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Acupuncture therapy improves health-related quality of life in patients with chronic obstructive pulmonary disease: A systematic review and meta-analysis

Po-Chun Hsieh[a,b], Mei-Chen Yang[c,d], Yao-Kuang Wu[c,d], Hsin-Yi Chen[c,d], I-Shiang Tzeng[e], Pei-Shan Hsu[a,b], Chang-Ti Lee[a,b], Chien-Lin Chen[a,b], Chou-Chin Lan[c,d,*]

[a] Department of Chinese Medicine, Taipei Tzu Chi Hospital, Buddhist Tzu Chi Medical Foundation, New Taipei, Taiwan
[b] School of Post-Baccalaureate Chinese Medicine, Tzu Chi University, Hualien, Taiwan
[c] Division of Pulmonary Medicine, Taipei Tzu Chi Hospital, Buddhist Tzu Chi Medical Foundation, New Taipei, Taiwan
[d] School of Medicine, Tzu-Chi University, Hualien, Taiwan
[e] Department of Research, Taipei Tzu Chi Hospital, Buddhist Tzu Chi Medical Foundation, New Taipei, Taiwan

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ABSTRACT

Background: Chronic obstructive pulmonary disease (COPD) is highly prevalent around the world and has a large impact on its patients, leading to a poor health-related quality of life (HRQL) and exercise capacity. Even under optimal medications, there are still many patients with poor HRQL. Body acupuncture therapy (BAT) is a non-invasive and a popular therapy. Therefore, we aimed to comprehensively analyze the effects of BAT in COPD.

Materials and methods: Eight electronic databases were searched. We included randomized controlled trials (RCTs) that evaluated the effect of BAT, medication (M), and pulmonary rehabilitation (PR). The primary outcome was HRQL evaluated by St. George's respiratory questionnaire (SGRQ) or COPD assessment test (CAT).

Results: Of the 922 articles, 12 studies were included with attesting a total of 798 participants. The result obtained indicated a significant improvement that favored the BAT + M group over the M group in CAT scores (MD: −4.77; 95% CI: −6.53 to −3.01; $p < 0.00001$).

Conclusions: BAT is an effective adjunctive non-pharmacological treatment to improve HRQL in patients under medical treatment for COPD. We suggested that BAT should be considered as one of the methods of management in patients with COPD.

1. Introduction

Chronic obstructive pulmonary disease (COPD) is a highly prevalent disease around the world and it has a large impact on the patients [1].COPD is predicted to be the third leading cause of death worldwide by 2020 [1]. COPD is characterized by airflow limitation along with systemic and airway inflammation [1]. Altogether, these features lead to muscle wasting, decreased physical activity, and worsening of dyspnea, which further lead to social isolation, anxiety, and depression [1]. However, even under pharmacologic and non-pharmacologic management as suggested by the GOLD guidelines [2], there are still many patients under poorly controlled functional status with a poor health-related quality of life (HRQL). Hence, it is necessary to develop another adjunctive treatment for COPD.

Pulmonary rehabilitation (PR) is regarded as an integral part of COPD management. In previous studies, we have suggested that PR results in several benefits which can improve the exercise capacity, HRQL, sleep quality, exertional dyspnea and cardiac autonomic function in patients with COPD [3–7]. Vieira et al. have also suggested that PR can improve the health status, functional capacity, respiratory muscle strength, and HRQL in most patients [8]. PR is therefore an important non-pharmacological management for COPD patients. However, PR has limited benefits gained from a home-based training programs [9]. Hospital-based PR results in greater benefits, but are more inconvenient and underutilized [10]. Only 1–2% of COPD patients receive PR [10]. Therefore, the application of other non-pharmacological management for COPD patients becomes necessary.

Acupuncture therapy is a popular, non-invasive therapy historically

* Corresponding author. Division of Pulmonary Medicine, Taipei Tzu Chi Hospital, Buddhist Tzu Chi Medical Foundation, New Taipei City, Taiwan, 289, Jianguo Road, Xindian City, Taipei County, 23142, Taiwan.
E-mail address: bluescopy@yahoo.com.tw (C.-C. Lan).

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used to treat various complaints [11]. The theory behind the use of acupuncture is to restore the balance of "vital flows" by inserting needles at particular points on the body surface where the "meridians" of these flows lie. It has been applied to many diseases, such as gut motility disorders [12], peripheral neuropathy [13], chronic pain [14], etc. There are also some studies about BAT in patients with COPD. We therefore aimed to comprehensively analyze the therapeutic effects of BAT in COPD.

2. Materials and methods

2.1. Search strategy

We searched five English databases, including PubMed, Embase, Medline, Cochrane Central Register of Controlled Trials (CENTRAL), Cumulative Index to Nursing, and Allied Health Literature (CINAHL), and three Chinese databases, including China National Knowledge Infrastructure (CNKI), Wanfang data, and Airiti library, from the earliest records to June 2018.

The search strategy comprised of the following keywords: "COPD" or "COAD" or "COBD" or "chronic obstructive pulmonary disease" or "chronic obstructive" or "chronic bronchitis" or "emphysema" or "pulmonary emphysema" or "lung emphysema" or "chronic airflow limitation" or "chronic airflow obstruction" or "chronic airflow obstructive" or "chronic obstructive lung disease" or "chronic obstructive airway disease" or "chronic obstructive respiratory disease" combined with "acupuncture" in English databases. Body acupuncture therapy (BAT) is a widely applied therapy in the Chinese cultural sphere; hence we used Chinese synonyms of COPD and acupuncture in Chinese databases.

2.2. Inclusion/exclusion criteria

Regarding the types of the studies, we included randomized controlled trials (RCTs) and excluded comparative experimental trials, single-armed follow-up studies, case series, and case reports. The target population comprised patients with stable COPD, which was defined as (1) COPD diagnosis based on the GOLD guidelines [15]; (2) stable from exacerbations without any further deterioration of respiratory symptoms (i.e., dyspnea, chest tightness, and cough), any increase in the use of rescue medication, and any unscheduled visits due to worsening COPD for at least three months [5]. All the retrieved studies were required to comprise at least two comparative treatment arms, one comprising BAT (including manual acupuncture and warm acupuncture), while the other comprising medication (M) or PR without BAT. We excluded interventions with Chinese herbal medicines, electroacupuncture, Acu-TENS, laser acupuncture, auricular acupuncture, acupressure, sham acupuncture, point application, and single-moxibustion. The bibliographies of included trials and related review articles were manually reviewed for relevant references.

