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REVIEW

Yoga has a solid effect on cancer-related fatigue in patients with breast cancer: a meta-analysis

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Abstract

Purpose This study was designed to critically evaluate the effect of yoga on cancer-related fatigue in patients with breast cancer.

Methods Eight databases (Cochrane Library, PubMed, Ovid-Medline, Web of Science, CBM, Wanfang, VIP, and CNKI) were systematically reviewed from inception to January 2019 for randomized controlled trials (RCTs). Two reviewers critically and independently assessed the risk of bias using Cochrane Collaboration criteria and extracted correlated data using the designed form. All analyses were performed with Review Manager 5.3.

Results A total of 17 qualified studies that included 2183 patients (yoga: 1112, control: 1071) were included in the meta-analysis. Yoga had a large effect on fatigue in post-treatment breast cancer patients and had a small effect on intra-treatment patients. The meta-analysis also indicated that supervised yoga class had a significant effect on CRF; the six-week program had a moderate beneficial effect while the 60/90 min/session supervised yoga class and the eight-week program demonstrated a large effect on fatigue in patients with breast cancer. Yoga could markedly mitigate the physical fatigue in breast cancer patients, had a medium impact on cognitive fatigue, and manifested a small effect on mental fatigue. Eight studies reported the adverse events, whereas ten studies did not.

Conclusions Yoga can be considered as an alternative therapy for relieving fatigue in breast cancer patients who have completed treatment or are undergoing anti-cancer treatment.

Keywords Yoga · Fatigue · Breast cancer · Meta-analysis

Introduction

Breast cancer is the most common cancer in women around the world, accounting for 25.1% of all cancers. It was estimated that 1.67 million new cases of breast cancer were identified and 0.52 million cases of deaths caused by breast cancer occurred in 2012 globally [1]. The incidence of breast cancer is predicted to increase to 85 per 100,000 women by 2021 [2]. Increased incidence and improved treatments have made breast cancer survivors more prevalent in the world [1]. Cancer-related fatigue (CRF) is defined as a distressing, persistent, subjective sense of physical, emotional, and/or cognitive tiredness or exhaustion related to cancer or cancer treatment that is not proportional to recent activity and interferes with usual functioning. It is one of the most common side effects in patients with cancer [3]. Women with breast cancer may be already experiencing fatigue before anti-cancer treatment. 60 to 90% of women with breast cancer may experience fatigue at the beginning of treatment [4]. Approximately one in four breast cancer survivors (BCS) suffer from severe fatigue [5]. It is obvious that the number of breast cancer patients with fatigue is enormous and the management of CRF is urgent.

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Yoga is an ancient oriental fitness method, which originated in India. Traditional Indian yoga involves several fields, including ethical thought, body posture, and spiritual practice, aiming at achieving the unity of thought, body, mental health, and self-consciousness [6]. Many studies have reported the effect of yoga on CRF in breast cancer patients, some of which had positive outcomes, while others did not. In addition, the relationship between the benefits of yoga and the type, duration, length, and frequency of yoga is still unspecific and ambiguous. Therefore, the purpose of this meta-analysis was to critically assess the effect of yoga interventions on CRF in patients with breast cancer.

Methods

The meta-analysis was performed following the PRISMA guidelines for systematic reviews and meta-analyses [7].

Searching strategies

Eight databases, namely the Cochrane Central Register of Controlled Trials, PubMed, Ovid-Medline, Web of Science, China Biology Medicine (CBM), Wanfang, VIP, and China National Knowledge Infrastructure (CNKI) databases, were systematically searched from inception through January 2019 for relevant randomized controlled trials (RCTs) without language restrictions. These searches were performed using the following keywords: "Breast Neoplasm," "Breast Tumor," "Breast Cancer," "Breast Carcinoma," "Mammary Cancer," "Mammary Carcinoma," "Mammary Neoplasm," "Mammary Tumor," "Fatigue," "Asthenia," "Lassitude," "Yoga," "Yogic," "Asana,". Two reviewers first screened the literature by scanning the titles and abstracts and then read the full text of potentially eligible trials to decide whether they should be included in the meta-analysis. The search strategy for the database PubMed is shown in the Appendix as an example. Additionally, further potentially relevant papers were searched using the reference lists of the identified articles.

Inclusion criteria

Participants

Studies including adult patients (≥ 18 years) who were diagnosed with breast cancer, regardless of cancer stage and current treatment, were eligible.

Interventions and controls

Trials that compared any type of yoga with any type of control group were included.

Outcomes

Trials regarding fatigue as a primary or secondary outcome and containing fatigue scores that could be extracted were included.

