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Qigong for women with breast cancer: An updated systematic review and meta-analysis

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Highlights

- This meta-analysis showed that Qigong had a slight but statistically significant effect on improving quality of life in breast cancer patients.
- Qigong program Baduanjin, less than 60 min a session, frequency over 5 times weekly over 3 months, might have more positive effect on quality of life.
- Qigong is better to relieve depression and anxiety, this finding may have important implications given the association between depression, anxiety, and survival in prospective studies.

Abstract

Objective

The purpose of this review was to evaluate the effectiveness of Qigong in improving the quality of life and relieving fatigue, sleep disturbance, and cancer-related emotional disturbances (distress, depression, and anxiety) in women with breast cancer.

Methods

The PubMed, Cochrane Central Register of Controlled Trials, Web of Science, Sinomed, Wanfang, VIP, and China National Knowledge Infrastructure databases were searched from their inceptions to March 2020 for controlled clinical trials. Two reviewers selected relevant trials that assessed the benefit of Qigong for breast cancer patients independently. A methodological quality assessment was conducted according to the criteria of the 12 Cochrane Back Review Group for risk of bias independently. A meta-analysis was performed by Review Manager 5.3.

Results

This review consisted of 17 trials, in which 1236 cases were enrolled. The quality of the included trials was generally low, as only five of them were rated high quality. The results showed significant effectiveness of Qigong on quality of life ($n=950$, standardized mean difference (SMD), 0.65, 95 % confidence interval (CI) 0.23–1.08, $P=0.002$). Depression ($n=540$, SMD = −0.32, 95 % CI −0.59 to −0.04, $P=0.02$) and anxiety ($n=439$, SMD = −0.71, 95 % CI −1.32 to −0.10, $P=0.02$) were also significantly relieved in the Qigong group. There was no significant benefit on fatigue ($n=401$, SMD = −0.32, 95 % CI 0.71 to 0.07, $P=0.11$) or sleep disturbance relief compared to that observed in the control group ($n=298$, SMD = −0.11, 95 % CI 0.74 to 0.52, $P=0.73$).

Conclusion

This review shows that Qigong is beneficial for improving quality of lifeand relieving depression and anxiety; thus, Qigong should be encouraged in women with breast cancer.

Previous article

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Keywords

Qigong; Breast cancer; Systematic review; Meta-analysis

1. Introduction

Breast cancer is the most common cancer affecting women, with an estimated 2.1 million cases worldwide in 2018.[1] This number indicates a heavy burden on humanity. Breast cancer survivors, a majority of the 2.1 million cases, are defined as patients who have received primary treatment but are not receiving end of life care.[2] Because they tend to receive multimodal

treatment, including surgery, chemotherapy, and/or radiotherapy, they are at particularly high risk for related morbidity over an extended period.[3],[4] Side effects related to conventional therapy may include pain, fatigue, insomnia, pulmonary symptoms, radiation burns, nausea, vomiting, and sexual dysfunction. Survivors also face a higher risk of infection and may tend to experience more prolonged and severe symptoms, as their immune function is inhibited.[5],[6] Not surprisingly, they are also at increased risk for anxiety and depression.[7], [8], [9]

Because of increasing survivorship years, breast cancer is now considered a form of chronic illness.[10] According to the key points of expert consensus at the 5th Breast Health Global Initiative Global Summit, it is recommended that breast cancer survivors maintain a healthy lifestyle, including staying physically active and a maintaining a healthy weight, as well as a good mindset.[11] Growing evidence suggests that stress-reduction techniques (e.g., aerobic exercise, physical movements, meditation, progressive relaxation, diaphragmatic breathing, and guided imagery) are not only important factors influencing treatment effects, but are a way to generally improve quality of life and reduce any complications, especially emotional disturbances, that may follow treatment.[12],[13]

Qigong is classified as a bioenergy therapy with a long history of use for many diseases, including cancer. Qigong is composed of two terms: *qi* meaning “energy flow”, and *gong* meaning “skill” or “achievement”.[14] The main components of Qigong include training in consciousness, breathing, body movement, and adjustment or stimulation of one’s own qi.[14] The most distinct advantage of Qigong programs is that inhaling they facilitate the inhalation of much oxygen into the body, which contributes to the inhibited the growth of tumor cells and is favorable to the rehabilitation of cancer patients.[15] Additionally, Qigong is very good at regulating patients’ emotions and boosting their spirits.[16] Other investigations also found that the effects of Qigong in cancer patients were associated with an increased of oxygen content of arterial blood, potentially further improving microcirculation and enhancing the immune function.[17], [18], [19] Although some sporadic reports claim that Qigong improves quality of life and extends survival in cancer patients, there is not yet scientific evidence of this. A review of clinical trials examining the effects of qigong in cancer patients receiving chemotherapy revealed generally positive findings.[20],[21] In contrast, a 2016 systematic review evaluating the effectiveness of Qigong for breast cancer claimed that although the eight trials enrolled (including four randomized controlled trials (RCTs)). displayed several methodological and design limitations, it was still too early draw conclusions on the contribution of Qigong to rehabilitation care of breast cancer survivors without meta-analysis or other quantitative analysis.[22] Because several trials evaluating the effect of Qigong on quality of life, fatigue, sleep disturbance, and cancer-related emotional disturbance (distress, depression, anxiety) in women with breast cancer were published between the years of 2016 and 2020, it is reasonable to update the results. Thus, the purpose of this review was to evaluate the effectiveness of Qigong

in improving quality of life, and relieving fatigue, sleep disturbance, and cancer-related emotional disturbances (distress, depression, and anxiety) in women with breast cancer.

2. Materials and methods

A systematic review was performed according to the Cochrane Systematic Reviews Guidelines and the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) checklist.[23,24]

3. Searching strategies

PubMed, the Cochrane Central Register of Controlled Trials, Web of Science, Sinomed, Wanfang, VIP, and China National Knowledge Infrastructure (CNKI) databases were searched from inception to March 2020 for relevant controlled clinical trials (CCTs), including RCTs or nonrandomized CCTs without language restrictions. These searches were performed using the following keywords: “qigong”, “chi gong”, “buduanjin”, “breast cancer”, “breast neoplasm”, “breast tumor”, “breast carcinoma”, “mammary cancer”, “mammary carcinoma”, “mammary neoplasm”, and “mammary tumor”. First, two reviewers (MT and WJJ) screened the literature by scanning the titles and abstracts independently. Then, the full texts of the potentially eligible studies were obtained, and it was decided whether they should be included in the review. Additionally, other potentially relevant papers were searched using the reference lists of the identified articles. Disagreements were resolved by discussions between the two reviewers and, if necessary, through discussion with the third reviewer (CYQ).

