises can be considered as a conventional rehabilitation nursing technique in clinical practice, and nurses should be aware of the importance of breathing exercises.

KEYWORDS lung cancer; breathing exercises; meta-analysis
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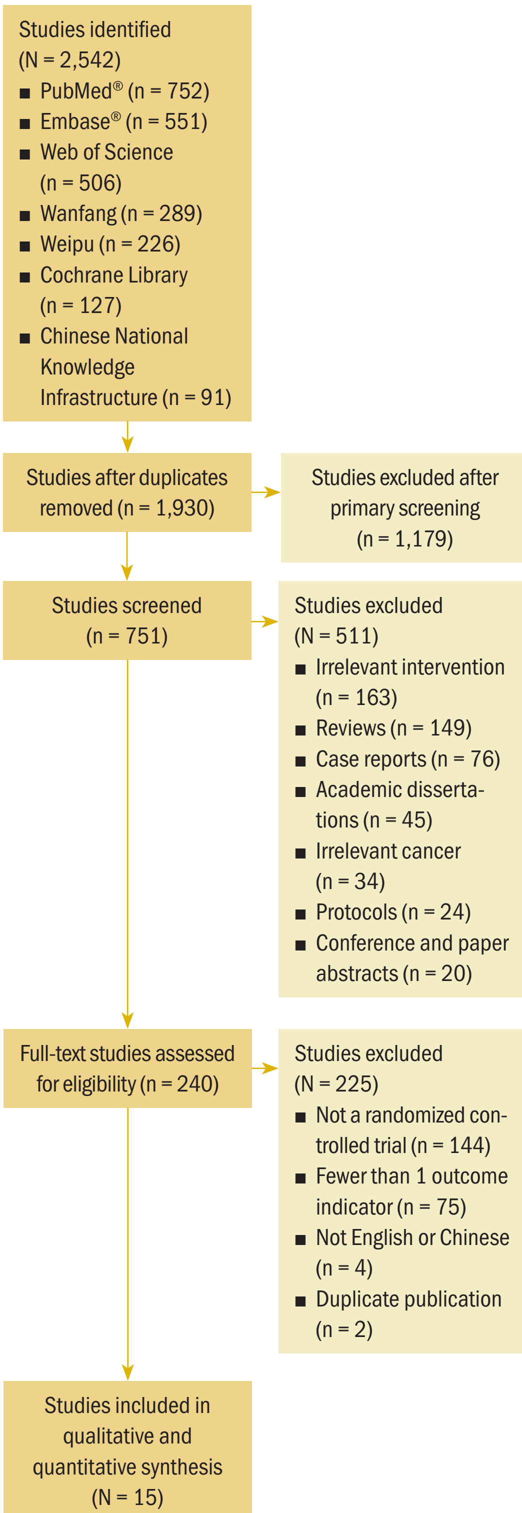
Lung cancer is not only one of the most common malignancies in the world, but it is also the number one cause of cancer-related death in the world (Mao, Yang, He, & Krasna, 2016; World Health Organization [WHO], 2019). In the past few years, the global burden of pulmonary cancer has been increasing, and the disease remains a main threat to public health worldwide (Gouvinhas et al., 2018; WHO, 2019). The treatments for lung cancer are surgery, chemotherapy, and radiation therapy. They aim to cure malignant tumors derived from lung tissue or to relieve the adverse effects (Kim, Boffa, Wang, & Detterbeck, 2012). Surgery is the optimal treatment for precancerous lesions and early- to middle-stage lung cancers (Boffa et al., 2008; Kim, Detterbeck, et al., 2012). However, many patients with advanced lung cancer refuse surgery because of the increased risk of postoperative pulmonary complications and lung function impairment; therefore, they choose chemotherapy, radiation therapy, and other treatment approaches (Baser et al., 2006; Boffa et al., 2008; Kim, Detterbeck, et al., 2012).

Regardless of the type of lung cancer treatment, the development of cancer and the invasion of lung tissue or surrounding tissues by cancer cells can interfere with normal breathing and lead to dyspnea or shortness of breath. In addition, most patients often experience other severe symptoms, such as decreased exercise capacity, anxiety, and depression, which lead to a significant decline in the quality of life (Ha, Ries, Mazzone, Lippman, & Fuster, 2018; Molassiotis, Charalambous, Taylor, Stamataki, & Summers, 2015).

Breathing is vital to maintaining the operation of the body organs and systems. However, surgery and other treatments targeting lungs inevitably present a substantial risk to the respiratory function of patients. The purpose of breathing exercises is to correct the incorrect breathing patterns, reestablish correct breathing methods, increase diaphragmatic activity, elevate alveolar ventilation, reduce energy consumption during the respiration, and ease shortness of breath in patients with lung cancer (Wei et al., 2013).

FIGURE 1. PRISMA Flow Diagram



PRISMA—Preferred Reporting Items for Systematic Reviews and Meta-Analyses

Several types of breathing exercises are reported in the literature. One of them, inspiratory muscle training (IMT), involves specific breathing exercises for respiratory muscles to improve their strength and, thereby, the respiratory function of lungs (Gosselink et al., 2011). Another approach, abdominal breathing exercises, can improve diaphragmatic descent and ascent during inhalation and exhalation, respectively. The physiological effect is achieved by breathing to sufficient vital capacity and maintaining the breath for three to five seconds to ensure the full expansion of lungs. This helps open the small-volume alveoli and stimulates the production of surfactants (Alaparthi, Augustine, Anand, & Mahale, 2016). Yet another approach, pursed-lip breathing, can prevent the premature closure of small airways and accelerates the discharge of residual gases from the lungs (Dellweg, Reissig, Hoehn, Siemon, & Haidl, 2017; Jones, Dean, & Chow, 2003).