Studies

Only RCTs were eligible.

Data extraction

The general information of the studies, the characteristics of the patients, the characteristics of the intervention and the control groups (form of intervention, type of yoga, duration and frequency of intervention, length of program, and adherence or contamination), the outcome measures, and the adverse events were independently extracted by two reviewers using a pre-designed information sheet.

Risk of bias assessment

Two reviewers independently evaluated the risk of bias in the included RCTs using the Cochrane assessment tool, which consists of the following seven domains: "adequate sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective reporting, and other bias" [7]. Each question can be rated as follows: yes (+), low risk of bias; unclear (?), unclear risk of bias; no (−), high risk of bias.

Data analysis

The meta-analysis was performed using Review Manager Software (version 5.3). Clinical heterogeneity (variability in the participants, interventions, and outcomes) and methodological heterogeneity (variability in the study design and risk of bias) were assessed first. Statistical heterogeneity is a consequence of clinical or methodological diversity or both among the studies [7]. If moderate clinical heterogeneity was identified, subgroup analyses were conducted on status of treatment, type of yoga, form of intervention, and dimension of fatigue if there were at least two studies on a stratum, considering that these variables might have influences on the fatigue outcomes. I^2 was used to measure the statistical heterogeneity among the trials in each analysis. If $P > 0.1$ and $I^2 < 50\%$, a fixed-effects model was adopted for the analysis due to the homogeneity of the studies; if $P < 0.1$ and $I^2 \geq 50\%$, then a random-effects model was adopted. If $P < 0.1$ and the sources of heterogeneity were unknown, a descriptive analysis was conducted without a meta-analysis. For continuous data, the weighted mean difference (WMD) and 95% confidence interval (CI) were determined for the

individual trials. The standardized mean difference (SMD) was used if the outcome assessment tools were different.

Reporting and publication bias were investigated by visually examining the degree of asymmetry of a funnel plot. A sensitivity analysis was performed in light of the fact that some of the trials (e.g., one with a larger sample) might impact the study results. Sensitivity analysis was used to explore the effects of the fixed-effects or random-effects model analyses for outcomes with heterogeneity and the effects of any assumptions.

Results

Literature search

A total of 690 records identified through database searching and three additional records identified through other sources were retrieved in the literature search, and 85 of them were duplicated (Fig. 1). After an initial review of the title and abstract, 583 records were excluded due to obvious nonconformity to the inclusion criteria. Of the remaining 25 articles, seven articles were excluded after reading the literature and critical appraisal, and thus 18 articles were included in systematic review. One article [22] was excluded from further analysis because it did not provide the total score of fatigue. Therefore, a total of 17 articles were included in the final meta-analysis [8–21, 23–25].

Characteristics of the included trials

The characteristics of the patients, treatments, controls, outcome measures, and adverse events are shown in Table 1.

Participants

Among the 18 studies included in systematic review, the mean age of the participants ranged from 47.38 to