4. Inclusion criteria

4.1. Participants

This trail included adult patients (≥18 years) who were diagnosed with breast cancer, regardless of breast cancer stage and previous or current treatment, including surgery or not, including chemotherapy and radiotherapy.

4.2. Interventions and controls

Trials that compared any type of Qigong with any type of control group were included. The Qigong type, length of program, length of session, frequency, and other details were not limited.

4.3. Outcomes

The primary outcome was quality of life, and the scales to evaluate quality of life were not limited. Secondary outcomes included fatigue, sleep disturbance, and cancer-related emotional disturbance (distress, depression, and anxiety), and the scales to evaluated these indexes were also not limited. Safety, which was recorded as adverse events, was also considered a secondary outcome.

4.4. Studies

Only RCTs or nonrandomized CCTs were eligible. Studies were excluded for the following reasons: (1) studies did not meet the above criteria; (2) reviews, meeting abstracts, and animal experiments; and (3) studies did not enroll control treatment.

4.5. Selection of studies

The selection of studies for inclusion was carried out by two authors (MT and WJJ) independently. They screened the abstracts of all identified potential studies. All articles with possible relevance were then retrieved in full text for comprehensive assessment of the inclusion criteria, and disagreement was resolved by discussion or consensus with a third reviewer (CHF).

4.6. Data extraction

Information was abstracted independently by two reviewers (MT and HSF). All study characteristics and outcome data were independently conducted according to predefined criteria using standard data extraction forms; disagreement was resolved by discussion or consensus with a third reviewer (CHF). Duplicate publications, missing data, changes in data, median data, and standard deviation were dealt with by methods from the Cochrane Handbook.[24]

4.7. Quality assessment

The risk of bias was assessed by two reviewers (MT and CYQ) independently, and disagreements were resolved by a third reviewer (CHF), in accordance with the use of the 12 Cochrane Back Review Group for risk of bias.[25] The 12 items for the risk of bias were divided into six domains, including A. Was the method of randomization adequate? B. Was the treatment allocation concealed? C. Was knowledge of the allocated interventions adequately prevented during the study? D. Were incomplete outcome data adequately addressed? E. Were reports of the study free of suggestion of selective outcome reporting? F. Other sources of potential bias. The judgment of each entry involved assessing the risk of bias as “low risk”, “high risk”, or “unclear risk”, indicating either a lack of information or uncertainty over the

potential for bias. We recommend that the studies be rated as having a “low risk of bias” when at least 6 of the 12 CBRG criteria have been met.

4.8. Statistical analysis

The Cochrane Collaboration software Review Manager 5.3 was used to perform the statistical analysis. Weighted mean differences (WMDs) with 95 % confidence intervals (CIs) were calculated for continuous data, and standardized mean differences (SMDs) were calculated for data measured in different ways by each trial. The I2 test was used to assess the heterogeneity of the data. If heterogeneity existed ($I^2 \geq 50\ \%$), a random model was applied; if not, a fixed model was applied.[19] If moderate clinical heterogeneity was identified and there were at least two trails on a stratum, subgroup analyses were conducted on the type of Qigong, length of program, length of session, frequency of session, and methodological quality, considering that these variables might have influenced the outcomes. Potential publication bias was investigated by visually examining the degree of asymmetry of a funnel plot.[24]

5. Results

5.1. Literature search

A total of 512 records identified through database searching and three additional records identified through other sources were retrieved in the literature search, and 252 of them were excluded as duplicates (Fig. 1). After an initial review of the title and abstract, 241 records were excluded. Of the remaining 22 articles, one article was excluded because it was only a protocol,[26] two articles were excluded as they did not report eligible outcomes,[27,28] and two articles were excluded as case series or case reports without controls,[29,30] Ultimately, 17 articles were included in this systematic review (Table 1).31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47