In 2013, Wei et al. performed a meta-analysis, which concluded that breathing exercises could improve the quality of life and postoperative pulmonary function in patients with lung cancer. Since the publication of these findings, several additional randomized controlled trials (RCTs) exploring the effects of breathing exercises in patients with lung cancer have been published (Bai, Ma, Zhang, & Tian, 2018; Brocki, Andreasen, Langer, Souza, & Westerdahl, 2016; Guo, Dong, & Song, 2016; Henke et al., 2014; Huang et al., 2017; Jastrzębski et al., 2015; Li, Gao, Li, Wang, & Kong, 2016; Li, Yu, Su, & Ma, 2018; Ma & Yin, 2013; Molassiotis et al., 2015; Sebio et al., 2017; Stefanelli et al., 2013; Yorke et al., 2015). Some of these studies provide novel data on dyspnea, six-minute walk distance (6MWD), anxiety, and depression, thereby justifying a new comprehensive review of the existing evidence. The purpose of this study was to perform a systematic review and meta-analysis to assess the effect of breathing exercises on dyspnea, 6MWD, anxiety, and depression in patients with lung cancer.

Methods

This evidence-based review was conducted in compliance with the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) statement (Liberati et al., 2009).

Search Strategy

The authors conducted a systematic literature search of the Cochrane Library, Web of Science, Embase®, PubMed®, Weipu, Wanfang, and Chinese National Knowledge Infrastructure databases for relevant studies included in the databases prior to April 6, 2018.

TABLE 1. Characteristics of Included Studies

Study and Location	Participants	Intervention	Outcomes
Bai et al., 2018 (China)	■ Patients with lung cancer ■ Treatment: surgery ■ EG: N = 34; 23 men and 11 women; mean age = 55.89 years (SD = 7.64) ■ CG: N = 34; 21 men and 13 women; mean age = 56.84 years (SD = 8.34)	Breathing exercises (pursed-lip breathing, diaphragmatic breathing exercises, and spirometer), oxygen therapy, aerosol inhalation, and expectoration; 5 times daily at 3–5 minutes per session during hospitalization; CG received CC.	Dyspnea, 6MWD, pulmonary functions (FEV_1, FVC), quality of life, length of stay, PPCs
Bredin et al., 1999 (United Kingdom)	■ Patients with NSCLC, SCLC, and mesothelioma ■ Treatment: surgery, chemotherapy, and radiation therapy ■ EG: N = 51; 41 men and 10 women; mean age = 68 years (range = 41–82) ■ CG: N = 52; 35 men and 17 women; mean age = 67 years (range = 41–83)	Detailed assessment, advice and support, exploration, training in breathing control techniques, progressive muscle relaxation, distraction exercises, goal setting, and early recognition of problems; once weekly for 3–8 weeks; CG received CC.	Dyspnea, anxiety, depression, World Health Organization performance status, quality of life
Brocki et al., 2016 (Denmark)	■ Patients with lung cancer ■ Treatment: surgery ■ EG: N = 34; 19 men and 15 women; mean age = 69.7 years (SD = 7.9) ■ CG: N = 34; 20 men and 14 women; mean age = 70.5 years (SD = 7.5)	IMT and physiotherapy twice daily for 2 weeks; CG received conventional physiotherapy.	Dyspnea, 6MWD, inspiratory muscle strength, PPCs, pulmonary functions (FVC% predicted, FEV_1% predicted, FEV_1/FVC), SpO_2
Corner et al., 1996 (United Kingdom)	■ Patients with NSCLC and SCLC ■ Treatment: chemotherapy and radiation therapy ■ EG: N = 11; 5 men and 6 women; mean age = 55 years ■ CG: N = 9; 7 men and 2 women; mean age = 69 years	Counseling, breathing retraining, relaxation, teaching coping, and adaptation strategies; once weekly for 1 hour per session for 3–6 weeks; CG: no intervention	Dyspnea, anxiety, depression, functional capacity
Guo et al., 2016 (China)	■ Patients with stage IIIA lung cancer ■ Treatment NR ■ EG: N = 40; 21 men and 19 women; mean age = 63.2 years (SD = 5.6) ■ CG: N = 39; 21 men and 18 women; mean age = 64.6 years (SD = 3.2)	Breathing exercises (pursed-lip breathing, diaphragmatic breathing exercises, breathing gymnastics, cough training) twice daily for 6 weeks; CG received CC.	Heart rate, oxygen saturation fraction, fatigue, dyspnea, 6MWD
Henke et al., 2014 (Germany)	■ Patients with NSCLC and SCLC stages IIIA, IIIB, and IV ■ Treatment: chemotherapy ■ EG: N = 18; demographics NR ■ CG: N = 11; demographics NR	Breathing techniques (active cycle of breathing), endurance training (walking exercise in the hallway, stair walking exercise), strength training (bridging exercise, diaphragmatic breathing exercises, biceps curl exercise, triceps extension exercise), physiotherapy; endurance training and breathing techniques performed 5 days weekly; strength training performed every other day of the week for 3 cycles of chemotherapy; CG received CC.	6MWD, quality of life, Barthel Index, muscle strength

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TABLE 1. Characteristics of Included Studies *(Continued)*