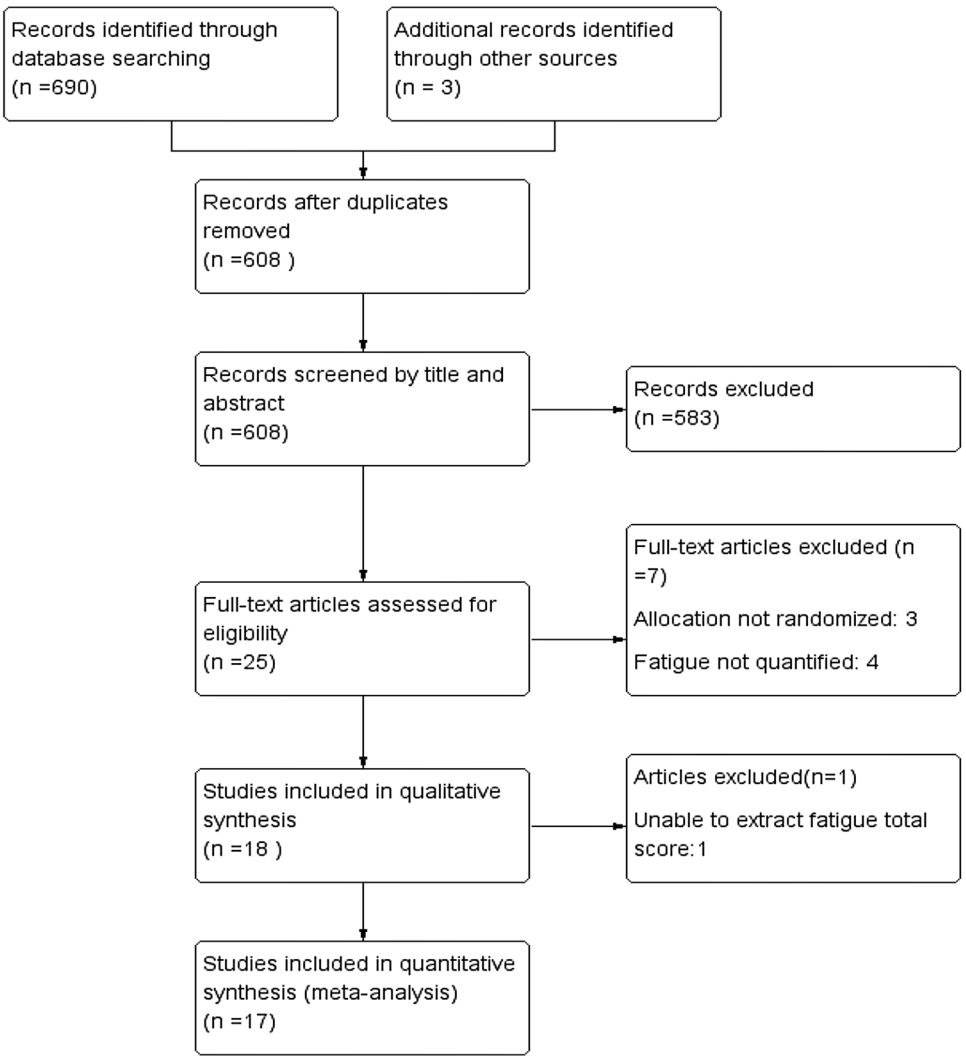

Fig. 1 Flow chart diagram of trial identification and selection

Table 1 Studies included in the systematic review

Author, year	Sample	Mean age (±SD) Gender	Ethnicity	Cancer stage	Current treatment	Treatment group: form of intervention, duration, frequency, length of program,	Control group: intervention, program length, contamination	Fatigue scale	Adverse events
Moadel, 2007 [8]	YG 84 CG 44	YG 55.11 ± 10.07 CG 54.23 ± 9.81 Female	%African American YG 42% CG 43% %Hispanic YG 30% CG 34% %Non-Hispanic white YG 22% CG 23% Others	I–IV	Surgery/chemotherapy/antiestrogen therapy/radiation treatment	Yoga class(Hatha yoga) + home-based yoga, 90 min + unclear, 1 time/week + daily, 12 weeks	Standard care, 12 weeks, not reported	FACIT-fatigue	Not reported
Vadiraja, 2009 [9]	YG 44 CG 44	Not reported Female	Not reported	I–III	Radiotherapy	Integrated yoga class + self-practice in the hospital,60 min + unclear, 3 times/week + unclear, 6 weeks	Supportive counseling, 6 weeks, not reported	EORTC-QOL-C30	Not reported
Danhauer, 2009 [10]	YG 22 CG 22	YG 54.3 ± 9.6 CD 57.2 ± 10.2 Female	%Non-Hispanic White YG 86.4% CG 90.9%	DCIS I–IV	Chemotherapy/radiation therapy	Restorative yoga class, 75 min, 1 time/week, 10 weeks	Wait-list, 10 weeks, not reported	FACT-fatigue	None
Banasik, 2011 [11]	YG 9 CG 9	YG 63.33 ± 6.9 CG 62.4 ± 7.3 Female	Caucasian	II–IV	Post-treatment	Iyengar yoga class, 90 min, 2 times/week, 8 weeks	Non-intervention, 8 weeks, not reported	Fatigue Likert Scale	not reported
Littman, 2012 [12]	YG 32 CG 31	YG 60.6 ± 7.1 CG 58.2 ± 8.8 Female	%Non-Hispanic White YG 93.7% CG 93.5%	In situ I–III	Post-treatment	Yoga class (viniyoga) +Home-based yoga, 65–85 min + 20–30 min, 5 times/week(yoga class + home-based yoga), 24 weeks	Wait-list, 24 weeks, not reported	FACIT-fatigue	None
Bower, 2012 [13]	YG 16 CG 15	YG 54.4 ± 5.7 CG 53.3 ± 4.9 Female	%White YG 94% CG 80%	0–II	Post-treatment	Iyengar yoga class, 90 min, 2 times/week, 12 weeks	Health education classes, 12 weeks, not reported	FSI	YG: back spasm1
Loudon, 2014 [14]	YG 12 CG 11	YG 55.1 ± 2.5 CG 60.5 ± 3.6 Female	Not reported	DCIS I–III	Chemotherapy/radiotherapy	Yoga class + home-based yoga sessions (Satyananda yoga), 90 min + 45 min, 1 time/week + daily, 8 weeks	Usual self-care, 8 weeks, not reported	VAS	None