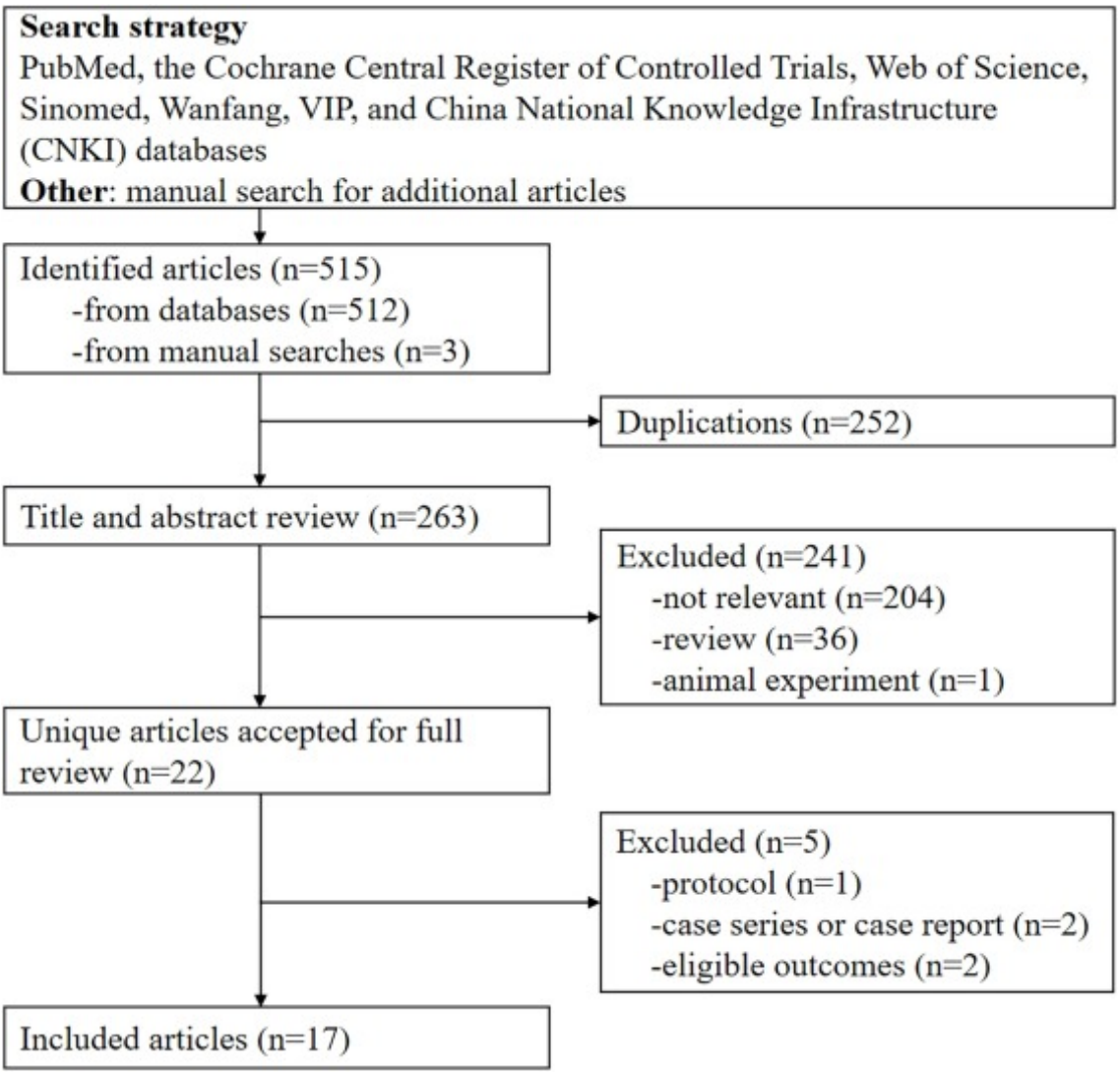

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Fig. 1. Flowchart of the search process of the review.

Table 1. The characteristics of trials included in the present review.

Study	Countries	Participant	Design	Intervention	Outcomes	Follow-up
Lee TI 2006 [26]	**China-Taiwan**	Breast cancer and preparing to have the first course of chemotherapy	Non-randomized CCT	**Chan-Chuang Qigong (n = 32)**	McCorkle and Young's symptom distress scale, the symptom checklist-90-revised	days 8, 15 and 22 after the beginning of chemotherapy

Study	Countries	Participant	Design	Intervention	Outcomes	Follow-up
				For at least 15 min but no more than 1 h per day during the first 21-day course of chemotherapy **Control (n = 35)** **No Chan-Chuang qigong, only chemotherapy** **Goulin New Qigong (n = 49)** **Five 40-min qigong classes each week during their 5 or 6 weeks of radiotherapy** **Control (n = 47)** **Waitlist, only radiotherapy**		
Chen Z 2013[27]	**China**	Breast cancer (stages 0-III)	RCT	**Tai Chi Qigong (n = 11)** **more than six months consecutively (three sessions per week, one hour per session)** **Control (n = 12)** **No Tai Chi Qigong**	FACT-General, BFI, PSQI, Center for Epidemiologic Studies Depression Scale, cortisol awakening response, Slope	Baseline, middle, last week of the trial, 1 and 3 months post the trial
Fong SS 2013[28]	**China-Hong Kong**	Breast cancer, received a mastectomy with or without chemotherapy or radiotherapy	Non-randomized CCT		FACT-Breast, Shoulder Mobility, rotator muscle strength, affected upper limb circumference, peripheral arterial resistance, side effects	Post the trial

Study	Countries	Participant	Design	Intervention	Outcomes	Follow-up
				Kuala Lumpur **Qigong (n = 32)** **30 minute twice a week during the 8-week intervention** **Control** **A. Exercise control (n = 31)** **Line-dancing program, same with Qigong group** **B. Usual care (n = 32)**		
Loh SY 2014 [29]	**Malaysia**	Primary diagnosis of early stage (I-II) breast cancer, had completed primary cancer treatment with no evidence of metastasis	RCT		FACT-Breast, FACIT-Fatigue short, Depression Anxiety, Stress Scale-short form	12 months post intervention
Larkey LK 2015 [30]	**USA**	Postmenopausal, breast cancer stages 0-III, 6 months to 5 years past primary treatment (surgery, radiation, or chemotherapy)	RCT	**Qigong/Tai Chi Easy (n=42)** **60 min over 12 weeks, meeting twice a week for the first 2 weeks, then once a week for the remainder of the period sham Qigong (n=45)** **The same with sham Qigong**	SF-36, BFI, PSQI, Beck Depression Inventory	Post intervention, and 3 months follow up
He GJ 2016 [31]	**China**	Unilateral breast cancer, received chemotherapy and no history of radiotherapy after modified radical mastectomy	RCT	**Baduanjin (n = 31)** **15-20 min, twice a day for 3 months** **Usual care (n = 33)**	BFI, Assessment of functional recovery of the affected limb	1 month, and 3 months after randomization
Huang	**China-**	Breast cancer	Non-	**Experimental**	SF-36,	1 month, and

Study	Countries	Participant	Design	group intervention	Outcomes	Follow-up
SM 2016 [32]	Taiwan.	who were about to start chemotherapy	randomized CCT	**A. Sporting qigong (n = 31)** **3 times lasted 30 min per week for 12 weeks** **B. Non-sporting qigong (n = 33)** **The same with SQG** **Control (n = 31)** **Postsurgical exercise, the same with SQG**	Edmonton Frail Scale	3 months after starting chemotherapy
Han Y 2017 [33]	**China**	Breast cancer, postoperative ≥ 1 month, in the period of chemotherapy	RCT	**Baduanjin (n = 30)** **20 min, once a day for 5 day per week for 3 months** **Usual care (n = 30)**	SAS, positive rates of anxiety-related serum protein, adverse events	3 months after randomization
Huang YQ 2017 [34]	**China**	6-8 courses of chemotherapy after modified radical mastectomy	RCT	**Baduanjin + Routine rehabilitation exercise (n = 40)** **30 min, twice a day for 4 months** **Routine rehabilitation exercise (n = 40)**	FACT-Breast, SDS	4 months after randomization
				Routine		

Study	Countries	Participant	Design	Intervention	Outcomes	Follow-up
				rehabilitation exercise in the middle and later stages of the affected limb		
Li Q 2017 [35]	**China**	Breast cancer, need radiotherapy after chemotherapy and modified radical mastectomy	RCT	**Baduanjin (n = 31)** **Once a day for 5 day per week for 3 months** **Usual care (n = 30)**	FACT-Breast, SAS, SDS	3 months after randomization
Liu P 2017 [36]	**China-Hong Kong**	Primary breast cancer stage 0-IIIb, completed surgical therapy, or/and radiotherapy, chemotherapy or a combination within the past one year	RCT	**Guolin-Qigong (n = 79)** **24-week intervention with GLQG (two 60-min sessions per week)** **Control (n = 79)** **Physical stretching, same with Qigong group**	FACT-Breast, Hospital Anxiety and Depression Scale, IL-2, IFN-γ, and TNF-α	12, 24 and 48 weeks follow-up
Shen LS 2017 [37]	**China**	Primary breast cancer stage I-Ⅱ, received modified radical mastectomy and chemotherapy	RCT	**Baduanjin (n = 30)** **30 min, once a day for 2 months**	FACT-Breast, Disability of the Arm, Shoulder and Hand Questionnaire, shoulder joint flexion range score, abduction rang score, extension rang score, pain	2 months after randomization
				Usual care (n = 30)		