Study and Location	Participants	Intervention	Outcomes
Huang et al., 2017 (China)	■ Patients with NSCLC and chronic obstructive pulmonary disease stages I–III ■ Treatment: surgery ■ EG: N = 30; 21 men and 9 women; mean age = 64.1 years (SD = 5.3) ■ CG: N = 30; 21 men and 9 women; mean age = 63.6 years (SD = 6.5)	IMT (diaphragmatic breathing exercises, thoracic breathing training) 3–4 times daily at 15–20 minutes per session for 1 week; CG received CC.	6MWD, quality of life, pulmonary functions (peak expiratory flow), index of fatigue in exercise, index of dyspnea in exercise, length of stay, PPCs
Jastrzębski et al., 2015 (Poland)	■ Patients with NSCLC and SCLC ■ Treatment: chemotherapy ■ EG: N = 12; 10 men and 2 women; mean age = 59 years (SD = 7) ■ CG: N = 8; demographics NR	Group A: aerobic exercises and respiratory exercises, Nordic walking, resistance training; group B: respiratory muscles exercise, peripheral muscles of upper and lower extremities; once daily for 8 weeks; CG: no intervention	6MWD, dyspnea, physical functioning, quality of life
Li et al., 2016 (China)	■ Patients with lung cancer ■ Treatment: surgery ■ EG: N = 40; 24 men and 16 women; mean age = 62.15 years (SD = 7.61) ■ CG: N = 40; 16 men and 24 women; mean age = 60.38 years (SD = 7.51)	Breathing exercises (pursed-lip breathing, diaphragmatic breathing exercises), cough and expectoration, and breathing gymnastics 3 times daily at 15–20 minutes per session from admission to discharge; CG received CC.	Dyspnea, 6MWD, pulmonary functions (FEV_1, FVC, FEV_1/FVC), postoperative hospital stay
Li et al., 2018 (China)	■ Patients with lung cancer stages I–III ■ Treatment: surgery ■ EG: N = 67; 37 men and 30 women; mean age = 60.3 years (SD = 5.2) ■ CG: N = 67; 39 men and 28 women; mean age = 61.1 years (SD = 4.8)	Breathing exercises (pursed-lip breathing, diaphragmatic breathing exercises), cough and expectoration, and upper limb movement during hospitalization; frequency NR; CG received CC.	Dyspnea, 6MWD, pulmonary functions (FEV_1, FVC, FEV_1/FVC), anxiety, depression
Ma & Yin, 2013 (China)	■ Patients with lung cancer; mean age = 65.69 years (SD = 12.39) ■ EG: N = 30; demographics NR ■ CG: N = 30; demographics NR	Health education, 3-line relaxing method, and breathing relaxation training 2–3 times daily until surgery; CG received CC.	Anxiety, blood pressure, pulse, sleep quality
Molassiotis et al., 2015 (United Kingdom)	■ Patients with NSCLC, SCLC, and mesothelioma ■ Treatment: surgery, chemotherapy, and radiation therapy ■ 9 men and 37 women; mean age = 69.5 years (SD = 8.35) ■ EG: N = 23 ■ CG: N = 23	IMT (pressure threshold device) 5 times weekly for 30 minutes per day for 12 weeks; CG received CC.	Dyspnea, anxiety, depression, pulmonary function, quality of life
Sebio et al., 2017 (Spain)	■ Patients with NSCLC ■ Treatment: surgery ■ EG: N = 10; 9 men and 1 woman; mean age = 70.9 years (SD = 6.1) ■ CG: N = 12; 11 men and 1 woman; mean age = 69.4 years (SD = 9.4)	Breathing exercises (volume-oriented incentive spirometer), endurance training (calibrated cycle ergometer), and resistance training (elastic bands, body-weight exercises) 3–5 times weekly until surgery (mean time = 53.5 days); CG received CC.	6MWD, quality of life, muscle strength, length of stay, PPCs

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TABLE 1. Characteristics of Included Studies *(Continued)*

Study and Location	Participants	Intervention	Outcomes
Stefanelli et al., 2013 (Italy)	■ Patients with lung cancer and chronic obstructive pulmonary disease stages I–II ■ Treatment: surgery ■ N = 40; 23 men and 17 women ■ EG: mean age = 65.5 years (SD = 7.4) ■ CG: mean age = 64.8 years (SD = 7.3)	Respiratory exercises and high-intensity training of the upper and lower limbs 5 times weekly for 3 hours per session Monday through Friday for 3 weeks; CG received CC.	Dyspnea, physical performance, pulmonary functions (FEV_1, FEV_1% predicted, DLCO, DLCO% predicted)
Yorke et al., 2015 (United Kingdom)	■ Patients with lung cancer ■ Treatment NR ■ EG: N = 50; 22 men and 28 women; mean age = 67.8 years (SD = 10.1) ■ CG: N = 51; 25 men and 26 women; mean age = 67.6 years (SD = 9.1)	Controlled breathing techniques (diaphragmatic breathing exercises, calming techniques practiced), cough-easing techniques (education, identifying warning signs of cough, using modified swallow technique and relaxed throat breathing), acupressure, and information pack twice daily for 12 weeks; CG received CC.	Dyspnea, quality of life, cough, fatigue, anxiety, depression

6MWD—6-minute walk distance; CC—conventional care; CG—control group; DLCO—diffusing capacity of the lungs for carbon monoxide; EG—experimental group; FEV_1—forced expiratory volume in the first second; FVC—forced vital capacity; IMT—inspiratory muscle training; NR—not reported; NSCLC—non-small cell lung cancer; PPC—postoperative pulmonary complication; SCLC—small cell lung cancer; SD—standard deviation; SpO_2—arterial oxygen saturation

Inclusion Criteria

The following inclusion criteria were applied for the articles in this study:

- The study is a full-text manuscript published in English or Chinese.
- The research design is RCT.
- Patients were diagnosed with lung cancer, or a mixed cancer cohort that included lung cancer was studied.
- The main intervention methods in the experimental group were breathing exercises of various forms (e.g., abdominal breathing, pursed-lip breathing).
- The primary outcome measures were dyspnea and 6MWD, and the secondary outcome measures were anxiety and depression; articles that reported any one of these outcome measures were included in this analysis.

When the same patient cohorts were reported by two articles, the most recently published study was included.

Data Extraction

When the title and abstract indicated that a study potentially may be eligible for inclusion, the full text was obtained and analyzed. The disagreements were resolved by discussion, and, when necessary, a third reviewer was invited to act as a mediator. Two authors extracted variables from the included studies independently. The extracted data included the following:

- Design: first author name, publication year, and country
- Participants: number, mean age, gender proportion, cancer type, cancer stage, and treatment method
- Intervention: type, frequency, and length of intervention

Outcome Measures

Relevant information was tabulated in the Microsoft® Excel spreadsheet predesigned for this review. The authors cross-checked the coding sheets, and any discrepancies were settled by discussion and consensus.