Table 1 (continued)

Author, year	Sample	Mean age (±SD) Gender	Ethnicity	Cancer stage	Current treatment	Treatment group: form of intervention, duration, frequency, length of program,	Control group: intervention, program length, contamination	Fatigue scale	Adverse events
Wang, 2014 [15]	YG 40 CG 42	Not reported Female	Not reported	Not reported	Chemotherapy	Yoga class (centralized intervention for inpatients/decentralized intervention for outpatients during the intermission of chemotherapy), 50 min, 4 times/week, 16 weeks	Usual care, 16 weeks, not reported	CFS	Not reported
Taso, 2014 [16]	YG 30 CG 30	49.27 ± 10.23 Female	Not reported	I–III	Chemotherapy/antihormone therapy	Anusara yoga class, 60 min, 2 times/week, 8 weeks	Standard care, 8 weeks, not reported	BFI	Not reported
Cramer, 2015 [17]	YG 19 CG 21	YG 48.3 ± 4.8 CG 50.0 ± 6.7 Female	Not reported	I–III	Anti-hormonal therapy	Yoga class(Hatha yoga) + home-based yoga, 90 min + unclear 1 time/week + daily, 12 weeks	Usual care, 12 weeks, not reported	FACIT-fatigue	YG: panic attack and foot pain2, transient muscle soreness3, unilateral hip pain1 CG: sciatica1, port pain1, elbow pain1, knee pain2, panic attacks1
Vardar Yağlı, 2015 [18]	YG 19 CG 21	YG 49.89 ± 4.65 CG 47.38 ± 7.57 Not reported	Not reported	I–II	Chemotherapy/radiotherapy	Aerobic exercise added to yoga, 60 min, 3 times/week, 6 weeks	Aerobic exercise, 6 weeks, not reported	FSS/EORTC-QOL-C30	Not reported
Vardar Yagli, 2015 [19]	YG 10 CG 10	YG 68.58 ± 6.17 CG 68.88 ± 2.93 Not reported	Not reported	I–II	Post-treatment	Classical yoga class, not reported, 2 times/week, 4 weeks	Exercise program, 4 weeks, not reported	VAS	Not reported
Lötzke, 2016 [20]	YG 45 CG 47	YG 51.0 ± 11.0 CG 51.4 ± 11.1 Female	Not reported	I–III	Chemotherapy/endocrine therapy/radiation	Yoga class (Iyengar Yoga) + home-based yoga, 60 min + 20 min, 1 time/week + 2 times/week, 12 weeks	Conventional physical exercise, 12 weeks, not reported	CFS-D/EORTC-QLQ-C30	Not reported
Stan, 2016 [21]	YG 18 CG 16	YG 61.4 ± 7.0 CG 63.0 ± 9.3 Female	Not reported	0–II	Chemotherapy/radiation/endocrine therapy/mastectomy	Home-based yoga, 90 min, 3–5 times/week, 12 weeks	Strengthening exercises, 12 weeks, not reported	MFSI-SF	YG: Flu-like symptom 3 Leg cramps 1 Swelling of the hand 1 Stomach pain 1 Shoulder pain 1 Side pain 2 CG: Flu-like symptom 2 Arm pain 1 De Quervain's tenosynovitis 1

Table 1 (continued)

Author, year	Sample	Mean age (±SD) Gender	Ethnicity	Cancer stage	Current treatment	Treatment group: form of intervention, duration, frequency, length of program,	Control group: intervention, program length, contamination	Fatigue scale	Adverse events
Jin, 2017 [22]	YG 50 CG 50	Unclear	Not reported	Not reported	Chemotherapy	Yoga added to usual care(centralized intervention for inpatients/decentralized intervention for outpatients during the intermission of chemotherapy), 60 min (centralized intervention), 3 times/week (centralized intervention), 16 weeks	Usual care, 16 weeks, not reported	CFS	Not reported
Zeng, 2017 [23]	YG 24 CG1 23 CG2 20 CG3 22	Not reported	Not reported	Not reported	Chemotherapy	Yoga added to usual care, 40 min, once every two days, 4 weeks	CG1: usual care, 4 weeks, not reported CG2: music relaxation training add to usual care, 4 weeks, not reported CG3: yoga combined with music relaxation training add to usual care, 4 weeks, not reported	CFS	Not reported
Chaoul, 2018 [24]	YG 74 CG1 68 CG2 85	YG 49.5 ± 9.8 CG1 50.4 ± 10.3 CG2 49 ± 10.1 Female	%White YG 58.1% CG1 68.7% CG2 65.4%	I–III	Chemotherapy	Yoga class (Tibetan yoga) + booster class + home-based practice, 75–90 min + unclear + unclear, unclear, unclear	CG1: stretch, unclear, not report CG2: usual care, unclear, not reported	BFI	None
Jong, 2018 [25]	YG 47 CG 36	YG 51 ± 8.0 CG 51 ± 7.3 Female	Not reported	I–III	Chemotherapy/hormone therapy/radiotherapy	Yoga class (Dru yoga) + home-based breathing and relaxation exercise, 75 min + a minimum of 5 min, 1 time/week + daily, 12 weeks	Standard care, 12 weeks, 13.8% were contaminated	MFI/FQL/EORTC-QLQ-C30	None