Study	Countries	Participant	Design	Intervention	Outcomes	Follow-up
				Usual care (n = 30)	score	
				Baduanjin (n = 46)		
				3 days/week for 60 min at hospital and 4 days/week at home for 6 months	FACT-Breast, Patient Health Questionnaire, Generalized Anxiety Disorder-7, Heart rate variability, lung capacity, arm circumferences, shoulder range of motion, step test index,	6 months after randomization
Wang Y 2018 [38]	**China**	Breast cancer stage I-III, completed surgery, chemotherapy, and/or radiation) within the past 2 years	RCT	**Maintain original physical activity (n = 40)**		
				Maintain original daily physical activity for no less than 30 min per day over the following 6-month period		
				Baduanjin (n = 31)		
Wu L 2018 [39]	**China**	Breast cancer stage I-III, completed aromatase inhibitors treatment at least 6 months	RCT	**60 min a day for at least 3 day per week**	EORTCQLQ-C30, PSQI, Symptom score	3 months after randomization
				Usual care (n = 30)		
				Baduanjin (n = 46)		
				60 min, 3 days/week for 12 weeks		
Lan H 2019 [40]	**China**	Postmenopausal, breast cancer stage I-III 0.5-8 years, completed aromatase inhibitors treatment at least 6 months	RCT	**Maintain original physical activity (n = 40)**	Piper Fatigue Scale, Kupperman Index, IL-6, IL-1β and TNF-α	12 weeks after randomization
				Maintain original daily physical activity for 12 weeks		
Myers	**USA**	Breast cancer	RCT	**Qigong (n = 19)**	FACT-Cog	8 weeks, and

Study	Countries	Participant	Design	Intervention	Outcomes	Follow-up
JS 2019 [41]		stage I-III, completed chemotherapy (and radiation if received) 2 months to 8 years prior to enrollment		**15 min at home twice a day for 8 weeks** **Control** **A. Gentle exercise (n = 20)** **Same with Qigong group** **B. Support (n = 11)** **Encouraged to share their concerns and discuss problem-solving strategies**	quality of life, Fatigue score, Sleep disturbance score, distress score	12 weeks after randomization
Sun J 2019 [42]	**China**	Breast cancer, estimated lifetime greater than 6 months	RCT	**Baduanjin (n = 33)** **30 min, once per week for 28 days** **Usual care (n = 34)**	EORTCQLQ-C30, SAS, SDS, $CD3^+$, $CD4^+$, $CD8^+$, $CD4^+/CD8^+$	28 days after randomization

CCTs, controlled clinical trial; RCT, randomized controlled trial; BFI, Brief Fatigue Inventory; FACT, Functional Assessment of Cancer Therapy; PSQI, Pittsburgh Sleep Quality Index; SF-36, the Medical Outcomes Survey Short Form 36; DASH, Hospital Anxiety and Depression Scale; SDS, Self-rating depression scale; SAS, Self-rating anxiety scale; IL-2, interleukin-2; IFN-γ, interferon-γ; IL-6, interleukin-6; IL-1β, interleukin-1β, TNF-α, tumor necrosis factor-α; EORTCQLQ-C30, European organization for the research and treatment of cancer QLQ-C30.

Fourteen of the trials were RCTs,[32,33, 34, 35, 36,38, 39, 40, 41, 42, 43, 44, 45, 46, 47] and the remaining trails were CCTs.[31,33,37] Among the 17 trials included in this systematic review, ethnicity was reported in all studies except one.[31] 14 studies were conducted in China,[31, 32, 33,36, 37, 38, 39, 40, 41, 42, 43, 44, 45,47] two trials were performed in the USA,[35,46] and one was performed in Malaysia.[34] Types of qigong included Baduanjin Qigong,[36,38, 39, 40,42, 43, 44, 45,47] Chan-Chuang Qigong,[31] Goulin New Qigong,[32,41] Tai Chi Qigong,[33,35] and Kuala Lumpur Qigong.[34] The course of qigong ranged from 21 days to more than six months. Four trials compared qigong to no treatment,[31, 32, 33,46] one sham Qigong,[35] seven compared to other types of exercise,[34,35,37,41,43,45,46] and six to usual care.[34,38,40,42,44,47]

5.2. Methodological quality of included studies

Ten of these trials reported an adequate method of randomization,[32,34,35,38, 39, 40, 41, 42, 43,47] while only three trials had an adequate description of allocation concealment using either free online random allocation software or A4 opaque paper in sealed envelopes.[34,41,42] The blinding of participants and care providers could not be conducted due to the characteristics of qigong, but blinding of the outcome assessor was conducted in three studies.[33,41,43] All but five studies stated that drop-out rates were acceptable.[37,39,44, 45, 46] Among the studies that reported drop-out rates, only two reported that all randomized participants were analyzed in the group to which they were allocated.[34,39] Only one study was free of suggestion of selective outcome reporting, as it registered the protocol before the study was conducted.[43] The groups were similar at baseline regarding the most important prognostic indicators in most of the studies, except in seven trials.[34,38,39,42,44,45,47] Co-intervention were either similar or avoided, and the timing of the outcome assessment was similar in all groups in all studies. Compliance was acceptable in all groups, except in three trials.[32,41,43]

5.3. Main results

5.3.1. Quality of life

Thirteen trials tested the effects of Qigong on quality of life with generic scales, including the Functional Assessment of Cancer Therapy (FACT)-General,[32] FACT-Breast,[33,34,39, 40, 41, 42, 43] Medical Outcomes Survey Short Form 36,[35,37] FACT-Cog quality of life subscale,[46,47] and European Organization for the Research and Treatment of Cancer scale.[44] The trials used different scales to measure functional capacity, thus we used SMD to pool the results. The meta-analysis showed a positive effect of Qigong on quality of life compared to control procedures (n = 950, SMD, 0.65, 95 % CI 0.23–1.08, P = 0.002, Fig. 2).