Risk-of-Bias Assessment

The authors used the Cochrane Collaboration risk-of-bias tool to evaluate the risk of bias in the included studies (Higgins & Green, 2011). The risk of bias in each included study was evaluated by two authors

TABLE 2. Risk-of-Bias Assessment for the Methodologic Quality of the Included Studies							
Study	Random Sequence Generation	Allocation Concealment	Blinding of Participants/ Personnel	Blinding of Outcome Assessment	Incomplete Outcome Data	Selective Reporting	Other Sources of Bias
Bai et al., 2018	No	Unknown	No	Unknown	Yes	Yes	Yes
Bredin et al., 1999	Unknown	Yes	No	Unknown	Yes	Yes	Yes
Brocki et al., 2016	Yes	Yes	No	Yes	Yes	No	No
Corner et al., 1996	Unknown	Unknown	Unknown	Unknown	Yes	Yes	Yes
Guo et al., 2016	Yes	Unknown	Unknown	Unknown	Yes	Yes	Yes
Henke et al., 2014	Yes	Unknown	Unknown	Unknown	Yes	Yes	Yes
Huang et al., 2017	Yes	Unknown	No	Yes	Yes	Unknown	Yes
Jastrzębski et al., 2015	Unknown	Unknown	No	Unknown	No	Yes	Unknown
Li et al., 2016	Yes	Unknown	No	Unknown	Yes	Yes	Yes
Li et al., 2018	Yes	Unknown	No	Unknown	Yes	Yes	Yes
Ma & Yin, 2013	Unknown	Unknown	No	Unknown	Yes	Yes	Yes
Molassiotis et al., 2015	Yes	Unknown	No	No	Yes	Yes	Yes
Sebio et al., 2017	Yes	Yes	No	Yes	No	Yes	Yes
Stefanelli et al., 2013	Unknown	Unknown	No	Unknown	Unknown	Unknown	No
Yorke et al., 2015	Unknown	Unknown	No	No	Yes	Yes	Yes

independently, and all disagreements were settled through discussion. Studies were assessed for the risk of bias in each of the following domains: sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective outcome reporting, and other biases.

Statistical Analyses

Statistical analysis was performed using Review Manager, version 5.3, and Stata, version 12.0. The mean difference (MD) or standardized MD (SMD), with 95% confidence interval (CI), were used to count for continuous outcomes. Forest plots were constructed to clarify the effect size. Cochran's Q test and I^2 test were used to assess the statistical heterogeneity of effects. A random effects model was used when the heterogeneity was significant ($I^2 > 50\%$). Otherwise, a fixed effects model was used.

Subgroup analysis: Exercise training was included in some of the interventions in the analysis. To evaluate whether the intervention methods based mainly on breathing training would improve dyspnea and 6MWD, the authors divided patients into two subgroups (the breathing exercises subgroup and the combined breathing exercises with other exercises subgroup) for this meta-analysis. In addition, to assess whether the treatment approaches would influence the results, the authors divided patients into two subgroups (the surgery subgroup and the other treatment approaches subgroup) for the meta-analysis.

Sensitivity analysis: The authors conducted a sensitivity analysis by examining each study to evaluate the stability of the analysis. The merged results before the changes and the adjusted results were compared to seek out the sources of heterogeneity.

Publication bias: The authors drew the funnel plot using Review Manager, version 5.3, and conducted Egger's test using Stata, version 12.0, to assess the symmetry and analyze the publication bias.

TABLE 3. Effect Size of Breathing Exercises Intervention

	Experimental Group			Control Group					
Study	**N**	**X̄**	**SD**	**N**	**X̄**	**SD**	**Weight (%)**	**MD**	**95% CI**
6MWD									
Bai et al., 2018	34	361.27	51.49	34	302.16	46.37	15.3	59.11	[35.82, 82.4]
Brocki et al., 2016	34	–48.1	71.9	34	–31.7	79.1	12.5	–16.4	[–52.33, 19.53]
Guo et al., 2016	40	492.64	95.83	39	411.97	59.79	12.7	80.67	[45.54, 115.8]
Henke et al., 2014	18	18.71	104.7	11	–47.5	157	3.7	66.21	[–38.42, 170,84]
Huang et al., 2017	30	476.5	86.5	30	500.8	82.3	11.1	–24.3	[–67.02, 18.42]
Jastrzębski et al., 2015	12	563.9	64.6	8	509.4	134.3	4	54.5	[–45.48, 154.48]
Li et al., 2016	40	360.1	45.23	40	309.65	79.59	14.2	50.45	[22.08, 78.82]
Li et al., 2018	67	365.74	51.73	67	316.68	64.02	16	49.06	[29.35, 68.77]
Sebio et al., 2017	9	1.88	34.7	10	–31.5	64.6	10.4	33.38	[–12.63, 79.39]
Study	**N**	**X̄**	**SD**	**N**	**X̄**	**SD**	**Weight (%)**	**SMD**	**95% CI**
Anxiety									
Bredin et al., 1999	50	–	4.5	52	9.5	4.25	20.3	–2.16	[–2.65, –1.66]
Corner et al., 1996	11	1.5	1.25	9	–	1	19	1.25	[0.27, 2.24]
Li et al., 2018	67	10.39	1.95	67	17.42	2.63	20.3	–3.02	[–3.52, –2.52]
Ma & Yin, 2013	30	46.86	5.2	30	60.46	7.14	20	–2.15	[–2.79, –1.51]
Yorke et al., 2015	31	0.81	2.75	40	–0.06	3.1	20.4	0.29	[–0.18, 0.76]
Depression									
Bredin et al., 1999	50	0.5	4.25	52	6	3.5	26.9	–1.4	[–1.84, –0.97]
Corner et al., 1996	11	2.5	0.75	9	–	1	19.1	2.75	[1.46, 4.05]
Li et al., 2018	67	9.61	2.61	67	12.73	3.54	27.4	–1	[–1.36, –0.64]
Yorke et al., 2015	31	0.7	3.14	40	1.22	3.97	26.7	–0.14	[–0.61, 0.33]
Dyspnea									
Bai et al., 2018	34	1.45	0.53	34	3.67	0.98	10.9	–2.79	[–3.46, –2.11]
Brocki et al., 2016	34	0.77	1.51	34	1.12	1.91	11.5	–0.2	[–0.68, 0.28]
Guo et al., 2016	40	1.95	0.88	39	2.56	1.37	11.6	–0.53	[–0.98, –0.08]
Huang et al., 2017	30	1.1	1.3	30	1.2	0.7	11.4	–0.09	[–0.6, 0.41]
Jastrzębski et al., 2015	12	0.6	0.5	8	1.8	1.3	9.7	–1.28	[–2.27, –0.28]
Li et al., 2016	40	1.43	0.96	40	2.25	1.17	11.6	–0.76	[–1.21, –0.3]