BFI brief fatigue inventory, *FSS* fatigue severity scale, *CFS* cancer fatigue scale, *CFS-D* the German version of the cancer fatigue scale, *CG* control group, *EORTC-QLQ-C30/EORTC-QOL-C30* European organization for research and treatment of cancer quality of life C30, *FACIT-Fatigue* the functional assessment of chronic illness therapy-fatigue, *FACT-Fatigue* functional assessment of cancer therapy-fatigue, *FQL* fatigue quality list, *FSI* fatigue symptom inventory, *MFI* multidimensional fatigue inventory, *MFSI-SF* multidimensional fatigue symptom inventory-short form, *VAS* visual analog scale, *YG* yoga group

68.88 years. Ethnicity was reported in six studies; one study was conducted with Caucasian populations; and four studies were performed in white populations. In the fifteen studies that reported cancer stage, most were Stages I–III. Only four studies focused on breast cancer patients who had completed anti-cancer treatment (post-treatment).

Interventions

Yoga types included Hatha yoga, Integrated yoga, Restorative yoga, Iyengar yoga, Viniyoga, Anusara yoga, Satyananda yoga, Dru yoga, and Tibetan yoga. Forms of intervention included supervised yoga class, home-based yoga, home-based breathing and relaxation exercise, self-practice in the hospital, and centralized intervention for inpatients/decentralized intervention for outpatients. The supervised yoga class ranged from 40 to 90 min and took place 1–5 times per week for 4–24 weeks.

Controls

Four studies used exercise as a control intervention [18–21]. One study used supportive counseling as a control intervention [9]. Health education classes were also used as the control intervention in one study [13]. The remaining 12 studies used standard care or usual care or non-intervention as the control intervention [8, 10–12, 14–17, 22–25]; in addition, more than one control group had been established in two of these 12 studies [23, 24].

Risk of bias in individual trial

The overall risk of bias as shown in Fig. 2 is moderate; blinding of participants and personnel was not applicable for yoga intervention, so the risk of performance bias is high in all studies. The individual risk of bias for each study is presented in Fig. 3. Ten studies reported the random sequence generation, one of which are high risk [19]. Seven studies had a low risk of allocation concealment [9, 13, 14, 16–18, 25]. In terms of detection bias, two studies had a low risk [13, 14] while one study had a high risk [12]. Four studies had a high risk of attrition bias [9, 14, 24, 25].

Analysis of overall effects

The effect sizes with scores of 0.2–0.5, 0.5–0.8, and > 0.8 were considered small, medium, and large effects, respectively [26].

The meta-analysis of the changes in fatigue scores from the 17 studies indicated that yoga had a small but statistically significant beneficial effect, suggesting that yoga could mitigate fatigue in breast cancer patients to some extent [SMD = − 0.31, 95% CI (− 0.52, − 0.10), $P = 0.003$] (Fig. 4). The funnel plot (Fig. 5) indicates that the publication bias is mild, and the sensitivity analysis reveals that the model is relatively stable.

Subgroup and sensitivity analysis

Status of treatment

The meta-analyses of the four studies with only post-treatment patients [SMD = − 0.80, 95% CI (− 1.52, − 0.09), $P = 0.03$] and of the 13 studies with patients undergoing anti-cancer treatment (intra-treatment) [SMD = − 0.25, 95% CI (− 0.47, − 0.03), $P = 0.03$] (Table 2) demonstrated that yoga had a large and a small effect on fatigue in post-treatment and intra-treatment breast cancer patients, respectively.