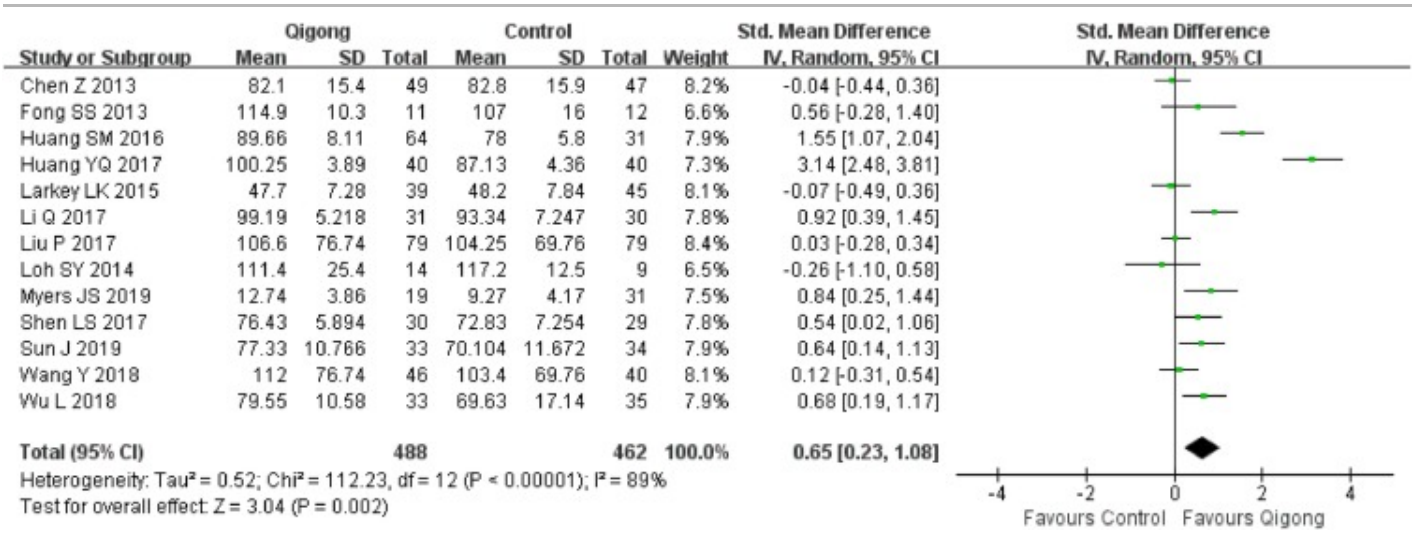

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Fig. 2. The forest plot of comparison between Qigong and control related to quality of life.

5.3.2. Fatigue

Six studies assessed the effect of Qigong on relieving fatigue, with the Brief Fatigue Inventory,[32,35,36] Piper Fatigue Scale,[45] and Fatigue score.[44,46] The meta-analysis showed that the included six studies (n = 401) had statistical heterogeneity (P = 0.003; I^2 = 73 %), indicating that the random-effects model should be considered. The pooled SMD showed a greater but not statistically significant effect in the participants of the Qigong groups (SMD, -0.32, 95 % CI -0.71 to 0.07, P = 0.11, Fig. 3).

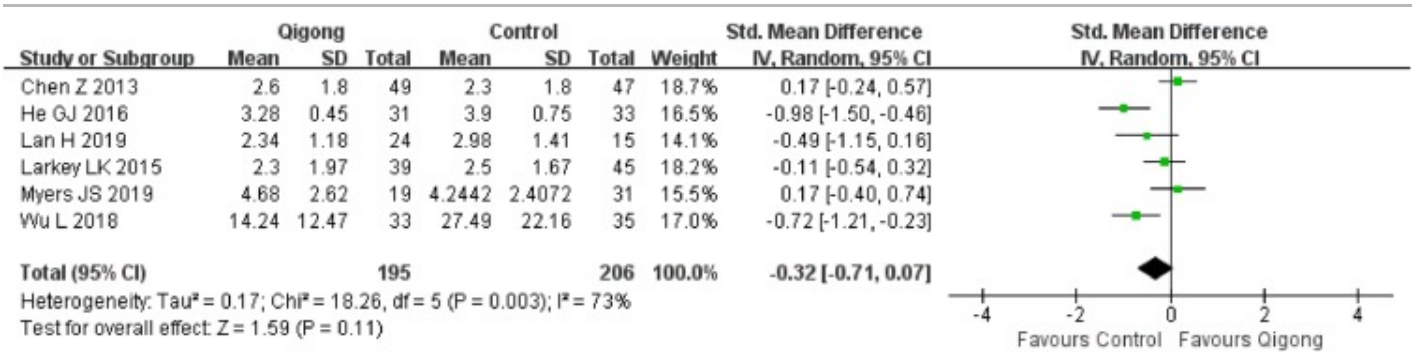

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Fig. 3. The forest plot of comparison between Qigong and control related to fatigue.

5.3.3. Sleep disturbance

Four studies assessed sleep disturbances by the Pittsburgh Sleep Quality Index,[32,35,44] and one used the sleep disturbance score.[46] Using random-model meta-analysis, it was found that there was no significant difference between Qigong and the control (n = 298, SMD = -0.11, 95 % CI -0.74 to 0.52, P = 0.73, Fig. 4).

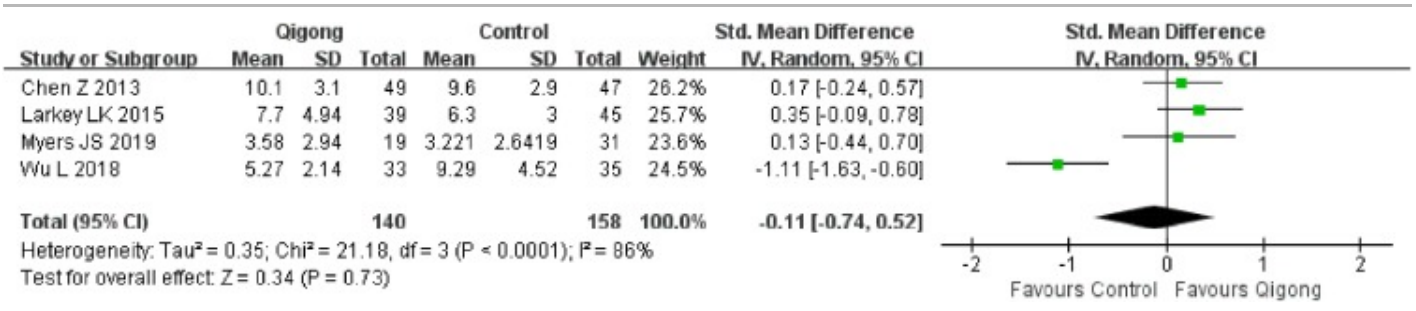

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Fig. 4. The forest plot of comparison between Qigong and control related to sleep disturbance.