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TABLE 3. Effect Size of Breathing Exercises Intervention *(Continued)*

	Experimental Group			Control Group					
Study	N	$\bar{X}$	SD	N	$\bar{X}$	SD	Weight (%)	SMD	95% CI
Dyspnea *(continued)*									
Li et al., 2018	67	1.42	0.23	67	2.31	0.4	11.5	–2.71	[–3.18, –2.24]
Molassiotis et al., 2015	18	2.5	1	18	3.4	1.4	10.9	–0.72	[–1.4, –0.05]
Stefanelli et al., 2013	20	0.9	1	20	1.8	0.7	10.9	–1.02	[–1.69, –0.36]

6MWD—6-minute walk distance; CI—confidence interval; MD—mean difference; SMD—standardized mean difference
Note. Heterogeneity for each category was as follows: 6MWD (I^2 = 27.32, t^2 = 731.46, I^2 = 71%, p = 0.0006), dyspnea (I^2 = 106.46, t^2 = 0.97, I^2 = 92%, p < 0.00001), anxiety (I^2 = 131.89, t^2 = 2.7, I^2 = 97%, p < 0.00001), and depression (I^2 = 44.92, t^2 = 0.9, I^2 = 93%, p < 0.00001).

Results

Study Selection

The electronic search yielded a total of 2,542 individual records (see Figure 1). From the pertinent literature, 15 RCTs (Bai et al., 2018; Bredin et al., 1999; Brocki et al., 2016; Corner, Plant, A'Hern, & Bailey, 1996; Guo et al., 2016; Henke et al., 2014; Huang et al., 2017; Jastrzębski et al., 2015; Li et al., 2016, 2018; Ma & Yin, 2013; Molassiotis et al., 2015; Sebio et al., 2017; Stefanelli et al., 2013; Yorke et al., 2015) met the eligibility criteria. These publications reported the data for a total of 870 participants.

Study Characteristics

The characteristics of included studies are reported in Table 1. The studies were published from 1996 through 2018 and described data reported from seven locations in the United Kingdom, China, Germany, Italy, Spain, Poland, and Denmark. In these studies, 12 RCTs assessed dyspnea, 9 RCTs evaluated 6MWD, 6 RCTs assessed anxiety, and 5 RCTs evaluated depression. The treatment approach was surgery in eight trials (Bai et al., 2018; Brocki et al., 2016; Huang et al., 2017; Li et al., 2016, 2018; Ma & Yin, 2013; Sebio et al., 2017; Stefanelli et al., 2013), with the sample size ranging from 22–80 patients. Chemotherapy was used as a treatment approach in two trials (Henke et al., 2014; Jastrzębski et al., 2015), and the sample size was 49 patients. The combination of chemotherapy and radiation therapy was used in one trial (Corner et al., 1996), and the sample size was 20 patients. Two trials (Bredin et al., 1999; Molassiotis et al., 2015) reported the combination of three treatments, and the sample size was 149 patients. The remaining trials (Guo et al., 2016; Yorke et al., 2015) did not refer to a specific treatment approach, and the sample size was 180 patients. The length of the intervention was 1 week to 12 weeks.

Methodologic Quality

Every included study attempted to randomize the participants into an experimental group and a control group, but some studies did not present the details of the randomization procedures. In addition, the risk of bias in some studies was predominately because of inadequate blinding of patients, therapists, or assessors. Owing to the ambiguity in the allocation concealment and the lack of blinding, the methodologic quality of some studies was poor. The results of the bias risk assessment are summarized in Table 2.

Primary Outcomes

Dyspnea: For the reported dyspnea scores (Bai et al., 2018; Brocki et al., 2016; Guo et al., 2016; Huang et al., 2017; Jastrzębski et al., 2015; Li et al., 2016, 2018; Molassiotis et al., 2015; Stefanelli et al., 2013), a random effects model was used on the basis of high heterogeneity (I^2 = 92%). The results revealed that breathing exercises could significantly improve dyspnea (SMD = –1.11; 95% CI [–1.79, –0.44]; p = 0.001) (see Table 3). Because of the use of different scales, the data from three of the articles could not be extracted for quantitative synthesis. In two RCTs (Bredin et al., 1999; Corner et al., 1996), the visual analog scale was used to assess dyspnea, and in one RCT (Yorke et al., 2015), dyspnea was assessed with a numeric rating scale and the Dyspnoea–12 scale. The results of these studies showed that dyspnea scores in the experimental groups were significantly improved.

6MWD: The studies' analysis (Bai et al., 2018; Brocki et al., 2016; Guo et al., 2016; Henke et al., 2014; Huang et al., 2017; Jastrzębski et al., 2015; Li et al., 2016, 2018; Sebio et al., 2017) demonstrated a considerable evidence of high heterogeneity (I^2 = 71%). Therefore, the authors used the random effects model for this analysis. The results showed considerable beneficial effects of breathing training, which increased the 6MWD by 37.72 meters on average (MD = 37.72; 95% CI [15.06, 60.37]; p = 0.001).