Type of yoga

Twelve studies reported the yoga types, two of which were Hatha yoga, three of which were Iyengar yoga, and the rest were Integrated yoga, Restorative yoga, Viniyoga, Anusara yoga, Tibetan yoga, Dru yoga, and Satyanada yoga, respectively. Therefore, the subgroup analyses of Hatha Yoga and Iyengar yoga were carried out. Hatha yoga had no effect on fatigue in patients with breast cancer [SMD = 0.35, 95% CI (− 0.13, 0.83), $P = 0.15$], and Iyengar yoga also demonstrated no effect [SMD = − 0.17, 95% CI (− 0.55, 0.21), $P = 0.37$]. When we excluded Lötzke's [20] study from the

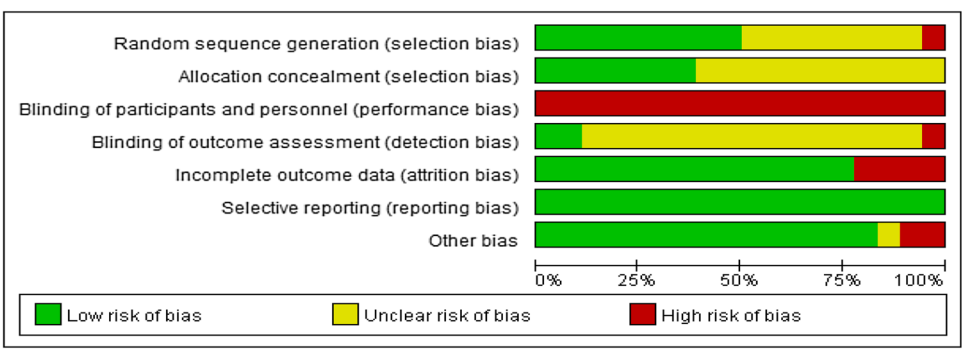

Fig. 2 Overall risk of bias assessment using the Cochrane tool

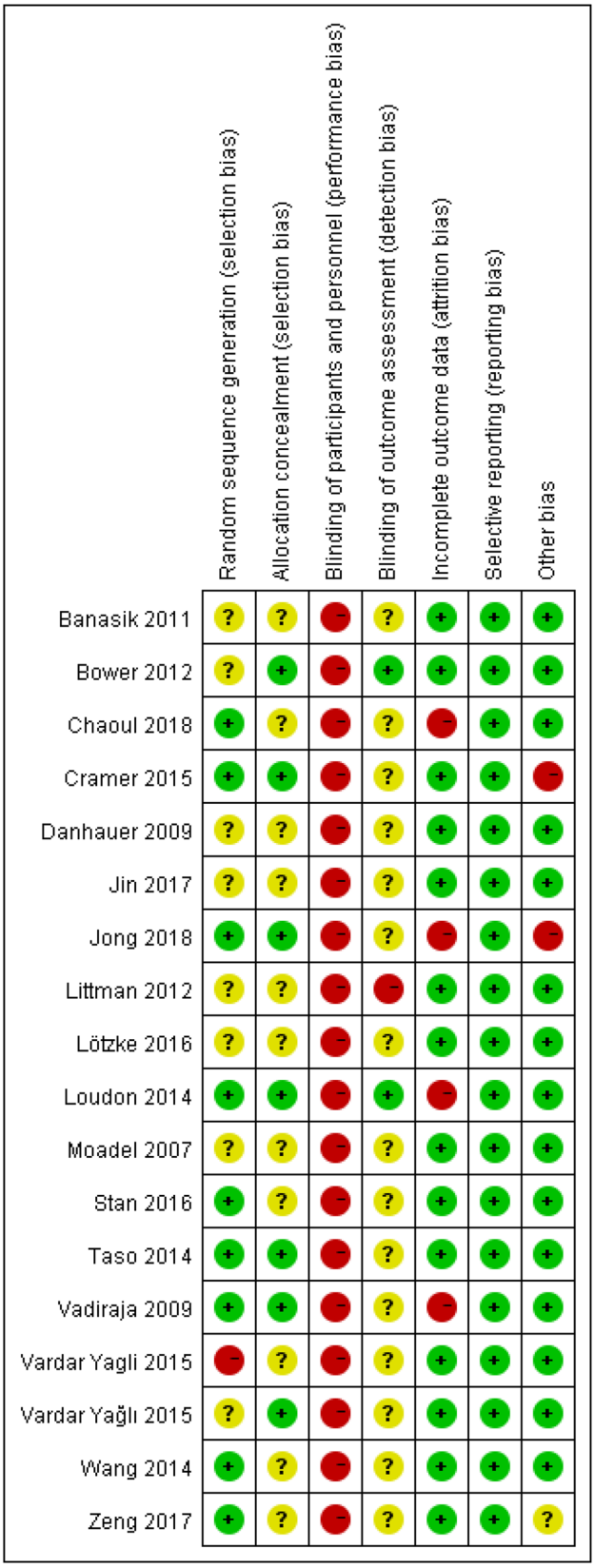

Fig. 3 Risk of bias assessment by individual trials

Iyengar yoga subgroup because it had a high dropout rate and used home-based yoga, and included intra-treatment patients while the other two studies were conducted with post-treatment patients [11, 13], the results indicated a large effect [SMD = − 0.98, 95% CI (− 1.46, − 0.49), $P < 0.0001$].

Form of intervention

Two forms of intervention were analyzed, supervised yoga class and supervised yoga class plus home-based yoga, the former demonstrated a large beneficial effect [SMD = − 0.92, 95% CI (− 1.53, − 0.32), $P = 0.003$] while the latter had no effect [SMD = 0.14, 95% CI (0.02, 0.25), $P = 0.02$] on CRF in breast cancer patients.

Duration of yoga class

60-min and 90-min yoga class indicated a significant positive effect on CRF in breast cancer patients [SMD = − 1.20, 95% CI (− 2.28, − 0.12), $P = 0.03$]/[SMD = − 0.98, 95% CI (− 1.46, − 0.49), $P < 0.0001$].