2.3. Data extraction

We examined all the retrieved articles and extracted data using a predetermined form. We recorded the first author, year, diagnosis, treatment arms, enrolled sample number, age of participants, duration of the disease, and outcome measurements. The intervention details of BAT, comparative arm regimens, and adverse effects were also recorded.

2.4. Assessment of risk of bias

The methodological quality of the enrolled studies was evaluated by the two reviewers independently using the Cochrane RoB 2.0 tool [16]. The tool used to assess the quality of RCTs contained five assessment domains for risk of bias that lead to an overall bias. Discrepancies between the reviewers were solved through discussions with a third reviewer who acted as an arbiter.

2.5. Data synthesis

Primary outcomes included the mean difference of HRQL: St. George's respiratory questionnaire (SGRQ) and COPD assessment test (CAT). Secondary outcomes included the mean differences between (1) the lung function: FEV_1% predicted, and FEV_1/FVC ratio, (2) six-minute walk test (6MWT) and (3) risk ratio (RR) of the presence of adverse effects.

2.6. Statistical analysis

Statistical analysis was conducted by RevMan 5.3 (Cochrane, London, UK). Continuous outcomes were presented as weighted mean difference, with 95% confidence intervals (CI). Dichotomous data were presented as RR, with 95% CI. If the data could not be applied to meta-analysis, we summarized them in the text. Subgroup analyses were conducted to assessment whether the treatment effects were different in subgroups. If the value of I^2 test was greater than 50% or a low p value ($p < 0.10$) was reported for the ??^{2} test, we regarded it as a substantial between-trial heterogeneity. The random-effects model was employed if statistical heterogeneity existed. The fixed-effect model was employed if there was no significant statistical heterogeneity. Statistical significance was defined as p values < 0.05, except for the determination of publication bias, that employed $p < 0.10$. Analysis were performed by intention-to-treat if possible. For continuous variables, we used simple sensitivity analysis. For dichotomous outcome (presence of adverse effect), patients with incomplete or missing data were included in sensitivity analyses by counting them alternately as presence or absence of adverse effect.

If more than 10 studies were included in the meta-analysis, publication bias was investigated by funnel plots. In addition, a meta-regression analysis was performed to explore potential associations between the effect size and covariates of interest (treatment total times, treatment period, publication year, and sample size).

3. Results

3.1. Study identification

We retrieved 922 identified citations through database searching by reviewing their titles and abstracts. After eliminating the duplicated references that violated the inclusion criteria, 32 articles were included to conduct meticulous full-text evaluation for eligibility. We excluded 20 studies: 4 non-RCT studies, 3 studies whose diagnosis was not COPD, 6 studies that diagnosed AECOPD and 7 studies without targeted outcomes. Therefore, 12 RCT studies [17–28] were included for conducting the meta-analysis. The flow diagram for searching and identification of included studies is outlined in Fig. 1.

3.2. Characteristics of included participants and treatment

The final quantitative analysis included 798 participants. The severity of the disease in the included studies ranged in all the stages as judged by the GOLD staging [15]. The baseline lung function and quality of life were generally well balanced between the treatment groups. The included studies had similar inclusion and exclusion criteria. Patients diagnosed with stable COPD were included in the study, whereas those suffering from diseases showing similar clinical manifestation such as asthma or respiratory infection (in the weeks before enrollment) were excluded. Patient characteristics and study methodology of the retrieved studies were listed in Table 1.

All of the retrieved studies were RCTs comparing the effects of BAT, M, or PR on HRQL and lung function. Intervention details are listed in Table 2.

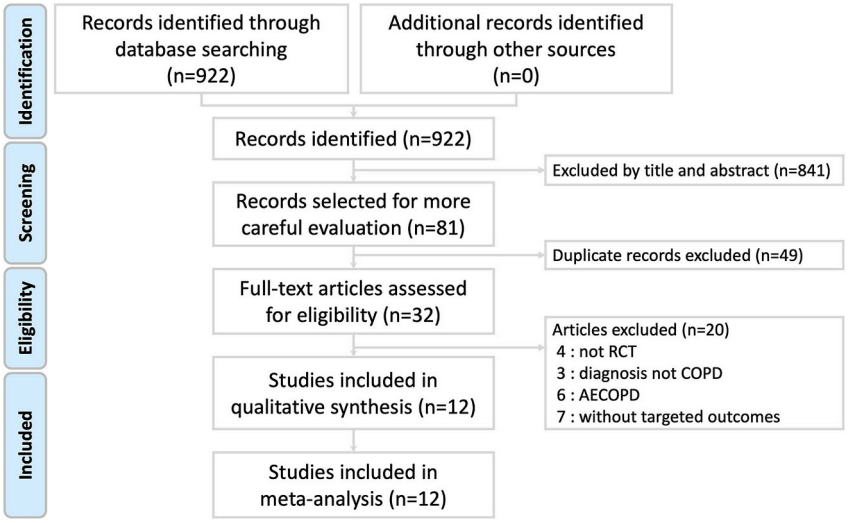

Fig. 1. Study flow diagram. Preferred reporting items for systemic reviews and meta-analysis (PRISMA) flow diagram for searching and identification of included studies.

3.3. Risk of bias assessment

The risk of bias assessment of the retrieved studies is shown in the risk of bias summary and risk of bias graph (Fig. 2A and B). The quality was variable, especially showing a high risk in the "bias due to deviations from intended interventions" domain. The possible reason for this is that none of the retrieved studies is patient-blinded study design.

3.4. Publication bias

Egger's test was not conducted as none of the meta-analysis included more than 10 studies. Although we conducted comprehensive searches, the potential publication bias cannot be avoided.

3.5. Primary outcome: HRQL

Between BAT + M group and M group: Two studies used CAT score as their outcome [23,25]. Pooled analysis did not show significant statistically heterogeneity (I^2 = 0%, $??^2$ = 0.04, p = 0.84); hence, the fixed-effect model was performed. The result obtained indicated a significant improvement that favored the BAT + M group over the M group in CAT scores (MD: −4.77; 95% CI: −6.53 to −3.01; Z = 5.32, p < 0.00001) (Fig. 3A).

Between BAT + PR group and PR group: Only one study used SGRQ score as its outcome [18]. The fixed-effect model was performed. The result obtained indicated that the BAT + PR group was equivalent to the PR group in SGRQ scores (MD: 0.30; 95% CI: −6.83 to 7.43) (Fig. 3B).