Secondary Outcomes

Anxiety: To analyze anxiety, a random effects model was used because of high heterogeneity (I^2 = 97%) observed in the studies (Bredin et al., 1999; Corner et al., 1996; Li et al., 2018; Ma & Yin, 2013; Yorke et al., 2015). The forest plots revealed that breathing exercises did not improve anxiety in patients with lung cancer (SMD = –1.18; 95% CI [–2.65, 0.28]; p = 0.11).

Depression: To analyze depression, a random effects model was used on the basis of the high heterogeneity (I^2 = 93%) observed in the studies (Bredin et al., 1999; Corner et al., 1996; Li et al., 2018; Yorke et al., 2015). The results revealed that depression level was not statistically different between the experimental group and the control group (SMD = –0.16; 95% CI [–1.15, 0.83]; p = 0.75).

Subgroup Analysis

Dyspnea: Seven studies (Bai et al., 2018; Brocki et al., 2016; Guo et al., 2016; Huang et al., 2017; Li et al., 2016, 2018; Molassiotis et al., 2015) provided detailed breathing exercises data, and two studies (Jastrzębski et al., 2015; Stefanelli et al., 2013) provided detailed breathing exercises with other exercises data (see Table 4). The analysis indicated that in the breathing exercises subgroup, a significant difference between the intervention group and the control group was observed (SMD = –1.11; 95% CI [–1.92, –0.29]; p = 0.008). Significant difference between two groups was also observed in the combined breathing exercises with other exercises subgroup (SMD = –1.10; 95% CI [–1.65, –0.55]; p < 0.0001).

Six studies (Bai et al., 2018; Brocki et al., 2016; Huang et al., 2017; Li et al., 2016, 2018; Stefanelli et al., 2013) provided detailed surgical data, and two studies (Jastrzębski et al., 2015; Molassiotis et al., 2015) provided detailed data for other treatment approaches (see Table 5). The analysis indicated that in the surgery subgroup, a significant difference between the intervention and control groups was observed (SMD = –1.25; 95% CI [–2.21, –0.3]; p = 0.01), and in the other treatment approaches subgroup, there was also a significant difference between the two groups (SMD = –0.9; 95% CI [–1.46, –0.34]; p = 0.002).

TABLE 4. Subgroup Analysis of Intervention Methods for Dyspnea

	Experimental Group			Control Group					
Study	N	$\bar{X}$	SD	N	$\bar{X}$	SD	Weight (%)	SMD	95% CI
Breathing exercises									
Bai et al., 2018	34	1.45	0.53	34	3.67	0.98	10.9	–2.79	[–3.46, –2.11]
Brocki et al., 2016	34	0.77	1.51	34	1.12	1.91	11.5	–0.2	[–0.68, 0.28]
Guo et al., 2016	40	1.95	0.88	39	2.56	1.37	11.6	–0.53	[–0.98, –0.08]
Huang et al., 2017	30	1.1	1.3	30	1.2	0.7	11.4	–0.09	[–0.6, 0.41]
Li et al., 2016	40	1.43	0.96	40	2.25	1.17	11.6	–0.76	[–1.21, –0.3]
Li et al., 2018	67	1.42	0.23	67	2.31	0.4	11.5	–2.71	[–3.18, –2.24]
Molassiotis et al., 2015	18	2.5	1	18	3.4	1.4	10.9	–0.72	[–1.4, –0.05]
Breathing and other exercises									
Jastrzębski et al., 2015	12	0.6	0.5	8	1.8	1.3	9.7	–1.28	[–2.27, –0.28]
Stefanelli et al., 2013	20	0.9	1	20	1.8	0.7	10.9	–1.02	[–1.69, –0.36]

CI—confidence interval; SMD—standardized mean difference

Note. Heterogeneity for each subgroup was as follows: breathing exercises (I^2 = 106.21, t^2 = 1.15, I^2 = 94%, p < 0.00001), breathing and other exercises (I^2 = 0.17, t^2 = 0.00, I^2 = 0%, p = 0.68).

6MWD: Six studies (Bai et al., 2018; Brocki et al., 2016; Guo et al., 2016; Huang et al., 2017; Li et al., 2016, 2018) provided detailed breathing exercises data, and three studies (Henke et al., 2014; Jastrzębski et al., 2015; Sebio et al., 2017) provided detailed breathing exercises with other exercises data (see Table 6). The analysis indicated that in the breathing exercises subgroup, a significant difference between the intervention and control groups was observed (MD = 35.66; 95% CI [8.12, 63.2]; p = 0.01), and in the combined breathing exercises with other exercises subgroup, there was also a significant difference between the two groups (MD = 41.2; 95% CI [2.49, 79.92]; p = 0.04).

Six studies (Bai et al., 2018; Brocki et al., 2016; Huang et al., 2017; Li et al., 2016, 2018; Sebio et al., 2017) provided detailed surgical data, and two studies (Henke et al., 2014; Jastrzębski et al., 2015) provided detailed data on other treatment approaches (see Table 7). The analysis indicated that in the surgery subgroup, a significant difference between the intervention and control groups was observed (MD = 28.54; 95% CI [2.6, 54.48]; p = 0.03), and in the other treatment approaches subgroup, there was no significant difference observed between the two groups (MD = 60.09; 95% CI [−12.2, 132.38]; p = 0.1).

Sensitivity Analysis

To evaluate the stability and find the sources of heterogeneity of this meta-analysis, the authors performed a sensitivity analysis based on the primary outcome measures. For dyspnea, the heterogeneity significantly decreased (I^2 = 41%) when the authors removed two studies (Bai et al., 2018; Li et al., 2016), demonstrating that these studies were the primary source of heterogeneity. In addition, there was a significant difference in the adjusted pooled estimates between the intervention and control groups (SMD = −0.57; 95% CI [−0.85, −0.29]; p < 0.0001). Similarly, the heterogeneity of 6MWD significantly decreased (I^2 = 0%) when the authors removed two studies (Brocki et al., 2016; Huang et al., 2017). Still, the adjusted pooled estimates have not changed significantly (MD = 54.75; 95% CI [42.91, 66.59]; p < 0.00001). The sensitivity analysis indicates that the results of this meta-analysis were relatively robust.