Length of program

Four-week and 12-week yoga class had no impact on fatigue in patients with breast cancer [SMD = − 0.81, 95% CI (− 1.86, 0.24), $P = 0.13$]/[SMD = − 0.09, 95% CI (− 0.30, 0.13), $P = 0.43$] (Table 2). The sensitivity analysis indicated that 4-week yoga class had a moderate effect [SMD = − 0.62, 95% CI (− 1.12, − 0.12), $P = 0.02$], i.e., the model is unstable; however, twelve-week yoga class still had no effect [SMD = − 0.04, 95% CI (− 0.17, 0.09), $P = 0.51$]. When we excluded Moadel's [8], Cramer's [17], Lötzke's [20], and Stan's [21] studies from the 12-week subgroup because they used home-based yoga, the outcome indicated a small effect [SMD = − 0.45, 95% CI (− 0.75, − 0.15), $P = 0.003$]. Six-week yoga class demonstrated a moderate effect [SMD = − 0.68, 95% CI (− 1.07, − 0.29), $P = 0.0006$] and eight-week yoga class manifested a large effect [SMD = − 1.32, 95% CI (− 2.48, − 0.16), $P = 0.03$] on fatigue.

Dimension of fatigue

Yoga has a significant beneficial effect on physical fatigue in patients with breast cancer [SMD = − 0.83, 95% CI (− 1.34, − 0.32), $P = 0.001$], a medium effect on cognitive fatigue [SMD = − 0.63, 95% CI (− 0.90, − 0.35), $P < 0.00001$], and a small effect on mental fatigue [SMD = − 0.47, 95% CI (− 0.75, − 0.19), $P = 0.001$] (Table 2). However, yoga has no impact on emotional fatigue [SMD = − 0.16, 95% CI (− 0.35, 0.03), $P = 0.10$], and the sensitivity analysis also indicated no effect [SMD = − 0.16, 95% CI (− 0.35, 0.03), $P = 0.09$].