Between BAT group and M group: Two studies used SGRQ scores [19,20] and another one study used CAT scores [28] as their outcome. Pooled analysis showed statistically heterogeneity (I^2 = 94%, $??^2$ = 34.25, p < 0.00001); hence, the random-effects model was performed. The result obtained indicated that the BAT group was equivalent to the M group in SGRQ and CAT scores (MD: −3.32; 95% CI: −9.20 to 2.55; Z = 1.11, p = 0.27). (Fig. 3C).

3.6. Secondary outcomes

3.6.1. FEV_1% predicted

Between BAT + M group and M group: Three studies used FEV_1% predicted [23–25] as their outcome. Pooled analysis did not show statistically significant heterogeneity (I^2 = 32%, $??^2$ = 2.92, p = 0.23); hence, the fixed-effect model was performed. The result obtained indicated an improvement that favored the M group over the BAT + M group in FEV_1% predicted (MD: 1.98; 95% CI: 0.26 to 3.70; Z = 2.25, p = 0.02). (Fig. 4A).

Between BAT group and M group: Four studies used FEV_1% predicted as their outcome [19–21,28]. Pooled analysis showed statistically heterogeneity (I^2 = 73%, $??^2$ = 11.14, p = 0.01); hence, the random-effects model was performed. The result obtained indicated that the BAT group was equivalent to the M group in FEV_1% predicted (MD: −0.33; 95% CI: −3.45 to 2.80; Z = 0.20, p = 0.84). (Fig. 4B).

Between BAT + PR group and M + PR group: Two studies used FEV_1% predicted as their outcome [22,27]. Overall pooled analysis did not show statistically significant heterogeneity (I^2 = 0%, $??^2$ = 0.33, p = 0.57); hence, the fixed-effect model was performed. The result obtained indicated a significant improvement that favored M + PR group over the BAT + PR group in FEV_1% predicted (MD: 7.80; 95% CI: 6.91 to 8.68; Z = 17.19, p < 0.00001). (Fig. 4C).

3.6.2. FEV_1/FVC ratio

Between BAT + M group and M group: Three studies used FEV_1/FVC ratio as their outcome [23–25]. Pooled analysis did not show statistically significant heterogeneity (I^2 = 20%, $??^2$ = 2.49, p = 0.29); hence, the fixed-effect model was performed. The result obtained indicated that the BAT + M group was equivalent to the M group in FEV_1/FVC ratio (MD: 1.53; 95% CI: −0.42 to 3.48; Z = 1.54, p = 0.12). (Fig. 5A).

Between BAT group and M group: Four studies used FEV_1/FVC ratio as their outcome [19–21,28]. Pooled analysis showed statistically heterogeneity (I^2 = 50%, $??^2$ = 6.01, p = 0.11); hence, the random-effects model was performed. The result obtained indicated that the BAT group was equivalent to the M group in FEV_1/FVC ratio (MD: 0.01; 95% CI: −2.00 to 2.03; Z = 0.01, p = 0.99). (Fig. 5B).

Between BAT + PR group and M + PR group: Two studies used FEV_1/FVC ratio as their outcome [17,26]. Pooled analysis showed statistically heterogeneity (I^2 = 91%, $??^2$ = 10.98, p = 0.0009); hence, the random-effects model was performed. The result obtained indicated that the BAT + PR group was equivalent to the M + PR group in FEV_1/FVC ratio (MD: −3.50; 95% CI: −10.11 to 3.12; Z = 1.04, p = 0.30). (Fig. 5C).

3.6.3. Six-minute walk distance (6MWD)

Only one study provided 6MWD data [24]. The fixed-effect model was performed. The result obtained indicated that the BAT + PR group was equivalent to the M + PR group in 6MWD (MD: 8.40; 95% CI: −5.88 to 22.68).

Table 1
Summary of the retrieved studies.

Author	Year	Study design	Double-blind	Diagnosis	Intervention arms			Sample number (Male/Female)	Average age year, M(SD)	Duration of COPD year, M(SD)	Outcome measurement
Jia	2004	RCT	No	COPD	BAT	M	–	22 (9/13)	61.0 (32.6)	11.7 (8.9)	FEV_1, FEV_1/FVC ratio, MVV, TLC, RV, RV/TLC, therapeutic effects assessment
				Stage II or III	–	M	PR	22 (8/14)	60.0 (34.8)	12.1 (7.2)	
					BAT	M	PR	22 (10/12)	61.0 (33.2)	11.6 (9.0)	
Deering et al.	2011	RCT	No	COPD	BAT	–	PR	16 (8/8)	65.1 (9.7)	–	ISWT, daily number of steps, FEV_1% predicted, FVC % predicted, IVC % predicted,
					–	–	PR	19 (12/7)	67.7 (5.3)	–	PiMax, mMRC, Borg scale, SGRQ, EQ-5D, Physical activity duration, sleep
					–	–	–	19 (12/7)	68.6 (5.5)	–	efficiency, sleep time, metabolic equivalents, Il-6, IL-8, TNF-α, CRP, total energy expenditure
Fan et al.	2011	RCT	No	COPD	BAT	–	–	29 (13/16)	64.96 (8.71)	10.27 (5.71)	FEV_1, FEV_1/FVC ratio, FEV_1% predicted, SGRQ, symptoms assessment
					–	M	–	30 (12/18)	65.25 (10.68)	10.79 (5.26)	
Gao et al.	2011	RCT	No	COPD	BAT	–	–	30 (13/17)	64.87 (8.73)	10.31 (5.82)	FEV_1, FEV_1/FVC ratio, FEV_1% predicted, PEF, SGRQ, symptoms assessment
					–	M	–	30 (12/18)	65.25 (10.66)	10.78 (5.53)	
Xie et al.	2014	RCT	No	COPD	BAT	–	–	40 (22/18)	68.9 (8.7)	11.8 (6.5)	FEV_1, FEV_1/FVC ratio, FEV_1% predicted, PEF, symptoms score
					–	M	–	40 (18/22)	68.5 (9.6)	12.3 (5.5)	
Yu	2014	RCT	No	COPD	BAT	–	PR	30 (18/12)	63.0 (8.5)	8.9 (3.7)	FEV_1, FEV_1% predicted, FVC % predicted, therapeutic effects assessment, PaO_2,
				Stage II or III	–	M	PR	30 (17/13)	62.0 (7.6)	8.4 (3.5)	$PaCO_2$
Lee et al.	2015	RCT	No	COPD	BAT	M	–	29 (19/10)	57.21 (6.68)	10.38 (4.9)	FEV_1/FVC ratio, FEV_1% predicted, CAT, symptoms assessment, therapeutic effects
					–	M	–	30 (17/13)	55.8 (7.23)	10.7 (4.88)	assessment
Liu et al.	2015	RCT	No	COPD	BAT	M	–	40 (24/16)	58.3 (12.4)	–	6MWD, FEV_1% predicted, FEV_1/FVC ratio, clinical signs and symptoms assessment
				Stage III or IV	–	M	–	40 (26/14)	63.2 (10.7)	–	
Yang et al.	2016	RCT	No	COPD	BAT	M	–	30 (19/11)	57.7 (8.41)	10.6 (5.06)	FEV_1/FVC ratio, FEV_1% predicted, CAT, symptoms assessment, therapeutic effects
					–	M	–	31 (18/13)	58.23 (7.77)	10.39 (5.12)	assessment
Chu	2017	RCT	No	COPD	BAT	–	PR	34 (20/14)	65.94 (7.56)	9.03 (4.17)	FEV_1, FVC, FEV_1/FVC ratio, therapeutic effects assessment, PaO_2, $PaCO_2$
					–	M	PR	34 (22/12)	63.18 (6.73	10.24 (3.38)	
Lee	2017	RCT	No	COPD	BAT	–	PR	45 (27/18)	65.81 (2.75)	–	FEV_1, FVC, FEV_1% predicted, PaO_2, $PaCO_2$
					–	M	PR	45 (24/21)	62.74 (2.15)	–	
Shi et al.	2017	RCT	No	COPD	BAT	–	–	30 (18/12)	57.77 (6.54)	11.43 (4.37)	FEV_1% predicted, FEV_1/FVC ratio, CAT, clinical signs and symptoms assessment,
					–	M	–	31 (17/14)	55.9 (6.86)	11.68 (3.64)	therapeutic effects assessment, PaO_2, $PaCO_2$