5.3.4. Distress

One trial used McCorkle and Young's symptom distress scale,[31] and another trailused Distress score[46] to evaluate the effect of Qigong on distress. In our meta-analysis, no significant difference was found between the Qigong group and the control group (n = 117, SMD = -0.20, 95 % CI -0.57 to 0.17, P = 0.29, Fig. 5).

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Fig. 5. The forest plot of comparison between Qigong and control related to distress.

5.3.5. Depression

Six trials assessed changes in depression after Qigong. The pooled SMD indicated statistical evidence supporting the role of Qigong in relief of depression in women with breast cancer (n = 540, SMD = -0.32, 95 % CI -0.59 to -0.04, P = 0.02, Fig. 6)

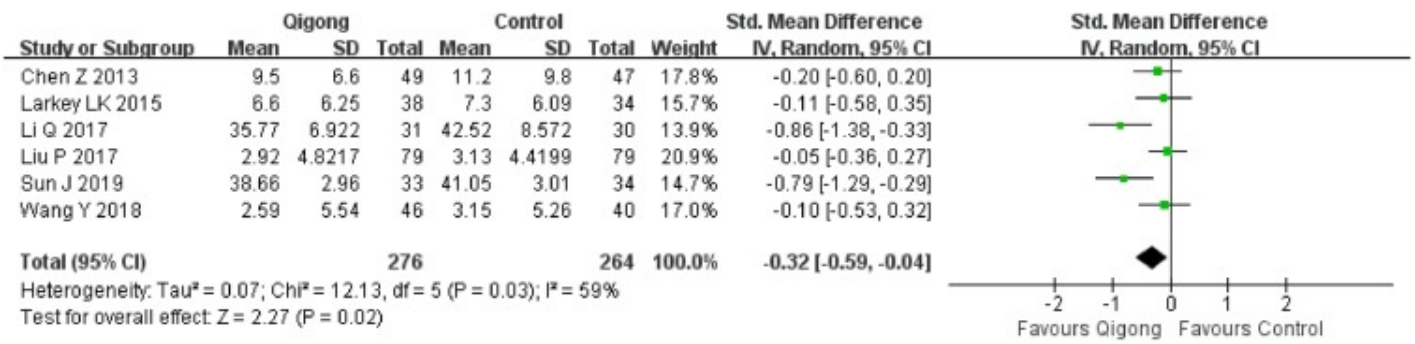

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Fig. 6. The forest plot of comparison between Qigong and control related to depression.

5.3.6. Safety

When assessing the safety of Qigong, only one trial reported adverse events to assess the safety of Qigong (Table 2). Four reported events may potentially have been attributed to Qigong: two subjects reported the recurrence of knee pain, and two others reported shoulder problems. Notably, these adverse events were relieved after further action guidance and correction by the certified Qigong master[41].

Table 2. The result of the risk of bias of the included trials.

Study	1	2	3	4	5	6	7	8	9	10	11	12	Score
Lee TI 2006 [26]	–	–	–	–	?	+	?	?	+	+	?	+	4
Chen Z 2013[27]	+	?	–	–	?	+	?	?	+	+	+	+	6
Fong SS 2013[28]	–	–	–	–	+	+	?	?	+	+	?	+	6
Loh SY 2014 [29]	+	?	–	–	?	+	?	?	+	+	?	+	5
Larkey LK 2015 [30]	+	+	–	–	?	+	+	?	?	+	?	+	6
He GJ 2016 [31]	–	?	–	–	?	+	–	?	+	?	?	+	3
Huang SM 2016 [32]	–	–	–	–	?	?	?	?	+	+	?	+	3
Han Y 2017 [33]	+	?	–	–	?	+	–	?	?	?	?	+	3
Huang YQ 2017 [34]	+	?	–	–	?	?	+	?	?	?	?	+	3
Li Q 2017 [35]	+	+	–	–	+	+	?	?	+	+	+	+	8
Liu P 2017 [36]	+	?	–	–	?	+	–	?	+	?	?	+	4
Shen LS 2017 [37]	+	+	–	–	?	+	–	?	?	?	?	+	4
Wang Y 2018 [38]	+	?	–	–	+	+	?	+	+	+	+	+	8
Wu L 2018 [39]	?	?	–	–	?	?	?	?	?	?	?	+	1
Lan H 2019 [40]	?	?	–	–	?	?	?	?	?	?	?	+	1
Myers JS 2019 [41]	?	?	–	–	?	?	?	?	+	+	?	+	3
Sun J 2019 [42]	+	?	–	–	?	+	–	?	?	?	?	+	3

1. Was the method of randomization adequate?

2. Was the treatment allocation concealed?

3. Was the patient blinded to the intervention?

4. Was the care provider blinded to the intervention?

5. Was the outcome assessor blinded to the intervention?

6. Was the drop-out rate described and acceptable?

7. Were all randomized participants analysed in the group to which they were allocated?

8. Are reports of the study free of suggestion of selective outcome reporting?

9. Were the groups similar at baseline regarding the most important prognostic indicators?

10. Were co-interventions avoided or similar?

11. Was the compliance acceptable in all groups?

12. Was the timing of the outcome assessment similar in all groups?

5.3.7. Anxiety

Five trials assessed anxiety, three with a self-rating anxiety scale,[38,40,47] one with a Hospital Anxiety and Depression Scale,[41] and another with generalized anxiety disorder-7.[43] Qigong had no benefit on anxiety relief ($n = 439$, SMD = -0.71, 95 % CI -1.32 to -0.10, $P = 0.02$, Fig. 7).

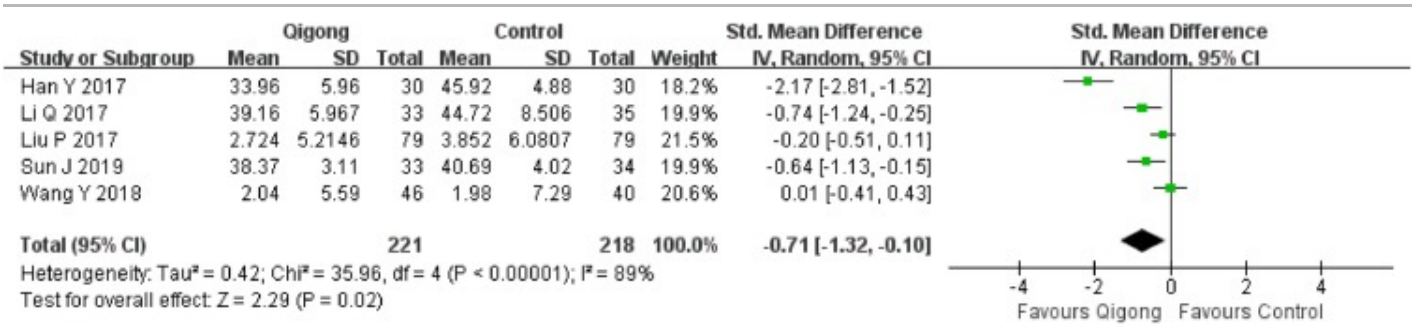

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Fig. 7. The forest plot of comparison between Qigong and control related to anxiety.