Publication Bias

The funnel plot drawn using Review Manager and the result of Egger's test demonstrate no publication bias (p = 0.861).

Discussion

All studies included in the review were RCTs. The results of analysis indicate that breathing training

TABLE 5. Subgroup Analysis of Treatment Approaches for Dyspnea

	Experimental Group			Control Group					
Study	N	$\bar{X}$	SD	N	$\bar{X}$	SD	Weight (%)	SMD	95% CI
Surgery									
Bai et al., 2018	34	1.45	0.53	34	3.67	0.98	12.3	−2.79	[−3.46, −2.11]
Brocki et al., 2016	34	0.77	1.51	34	1.12	1.91	13	−0.2	[−0.68, 0.28]
Huang et al., 2017	30	1.1	1.3	30	1.2	0.7	12.9	−0.09	[−0.6, 0.41]
Li et al., 2016	40	1.43	0.96	40	2.25	1.17	13	−0.76	[−1.21, −0.3]
Li et al., 2018	67	1.42	0.23	67	2.31	0.4	13	−2.71	[−3.18, −2.24]
Stefanelli et al., 2013	20	0.9	1	20	1.8	0.7	12.4	−1.02	[−1.69, −0.36]
Surgery, chemotherapy, or radiation therapy									
Jastrzębski et al., 2015	12	0.6	0.5	8	1.8	1.3	11.1	−1.28	[−2.27, −0.28]
Molassiotis et al., 2013	18	2.5	1	18	3.4	1.4	12.3	−0.9	[−1.46, −0.34]

CI—confidence interval; SMD—standardized mean difference

Note. Heterogeneity for each subgroup was as follows: surgery (I^2 = 99.3, t^2 = 1.36, I^2 = 95%, p < 0.00001); surgery, chemotherapy, or radiation therapy (I^2 = 0.81, t^2 = 0.00, I^2 = 0%, p = 0.37).

TABLE 6. Subgroup Analysis of Intervention Methods for 6WMD

	Experimental Group			Control Group					
Study	N	$\bar{X}$	SD	N	$\bar{X}$	SD	Weight (%)	MD	95% CI
Breathing exercises									
Bai et al., 2018	34	361.27	51.49	34	302.16	46.37	15.3	59.11	[35.82, 82.4]
Brocki et al., 2016	34	–48.1	71.9	34	–31.7	79.1	12.5	–16.4	[–52.33, 19.53]
Guo et al., 2016	40	492.64	95.83	39	411.97	59.79	12.7	80.67	[45.54, 115.8]
Huang et al., 2017	30	476.5	86.5	30	500.8	82.3	11.1	–24.3	[–67.02, 18.42]
Li et al., 2016	40	360.1	45.23	40	309.65	79.59	14.2	50.45	[22.08, 78.82]
Li et al., 2018	67	365.74	51.73	67	316.68	64.02	16	49.06	[29.35, 68.77]
Breathing and other exercises									
Henke et al., 2014	18	18.71	95.83	11	–47.5	157	3.8	66.21	[–36.59, 169.01]
Jastrzębski et al., 2015	12	563.9	64.6	8	509.4	134.3	4	54.5	[–45.48, 154.48]
Sebio et al., 2017	9	1.88	34.7	10	–31.5	64.6	10.4	33.38	[–12.63, 79.39]

6WMD—6-minute walk distance; CI—confidence interval; MD—mean difference
Note. Heterogeneity for each subgroup was as follows: breathing exercises (I^2 = 26.91, t^2 = 933.72, I^2 = 81%, $p < 0.0001$), breathing and other exercises (I^2 = 0.41, t^2 = 0.00, I^2 = 0%, $p = 0.82$).

can bring many benefits to patients with lung cancer, because they improve dyspnea symptoms and increase 6MWD, even though they did not improve anxiety and depression scores. The previously published meta-analysis (Wei et al., 2013) covered two RCTs and six cohort studies; its results demonstrated that breathing exercises could significantly improve quality of life and the postoperative pulmonary function in patients with lung cancer. Because a small number of RCTs and limited research outcome indicators were used in this meta-analysis, more detailed evaluation of the effects of breathing training on patients with lung cancer is needed.

Because weakened breathing muscles cause dyspnea and reduce exercise capacity, breathing exercises should be regularly used in patients with lung cancer to reduce respiratory distress and improve 6MWD. Dyspnea is a common symptom in individuals with lung cancer in the early and intermediate stages of the disease. In addition, with conservative or aggressive management of pulmonary cancer, most patients with advanced disease usually suffer from dyspnea (Ban et al., 2016). This is an important concern because dyspnea can cause a deleterious effect on the quality of life of patients and their caregivers (Edmonds, Higginson, Altmann, Sen-Gupta, & McDonnell, 2000). Breathing exercises have a long history of research, particularly among patients with poor lung function or chronic obstructive pulmonary disease. There are several types of breathing exercises, such as IMT and abdominal breathing exercises. Other previous studies (Beaumont, Forget, Couturaud, & Reychler, 2018; Gosselink et al., 2011) demonstrated that breathing exercises improve dyspnea symptoms in patients, supporting the authors' conclusions.

Following the sensitivity analysis based on dyspnea, the authors discovered that two studies (Bai et al., 2018; Li et al., 2016) in the analysis were the sources of heterogeneity. The patients in both studies were all from China, and this may have caused the clinical heterogeneity because of the differences in the research centers and patient acceptance.

Breathing exercise for patients with lung cancer is a form of pulmonary rehabilitation. The analysis found that breathing exercises may increase 6MWD. Some other studies (Kumar et al., 2016; Rodrigues, Gurgel, Gonçalves, & da Silva Soares, 2018; Zeren, Demir, Yigit, & Gurses, 2016) also revealed that breathing exercises may significantly improve 6MWD.