RCT: randomized control trial, COPD: chronic obstructive pulmonary disease, BAT: body acupuncture therapy, M: medication, PR: pulmonary rehabilitation, FEV_1: forced expiratory volume in 1 s, FVC: forced vital capacity, PEF: peak expiratory flow, MVV: maximal voluntary ventilation, TLC: total lung capacity, RV: residual volume, IVC: inspiratory vital capacity, PiMax: Maximal inspiratory mouth pressures, 6MWD: six-minute walk distance, ISWT: incremental shuttle walk test, SGRQ: St. George's respiratory questionnaire, CAT: COPD assessment test, mMRC: Modified Medical Research Council.

Table 2
Summary of the intervention details.

Author	Year	Intervention arms			Intervention details	Acupuncture points	Acupuncture time (min.)	Intervention time
Jia	2004	BAT	M	–	(a) BAT: 2–3 Main Points + 1–2 Matching Points. Neutral supplementation and draining method with lifting-thrusting and twirling method till de qi, repeat once every 10 min during lasting needle. (b) M: With conventional medication for COPD.	Main points: BL13, BL43, LU9, KI3, BL23, ST36 Matching points: LU7, LU5, CV17, EX-B1	30	(a) every other day for 100 days, total: 50 times (b) not mentioned
		–	M	PR	(b) + (c) PR: Endurance Exercise, Breathing Exercise. With conventional medication for COPD.			(c) 100 day
		BAT	M	PR	(a) + (b) + (c)	Main points: BL13, BL43, LU9, KI3, BL23, ST36 Matching points: LU7, LU5, CV17, EX-B1	30	(a) every other day for 100 days, total: 50 times (b) not mentioned (c) 100 day
Deering et al.	2011	BAT	–	PR	(d) BAT: Using European standard, sterile, single use needles in the direction and depth recommended. + (e)	LI11, LI10, TE10, TE6, L5, L7	20	(d) once per week after class, total: 7 times (e) 2 h, twice per week for 7 weeks
		–	–	PR	(e) PR: Pulmonary rehabilitation was undertaken for 2 h, twice per week for 7 weeks, with a recommendation for 3 additional days (for 30 min), unsupervised, home exercise programming. The first hour of each PR session consisted of a prescribed exercise training program based on the results of an incremental shuttle walk test (ISWT). The second hour consisted of a multidisciplinary interactive educational session based on international guidelines. Patients also undertook inspiratory muscle training ranging between 15% and 30% of maximum inspiratory pressure (PiMax) for 10–15 min per day, 5 days per week; progressing to a maximum of 60% of PiMax for 30 min (or 2–15 min).			(e) 2 h, twice per week for 7 weeks
		–	–	–	no specific intervention as control group			
Fan et al.	2011	BAT	–	–	(f) BAT: 3 to 5 acupoints per session, manipulate till de qi., warming needle moxibustion was applied to the acupoints at back and ST36. The moxa sticks (10 mm in length) were inserted into the needle handle, ignited it and removed ashes when it burned out, two sticks for every point.	EX-B1, BL13, BL12, BL43, BL15, CV17, CV22, BL20, BL23, ST36	30	(f) every other day, 3 times a week for 8 weeks, total: 24 times
		–	M	–	(g) M: Seretide (Salmeterol 50 μg + Fluticasone 250 μg), 1 puff per time.			(g) 2 times a day for 8 weeks
Gao et al.	2011	BAT	–	–	(h) BAT: Main points + 2–3 Matching Points. Warming needle moxibustion was applied to the acupoints at back and ST36. The moxa sticks (10 mm in length) was inserted into the needle handle, ignited it and removed ashes when it burned out, two sticks for every point.	Main point: EX-B1, BL13, ST36, Matching point: BL12, GV14, BL43, BL15, CV17, CV22, BL20, BL23	30	(h) every other day, 3 times a week for 8 weeks, total: 24 times
		–	M	–	(i) M: Seretide (Salmeterol 50 μg + Fluticasone 250 μg), 1 puff per time.			(i) 2 times a day for 8 weeks
Xie et al.	2014	BAT	–	–	(j) BAT: Warming needle moxibustion was applied to the acupoints at back and ST36. The moxa sticks (10 mm in length) was inserted into the needle handle, ignited it and removed ashes when it burned out, two sticks for every point.	Main point: ST36, BL13, EX-B1 Matching point: BL43, BL15, GV14, BL12	30	(j) every other day, 3 times a week for 8 weeks, total: 24 times
		–	M	–	(k) M: Seretide (Salmeterol 50 μg + Fluticasone 250 μg), 1 puff per time.			(k) 2 times a day for 8 weeks
Yu	2014	BAT	–	PR	(l) BAT: Warming needle moxibustion was applied to the acupoints. The moxa sticks (10 mm in length) was inserted into the needle handle at a distance of 2–3 cm from skin, ignited it and removed the ashes when it burned out. 3–4 sticks for every point. + (m)	Main point: BL13, BL12, CV17, EX-B1, BL43, BL23, ST36 Matching point: LU7, LU5, ST40, SP10	–	(l) once a day, 5 times a week for 3 months, total: 60 times (m) once a day for 3 months
		–	M	PR	(m) PR: Breathing retraining including diaphragmatic breathing and pursed lip breathing. Endurance training including oxygen endurance training and upper extremity exercise, once a day. (n) M: With conventional medication of COPD.			(m) once a day for 3 months (n) not mentioned
Author	Year	Intervention arms			Intervention details	Acupuncture points	Acupuncture time (min.)	Intervention frequency
Lee et al.	2015	BAT	M	–	(o) BAT: Treatment started from Winter Solstice Festival (2014.7.18 to 2014.8.16). Warming needle moxibustion was applied to the acupoints. The moxa sticks (20 mm in length) was inserted into the needle handle, ignited it and removed ashes when it burned out, two sticks for every point. + (p)	GV14, BL13, BL20, BL23, BL17	30	(o) every other day for 30 days, 15 times for total (p) once a day for 30 days
		–	M	–	(p) M: Tiotropium Bromide Powder for Inhalation, 1 puff (18 μg) per time.			(p) once a day for 30 days