5.3.8. Subgroup analysis

Subgroup analysis revealed that among the different types of Qigong, Baduanjin Qigong was included in six trials and resulted in a positive effect on quality of life compared to the control condition ($n = 421$, SMD = 0.98, 95 % CI 0.26–1.70, $P = 0.008$, Table 3). Goulin New Qigong (2

trials, $n = 254$, SMD = 0.00, 95 % CI -0.24 to 0.25; $P = 0.98$, Table 3), and Tai Chi Qigong (2 trials, $n = 107$, SMD = 0.06, 95 % CI -0.32 to 0.45, $P = 0.74$, Table 3) showed no benefit.

Table 3. Subgroup analysis of Qigong to improve quality of life related to breast cancer.

Subgroup	Study	Participant	Heterogeneity	SMD, 95 % CI	*P*
Qigong type					
Baduanjin Qigong	6	421	92%, < 0.00001	0.98 [0.26, 1.70]	0.008
Goulin New Qigong	2	254	0%, 0.77	0.00 [-0.24, 0.25]	0.98
Tai Chi Qigong	2	107	41%, 0.19	0.06 [-0.32, 0.45]	0.74
Length of program					
Less than 3 months	5	295	61%, 0.04	0.37 [-0.02, 0.75]	0.06
Over 3months	8	655	93%, < 0.00001	0.85 [0.21, 1.49]	0.0009
Length of session					
Less than 60 min	7	470	93%, < 0.00001	0.92 [0.16, 1.67]	0.02
Over 60 min	5	419	43%, 0.13	0.16 [-0.03, 0.35]	0.11
Frequency weekly					
Less than 5 times	10	750	80%, < 0.00001	0.40 [0.06, 0.74]	0.02
Over 5 times	3	200	95%, < 0.00001	1.52 [0.06, 2.98]	0.04
Methodological quality					
Less than 6 points	9	650	91%, < 0.00001	0.91 [0.36, 1.45]	0.0001
Over 6 points	5	386	0%, 0.69	0.05 [-0.16, 0.25]	0.66

It was concluded that a Qigong program running less than 3 months showed no positive effect on quality of life compared to the control group (5 trials, $n = 295$, SMD = 0.37, 95 % CI -0.02 to 0.75, $P = 0.06$) (Table 3). These results differ from that of program lasting over 3 months (8 trials, $n = 655$, SMD = 0.85, 95 % CI 0.21–1.49, $P = 0.0009$, Table 3).

A Qigong session less than 60 min seemed to improve quality of life (7 trials, $n = 470$, SMD = 0.92, 95 % CI 0.16–1.67, $P = 0.02$, Table 3). Sessions lasting longer than 60 min yielded meaningless results (5 trials, $n = 419$, SMD = 0.16, 95 % CI -0.03 to 0.35, $P = 0.11$, Table 3).

Both measures of frequency (frequency less than 5 times and over 5 times weekly) were shown to improve quality of life compared to control.However frequency over 5 times weekly (3 trials, $n = 200$, SMD = 1.52, 95 % CI 0.06–2.98, $P = 0.04$, Table 3) appeared to show greater improvement (10 trials, $n = 750$, SMD = 0.40, 95 % CI 0.06 to 0.74, $P = 0.02$, Table 3).

For the trials scoring less than 6 points related to methodological quality, the pooled SMD indicated evidence suggesting that Qigong improves quality of life (9 trials, $n = 650$, SMD, 0.91, 95 % CI 0.36–1.45, $P = 0.0001$, Table 3), while the trials that scored over 6 points, the result was negative (5 trials, $n = 386$, SMD, 0.05, 95 % CI -0.16 to 0.25, $P = 0.66$, Table 3).

5.3.9. Publication bias

The funnel plot was asymmetric, which indicates that the publication bias is mild (Fig. 8).

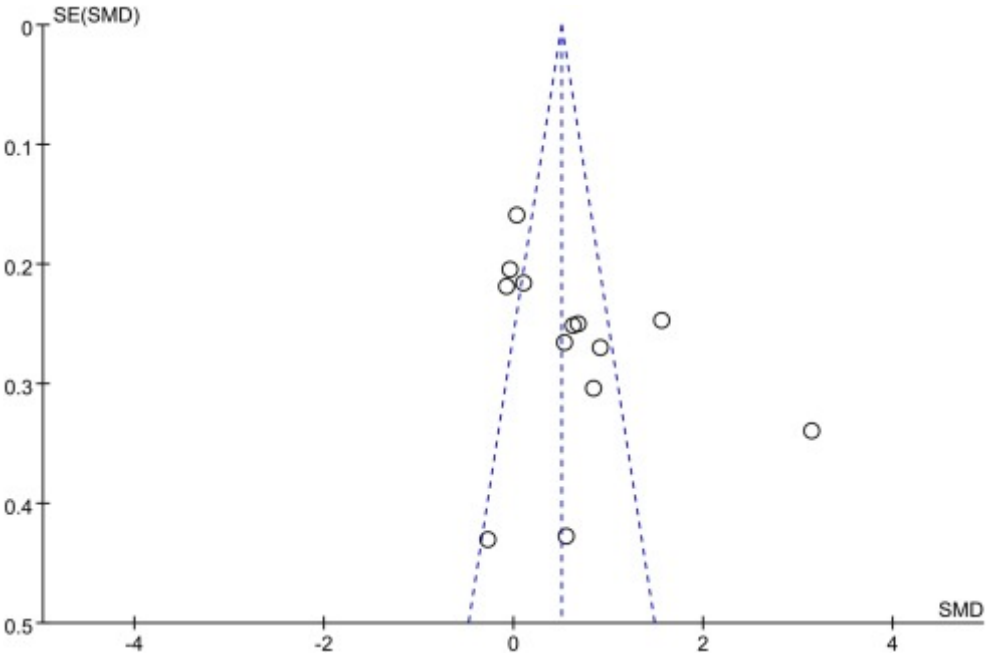

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Fig. 8. Funnel plot for publication bias.