In addition, one study (Wu, Kuang, & Fu, 2018) found that breathing exercises may relieve dyspnea and improve 6MWD and quality of life.

It is worth mentioning that breathing exercises may significantly improve 6MWD in the surgery subgroup. In the other treatment approaches subgroup, statistical significance was not reached. One possible reason is that the other treatment approaches subgroup included only two studies, with chemotherapy as a treatment approach. Patients with lung cancer often refuse surgery because of advanced stage of disease or advanced age, instead choosing chemotherapy. The lack of improvement in 6MWD may have occurred because of either the lack of motivation for patients to live a positive life or the reluctance of patients to participate in daily training because of fear of symptom exacerbation. Additional, more detailed studies are needed to clarify this issue.

Studies investigating the anxiety and depression improvements caused by breathing training have conflicting results. Corner et al. (1996) suggested that breathing exercises do not improve anxiety and depression. Bruurs, van der Giessen, and Moed (2013) found that breathing exercises could reduce hyperventilation, anxiety, and depression; improve quality of life; and lower the rate of medication use. However, these effects were not observed in the current analysis. It is worth mentioning that, because of missing data, the data from one article (Molassiotis et al., 2015) could not be extracted for quantitative synthesis. In this study, the anxiety and depression scores were significantly different between the two groups, with better scores in the breathing exercises group. These results should be interpreted with caution. Larger, longer, multicenter, parallel RCTs are needed to verify the impact of breathing exercises on anxiety and depression.

Limitations

This review has several limitations. The sample size of 870 patients with lung cancer was smaller than that in other reviews, which could limit analytical power. Many influencing factors could have given rise to clinical heterogeneity, such as diversities in the characteristics of interventions, controls, and the participants. The quality of studies and the differences in the research designs also could have resulted in methodologic heterogeneity. The authors did not assess lung function, pain, and long-term outcomes in the patients. These questions can be addressed in future studies. On account of differences in the interventions, it is unclear which of the interventions were specifically accountable for overall effect. Further research will need to be performed to investigate this question. Some studies had low methodologic

TABLE 7. Subgroup Analysis of Treatment Approaches for 6WMD

	Experimental Group			Control Group					
Study	**N**	**$\bar{X}$**	**SD**	**N**	**$\bar{X}$**	**SD**	**Weight (%)**	**MD**	**95% CI**
Surgery									
Bai et al., 2018	34	361.27	51.49	34	302.16	46.37	17.7	59.11	[35.82, 82.4]
Brocki et al., 2016	34	–48.1	71.9	34	–31.7	79.1	14.3	–16.4	[–52.33, 19.53]
Huang et al., 2017	30	476.5	86.5	30	500.8	82.3	12.6	–24.3	[–67.02, 18.42]
Li et al., 2016	40	360.1	45.23	40	309.65	79.59	16.4	50.45	[22.08, 78.82]
Li et al., 2018	67	365.74	51.73	67	316.68	64.02	18.7	49.06	[29.35, 68.77]
Sebio et al., 2017	9	1.88	34.7	10	–31.5	64.6	11.8	33.38	[–12.63, 79.39]
Surgery, chemotherapy, or radiation therapy									
Henke et al., 2014	18	18.71	95.83	11	–47.5	157	4.1	66.21	[–38.42, 170.84]
Jastrzębski et al., 2015	12	563.9	64.6	8	509.4	134.3	4.4	54.5	[–45.48, 154.48]

6WMD—6-minute walk distance; CI—confidence interval; MD—mean difference
Note. Heterogeneity for each subgroup was as follows: surgery (I^2 = 22.11, t^2 = 774.16, I^2 = 77%, p = 0.0005); surgery, chemotherapy, or radiation therapy (I^2 = 0.03, t^2 = 0.00, I^2 = 0%, p = 0.87).

quality, which was largely attributed to the inadequate blinding of patients, therapists, or assessors, and the inability to blind personnel and participants to the breathing exercise interventions. Sham breathing exercises can be used in future trials to blind participants, thereby improving methodologic quality. More research may be required to address this question.

Implications for Nursing

Patients with lung cancer often suffer from adverse symptoms, such as dyspnea and decreased exercise capacity, which seriously impair quality of life. The results of this meta-analysis support the beneficial effects of breathing exercises on dyspnea and 6MWD. Nurses need to be aware of the benefits of evidence-based breathing exercises for these adverse symptoms, and they need to deliver breathing exercise programs for patients with this disease. For more effective implementation of breathing exercises, nurses can provide different intensity or frequency of interventions that could be adopted by the patients with lung cancer at different stages of the disease. Nurses can make it easier for patients to receive and master breathing exercises in intuitive ways, such as live demonstration and video teaching. In patients with advanced disease, the degree of dyspnea is high and may result in decreased training. To improve adverse symptoms, individualized breathing training can be used. In addition, breathing exercises should be developed by using various management methods, such as encouraging patients to form partnerships with other patients in the same ward to supervise the implementation of training and ensure benefits from breathing exercises. Meanwhile, nurses can provide encouragement and advice about maintaining the daily breathing exercises to help patients address training barriers. Nurses' intervention is hoped to improve patients' understanding of breathing exercises, enhance confidence in rehabilitation, and improve effects of training. Long-term follow-up is needed to sustain the maintenance of long-term benefit from breathing exercises.

Conclusion

The analysis found that breathing exercises for patients with lung cancer may significantly improve dyspnea symptoms and increase 6MWD. No difference was observed in anxiety and depression scores between the experimental and control groups. Breathing exercises are effective treatment approaches and could be considered as a conventional rehabilitation nursing technique for patients with lung cancer in clinical practice.

KNOWLEDGE TRANSLATION

- Breathing exercises for patients with lung cancer may have beneficial effects on improving dyspnea and six-minute walk distance (6MWD).
- The 6MWD of patients with lung cancer who received surgery improved more than of those who received chemotherapy.
- Breathing exercises did not significantly improve psychological outcomes in this study.

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