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Table 2 (*continued*)

Author	Year	Intervention arms			Intervention details	Acupuncture points	Acupuncture time (min.)	Intervention time
Liu et al.	2015	BAT	M	–	(q) BAT: Disposable filiform needles of 0.25 mm in diameter and 40 mm in length were used to puncture patients in a supine position. Qihai (CV 6) and Guanyuan (CV 4) were punctured 1.0–1.3 cun perpendicularly, followed by even reinforcing-reducing manipulation upon arrival of qi. The needles were removed after 10 min. Then the patient was asked to sit and bend the head. Feishu (BL 13), Shenshu (BL 23), Dingchuan (EX-B 1), Danzhong (CV 17) and Zusanli (ST 36) were punctured. Feishu (BL 13) was punctured 0.5–0.8 cun obliquely toward the spine; Shenshu (BL 23) was punctured 0.5–1 cun perpendicularly; Dingchuan (EX-B 1) was punctured 0.5–1 cun obliquely toward the spine; Danzhong (CV 17) was punctured 0.5–0.8 cun subcutaneously; and Zusanli (ST 36) was punctured1-1.3 cun perpendicularly. Even reinforcing-reducing manipulation was applied upon arrival of qi. The needles were retained for 10 min + (r)	BL13, BL23, CV6, CV4, EX-B1, CV17, ST36	20	(q) 2 times a week for 3 months, total: 24 times (r) 2 doses a day (once in the morning and once in the evening), for 3 months
		–	M	–	(r) M: Seretide inhaler, 50μg/250 μg for each dose			(r) 2 doses a day (once in the morning and once in the evening), for 3 months
Yang et al.	2016	BAT	M	–	(s) BAT: Treatment started from Winter Solstice Festival (2015.12.22 to 2016.1.17). Warming needle moxibustion was applied to the acupoints. The moxa sticks (20 mm in length) was inserted into the needle handle, ignited it and removed ashes when it burned out. Two sticks for every point. + (t)	GV14, BL13, BL20, BL23, BL17	30	(s) very other day for 27 days, 14 times for total (t) once a day for 27 days
		–	M	–	(t) M: Tiotropium Bromide powder for inhalation, 1 puff (18 μg) per time.			(t) once a day for 27 days
Chu	2017	BAT	–	PR	(u) BAT: Warming needle moxibustion was applied to the acupoints. The moxa sticks (10 mm in length) was inserted into the needle handle at a distance of 2.5 cm from skin, ignited it and removed ashes when it burned out. 3–4 sticks for every point. + (v)	Main point: ST36, BL23, BL43, EX-B1, CV17, BL12, BL13 Matching points: SP10, ST40, LU5, LU7	–	(u) once a day, 5 times a week for 3 months, 60 times for total (v) once a day for 3 months
		–	M	PR	(v) PR: Breathing retraining, endurance training, oxygen endurance training, upper extremity exercise, diaphragmatic breathing, pursed lip breathing, once a day. (w) M: Conventional medication of COPD.			(v) once a day for 3 months (w) not mentioned
Lee	2017	BAT	–	PR	(x) Warming needle moxibustion was applied to the acupoints. The moxa sticks was inserted into the needle handle. + (y)	BL13, BL12, CV17, EX-B1, BL43, BL23, ST36, LU5, ST40, SP10	–	(x) once a day, 3–5 times a week for 4 weeks, total: 12–20 times (y) for 4 weeks
		–	M	PR	(y) PR: slow walking exercise for 60 min per day. (z) M: Salbutamol Aerosol, 1–2 puff (100–200 μg) per time, less than 12 puff.			(y) for 4 weeks (z) for 4 weeks
Shi et al.	2017	BAT	–	–	(α) Adopted the “Shengsan Prescription” for acupuncture.	Main point: CV17, CV12, CV6, GV20, LI6, LU7 Matching point: LU9, ST36	30	(α) 3 times a week for 2 months, total: 24 times
		–	M	–	(β) Tiotropium Bromide powder for inhalation, 1 puff (18 μg) per time			(β) once a day for 2 months