6. Discussion

6.1. The summary of this systematic review

The meta-analysis included1236 participants and demonstrated that Qigong shows a slight but statistically significant improvement in quality of life in breast cancer patients, while its role in eliminating fatigue and reducing sleep disturbance was not been determined. Subgroup

analysis revealed that Baduanjin Qigong might have a greater effect on quality of life than other forms of Qigong; specifically, a Baduanjin program less than 60 min a session, frequency over 5 times weekly, over 3 months might have a positive effect on quality of life. However, methodological quality has an impact on the certainty of this conclusion. In regards to breast cancer-related emotional disturbances (distress, depression, and anxiety), there was evidence that Qigong can relieve depression and anxiety,but because only two trials reported on distress, it could not be proven that Qigong can temporarily relieve distress. For anxiety, one trial also checked for anxiety-related serum protein and found that the positive rate was significantly lower in the Qigong group than in the control group ($P < 0.01$).[38] This finding may have important implications given the association between depression, anxiety, and survival in prospective studies. Future research is also needed to uncover the psychosocial and biological mechanisms by which Qigong affects symptom relief, and the safety of Qigong should also be observed in future studies.

A systematic review of Qigong for breast cancer published in 2016claimed that because the 8 studies reviewed contained several methodological and design limitations, it is still too early to draw conclusions on the contribution of Qigong to the rehabilitation care of breast cancer survivors.[22] In this systematic review, the scientific evidence reflects the effectiveness of Qigong as a physical rehabilitation strategy for women with breast cancer, especially Baduanjin. Baduanjin is a conventional Chinese form of aerobic exercise that consists of eight slow movements. It is one of the most common forms of Chinese Qigong exercise and was developed in the Song Dynasty;it has a history of more than 1000 years.[48] In traditional Chinese medicine theory, Baduanjin uses natural energies to balance the coordination of the body, breathing, energy and mind. A recent systematic review indicated the efficacy of Baduanjin in reducing depression and anxiety symptoms in people with physical or mental illnesses.[49] The health benefit of Baduanjin has been proven in many diseases, such as low back pain, knee osteoarthritis, hypertension, chronic obstructive pulmonary disease, and insomnia.[49], [50], [51], [52], [53] This systematic review added the evidence that Baduanjin has a beneficial effect inbreast cancer patients as well.

6.2. Possible psychosocial mechanisms related to Qigong for breast cancer

Two studies tested the immune responses of breast cancer patients after treatment; compared with controls, IL-2, IFN-γ, IL-6, IL-1β, and TNF-α levels were reduced in breast cancer patients following Qigong.[41],[45] Inflammation was consistently found to affect the basal ganglia and cortical reward and motor circuits, leading to reduced motivation and motor activity. Inflammation was alse found to affect anxiety-related brain regions (including the amygdala, insula and anterior cingulate cortex), which may result from the effect of cytokines on monoamines and glutamate. Similar relationships between inflammation and altered

neurocircuitry have been observed in anxiety and depression patients with increased peripheral inflammatory markers, and further work is on the horizon.[54] Exercise has also been shown to reduce inflammation via several different processes (inflammation, cytokines, Toll-like receptors, adipose tissue and via the vagal tone), which can contribute to better health outcomes in people suffering from mood disorders.[55]

6.3. Possible reasons for ineffective outcomes in physiological problems related to Qigong for breast cancer

There are a few possible reasons for ineffective outcomes in physiological problems.First, the effect of Qigong is not enough to improve fatigue and sleep, as there are too many factors involved in fatigue and sleep disturbance. Second, the ceiling and floor effects in fatigue (measured with the FACIT-Fatigue Scale or BFI),[56,57] may have confounded the result, leading to an insignificant change in fatigue levels. Third, some of the participants may have adjusted to symptoms of fatigue, since their mean-year postdiagnosis was long (over one year in most of the trials). A larger sample size may be required to demonstrate a clearer significant effect of Qigong on fatigue.

6.4. Limitations of this review

There are several limitations in this study. Most of the trials included in the review were not strictly designed, as only five trials earned over 6 points for methodological quality. The impact of the substandard design on the certainty of the conclusions cannot be ignored. The subgroup analysis of methodological quality also proved this. Additionally, due to the characteristics of the Qigong intervention, placebo could not be applied in the trials; thus, blinding of participants and care providers could not be conducted. When it is not possible to buildparticipants and care providers, researchers can still make arrangements to compensate as much as possible for the lack of blinding. Trial staff/health care providers, data collectors, outcome assessors, and data analysts (including statisticians), are also important steps to prevent bias. For example, blinding of assessors prevents observer-related bias, as it was demonstrated that nonblinded assessors overrate patients in the treatment group andunderrate patients in the control group.[58] However, blinding of assessors was only conducted in three trials reviewed in this study. These defects (including failed allocation concealment, blinding of participants and personnel, blinding of outcome assessment, and failure to register the protocol before conducting the study), may have resulted in the emergence of bias and overestimation of the efficacy of the treatment group, especially in regard to the subjective outcomes.[25] Additionally, the sample sizes of the trials included were not large enough; only one trial enrolled more than 100 participants. Finally, the funnel plot was asymmetric; thus, potential publication bias cannot be ruled out.

7. Conclusion

This review shows that Qigong is effective at improving quality of life and relieving depression and anxiety; thus, Qigong should be encouraged in women with breast cancer. Specifically, Baduanjin Qigong program, less than 60 min a session, with a frequency over 5 times weekly over the course of 3 months, might have a positive effect on quality of life. Future RCTs assessing the efficacy of Qigong in breast cancer care should adhere to accepted standards of trial methodology.

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Data availability

All data generated or analyzed during this study are included in this published article.

Declaration of Competing Interest

The authors report no declarations of interest.

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> …Results of the risk of bias assessment are shown in Table II and Figure 2. For the overall quantitative synthesis, we considered 23 meta-analysis results from 20 systematic reviews,35–54 excluding the studies focused on nutritional supplements.55,56 The decision to exclude nutritional supplements from the analysis was made because these therapies differ greatly from the other interventions in terms of mechanism of action.…

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> …Thus, there is a great need to explore a non-pharmacological approach that can be energy-saving, cost-effective and easy to implement in alleviating the FSDSC. Traditional Chinese exercises (TCEs) have been reported to be effective in relieving cancer-related symptoms, such as fatigue, sleep disturbance and depression (Cheung et al., 2021a; Meng et al., 2021). TCEs can also be delivered with low intensity and are shown to be cost-effective and safe (Yao et al., 2020)….

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