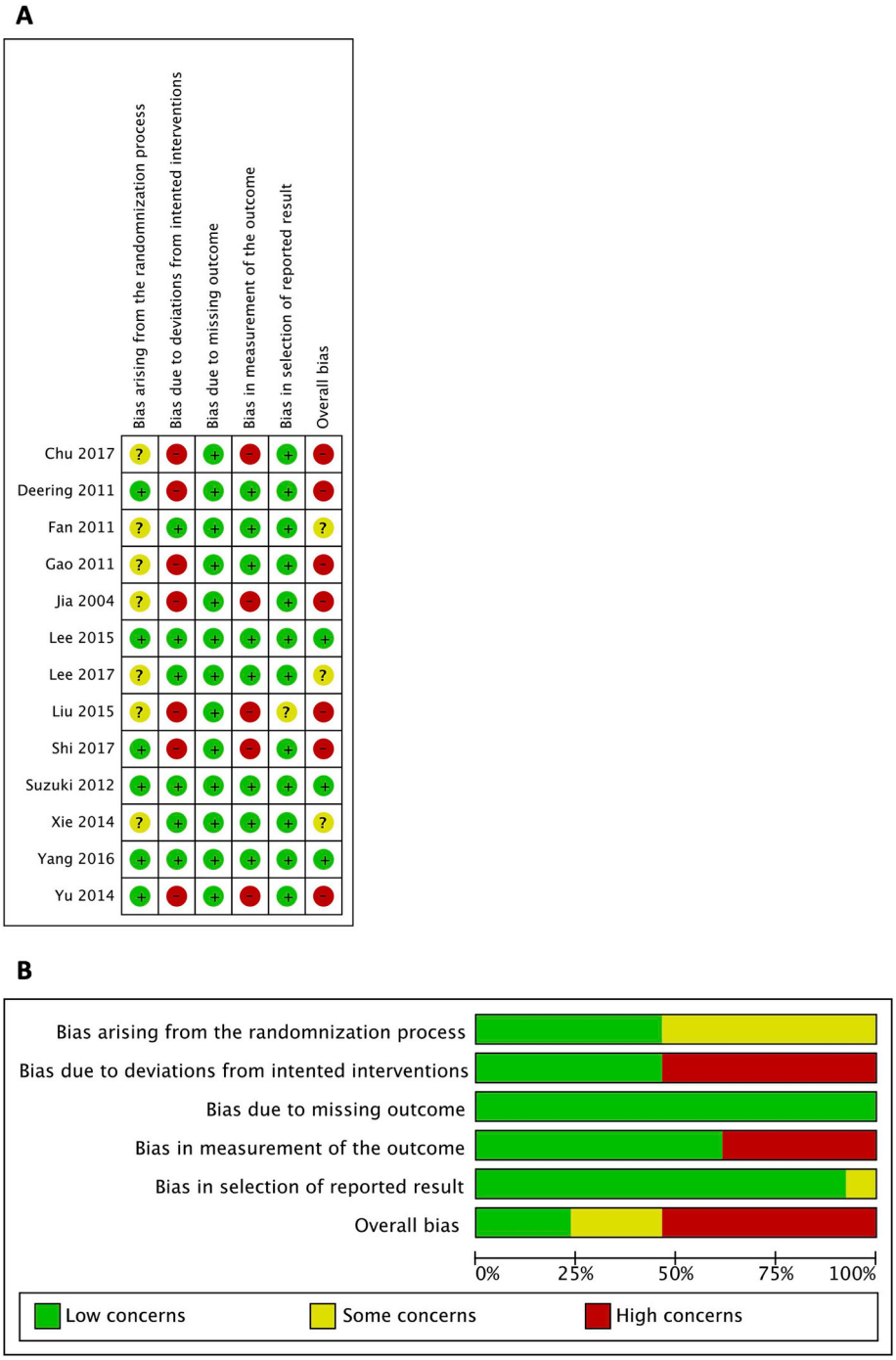

Fig. 2. Risk of bias summary and risk of bias graph. Review authors' judgement about each risk of bias item for each included study (RoB 2.0).

3.6.4. Presence of adverse effects

Three studies provided the information regarding adverse effects [23,25,28]. None of the studies reported the occurrence of any adverse effects during and after the trial. Hence the meta-analysis was not conducted.

3.6.5. Meta-regression analysis

The meta-regression analysis based on all included studies indicated potential associations between effect size and covariates of interest (treatment total times, treatment period, publication year, and sample size) (Table 3). However, the results showed that there were no statistically significant associations between effect size and those covariates except the treatment total times. Treatment total times showed a significant association and may lead to the heterogeneity of studies included.

4. Discussion

Our results indicate that BAT can further improve HRQL in patients under medical treatment. However, BAT cannot further improve the lung function (FEV_1% and FEV_1/FVC). Therefore, we suggested that BAT is a useful modality to improve HRQL in COPD.

A recent quantitative analysis evaluating the effects of acupuncture therapy in COPD patients [29] revealed that acupuncture therapy may

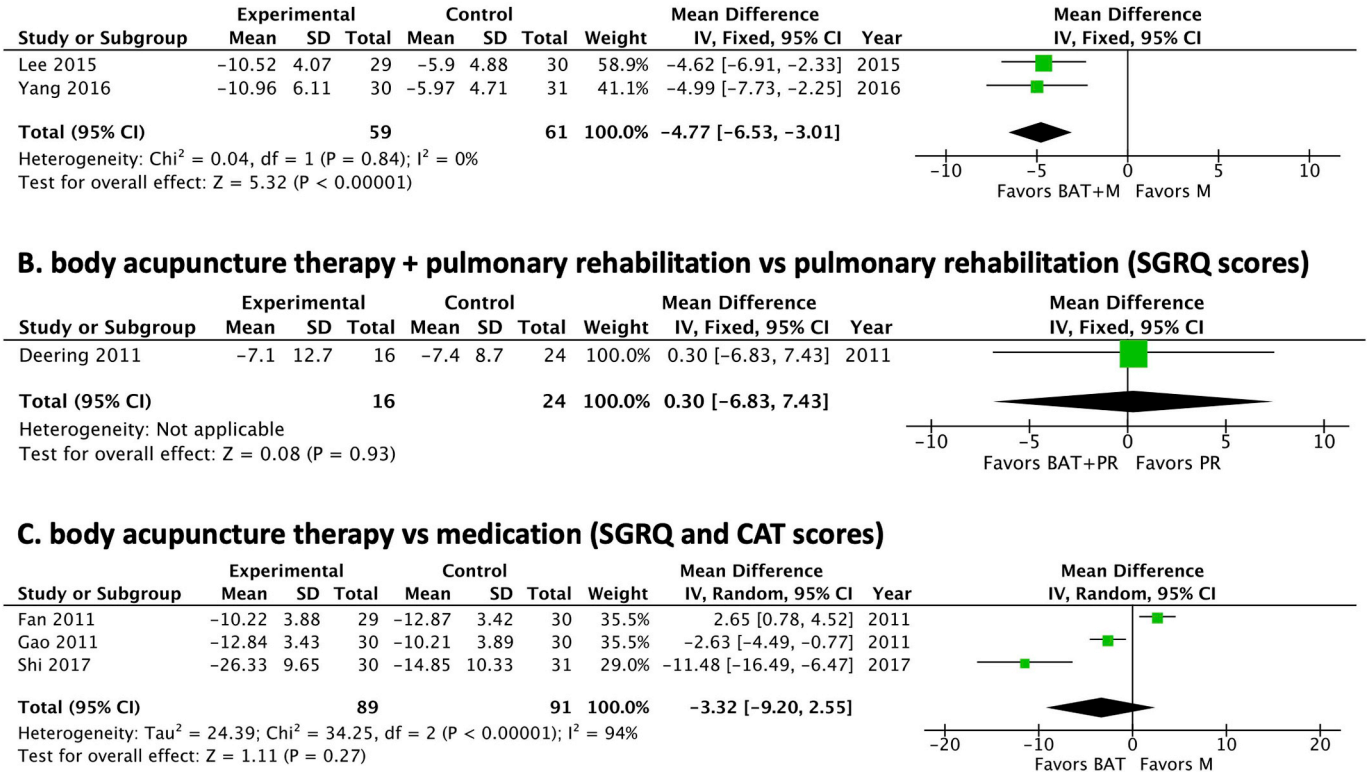

Fig. 3. Comparisons of HRQL

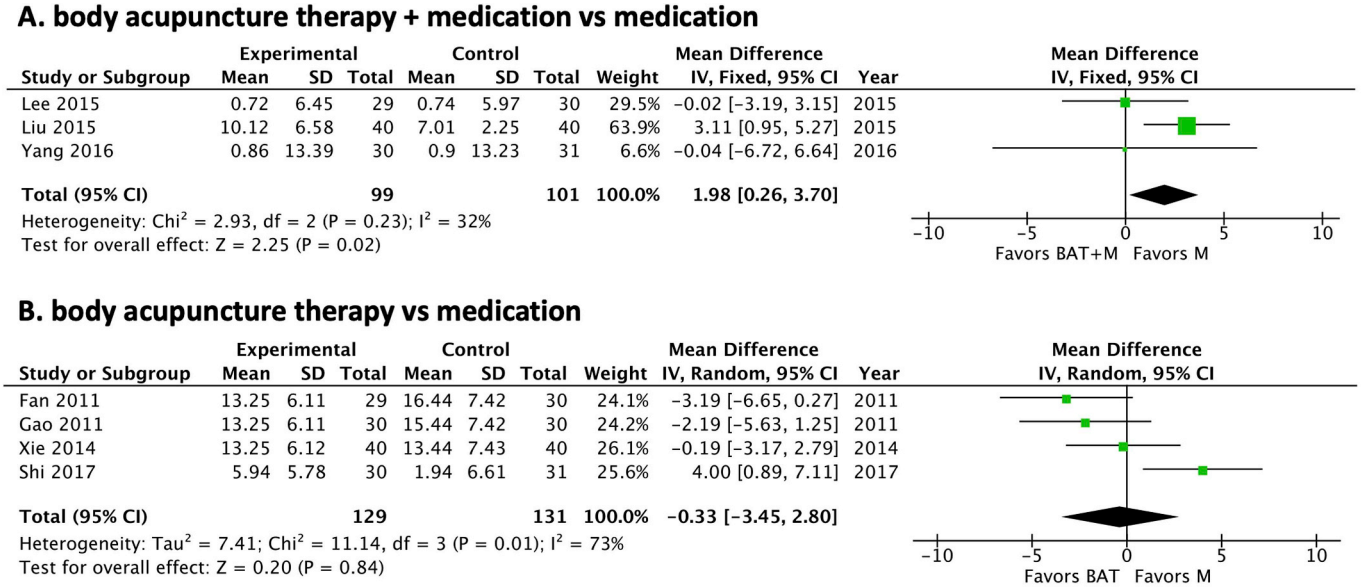

Fig. 4. Comparisons of FEV_1% predicted.

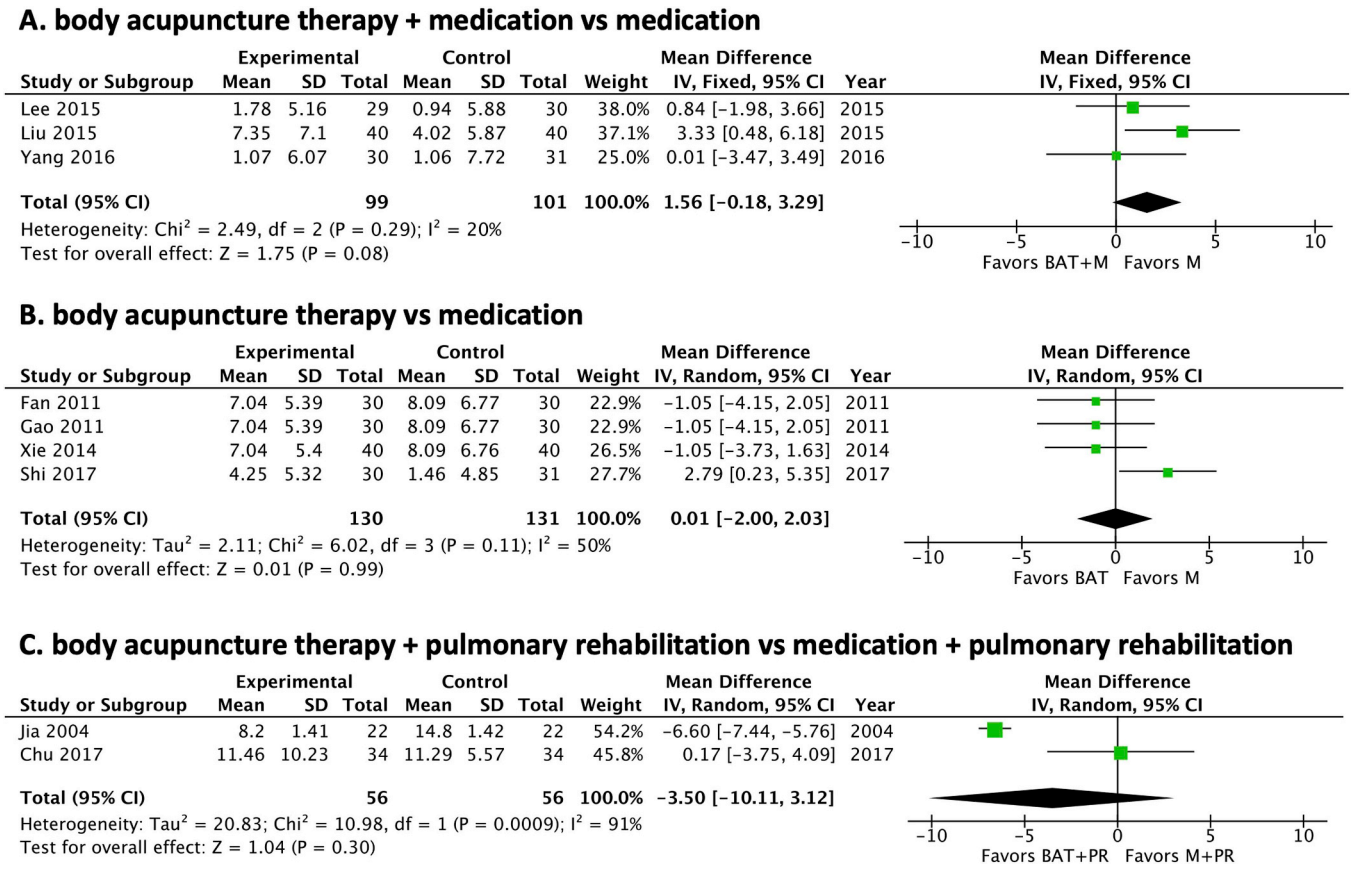

Fig. 5. Comparisons of FEV_1/FVC ratio.

be effective in improving the functional effects, pulmonary function, and quality of life in COPD patients. However, the comparative groups in the pooled analysis comprised of various types of treatment, such as Chinese herbal medicine, spreading moxibustion, manual acupuncture, electroacupuncture, auricular acupuncture, and warm acupuncture. It is difficult to define the pure effect of BAT in patients with COPD. Hence, to provide a clear recommendation regarding BAT, we conducted the meta-analyses to clarify the therapeutic effects of BAT in combination with M and PR. According to our study, BAT is an effective management for patients with COPD. In the retrieved studies, BL13, BL23, ST36, CV17, EX-B1, BL43, BL12, LU5, and LU7 were the most common acupuncture points [17–28]. Those points are also mainly used in treating respiratory system related symptoms and diseases in clinical practice [30].

The SGRQ is a questionnaire designed to measure the influence of COPD on HRQL [31]. A higher SGRQ score corresponds to poor HRQL. In our analysis, BAT significantly improved the HRQL even in patients under medical treatment. A decrease by 4 U in the SGRQ score met the minimal clinically important difference (MCID) [31,32]. Suzuki et al. showed that the SGRQ score decreased by 16.0 U in patients who underwent BAT [33]. They also suggested that BAT improved the 6MWD, and decreased exertional dyspnea [33]. Deering and colleagues also reported significant improvements in the functional capacity, HRQL; and breathlessness [18]. Liu et al. has proven that BAT combined with Seretide can further improve clinical signs, symptoms, and 6MWD [24]. Therefore, the effects of BAT on the exercise capacity, HRQL, and breathlessness were satisfactory in these studies.

PR with exercise training is an important management in COPD. In many previous studies, PR is known to improve the HRQL, exercise capacity, breathlessness, and health status [3–6,8]. However, PR with exercise training is relatively inconvenient and hinder many patients from attending the training program [10]. Through this meta-analysis, we compared the effects of PR and BAT. We suggested that PR and BAT have similar benefits in patients with COPD. However, BAT is a convenient and feasible intervention [34].

It is interesting to address the mechanisms associated with therapeutic effects of BAT. Several factors are thought to relate to poor HRQL and breathlessness in patients with COPD, including dynamic hyperinflation, poor respiratory muscle strength, and the limitation of rib cage movement [1,35,36]. Dynamic hyperinflation is one of the

Table 3
Meta-regression model with univariate analysis of interested covariates.

Covariates of interest	Coefficient	Std. error	*p* value	95% confidence intervals (CI)	
				Lower limit	Upper limit
Treatment total times	0.06387	0.01432	0.00211*	0.03085	0.09690
Treatment period	−0.04860	0.03143	0.17300	−0.12550	0.02831
Sample size	0.01913	0.03586	0.64700	−0.13517	0.17343
Publication year	0.07494	0.15785	0.64800	−0.28906	0.43894

*$p < 0.05$.

common causes of dyspnea and functional limitation [35]. Patients with COPD often develop lung hyperinflation, impairment of the inspiratory respiratory muscles, and an increased in work of breathing [35]. Kawakita et al. suggested that BAT suppressed electromyogram activity of the respiratory muscles that were hyper-activated by repeated eccentric contraction [37]. Decreased muscle tone consequently caused the recovery of the muscle strength in the rib cage, resulting in an increased mobility of the rib cage [37]. Relaxation of the respiratory muscles also resulted in a further reduction in energy expenditure, a reduction in oxygen consumption, and an improvement in breathlessness [33]. Therefore, BAT can improve respiratory muscle strength, decrease respiratory muscle hyper-activation as well as dynamic hyperinflation and breathlessness.

Poor nutrition is highly prevalent and correlated with skeletal muscle dysfunction, poor health status, and poor prognosis in patients with COPD [36]. In a previous study, the nutritional status in COPD patients was recovered after 12 weeks of BAT [33]. It was reported that BAT improves the gastrointestinal function, consequently facilitating food ingestion [12]. Suzuki et al. therefore suggested that improvement in gastrointestinal function and reduced dyspnea may facilitate food intake, resulting in a better nutritional status for these patients [33].

COPD is characterized by not only the airflow limitation but also by the airway and systemic inflammation [1]. The inflammatory markers, including interleukins (IL) (IL-6 and IL-8), tumor necrosis factor, and C-reactive protein levels are raised in patients with COPD compared to those of the healthy controls [1]. A previous study suggested that acupuncture can modulate the immune system by suppressing the inflammatory cytokines [38]. Another previous study also found that the phlegm expectoration, and shortness of breath were more significantly improved after BAT, indicating the improvement in airway inflammation by BAT [24].

5. Conclusions

Patients with COPD often suffer from poor HRQL, exercise capacity, and breathlessness. BAT is a convenient and feasible intervention to improve HRQL in patients under medication.

6. Limitation of study

Although, we suggested that BAT is effective in improving HRQL in COPD patients, a few limitations of this analysis still exist. Firstly, the standard treatment times of BAT for patients with COPD are unknown. The total times of treatment in the involved studies varied from 12 times to 50 times, and the greater the treatment times, greater were the benefits. However, the standard treatment times are still unknown. Secondly, these studies did not assess the effects of BAT in different severities of COPD. It is still unclear whether BAT is beneficial in severe or mild COPD. Therefore, further studies addressing the duration or severity of COPD are necessary.

Declarations of interest

None.

Contributors

PCH, CCL, MCY, YKW and HYC designed the review protocol. PCH, CCL and IST conducted the literature search, data extraction, quality assessment. PCH, CCL, PSH, CTL and CLC performed the analyses. PCH, CCL, CLC and YKW drafted the paper.

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