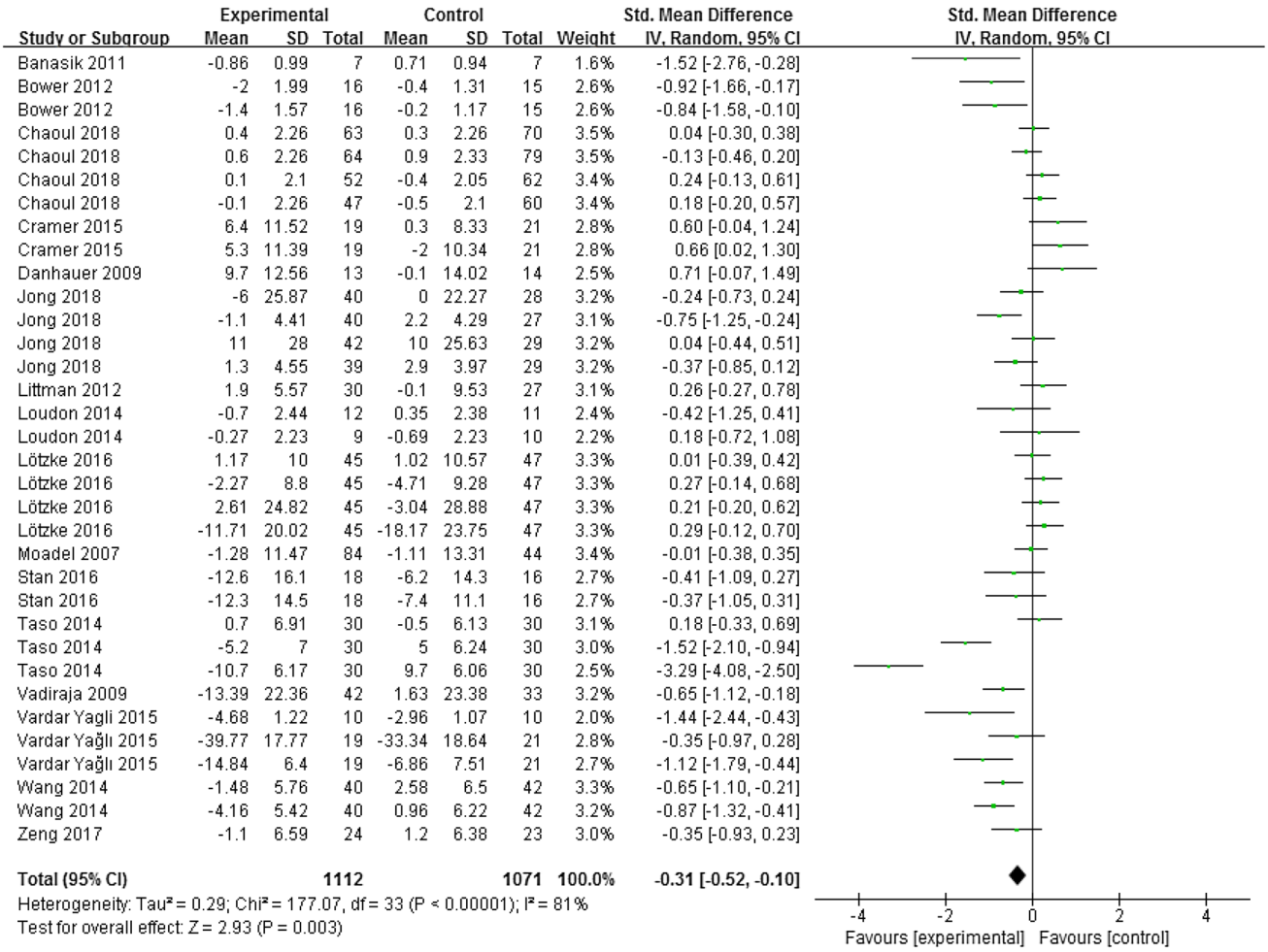

Fig. 4 Overall effect of yoga on fatigue score changes in breast cancer patients

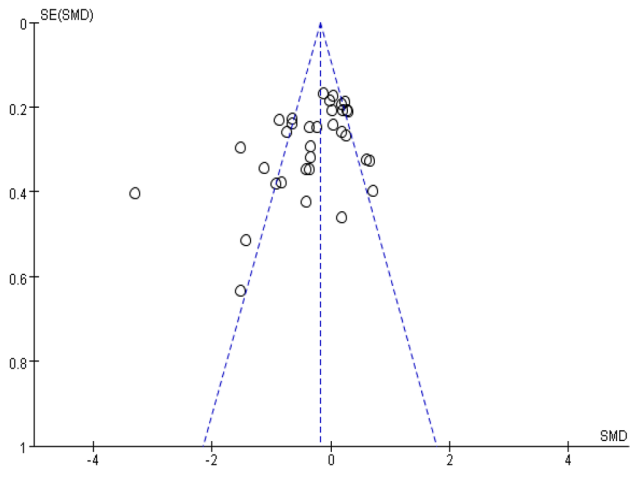

Fig. 5 Funnel plot of comparison: overall effect of yoga on fatigue score changes in breast cancer patients

Adherence and contamination

Twelve studies reported the adherence to the yoga intervention; adherence was higher than 80% in four studies [11, 14, 16, 17]; five studies reported specific compliance that could not be simply described in percentage terms [8, 9, 12, 24, 25], three of which had a low adherence [8, 12, 24]. Six studies did not report the adherence to yoga [15, 18–20, 22, 23]. Only one study reported the contamination rate of the control group (13.8%) [25].

Adverse events

Eight studies reported the adverse events, five of which had no adverse events [10, 12, 14, 24, 25] and three of which reported a total of 26 adverse events [13, 17, 21]. Fourteen of these events may be related to the yoga intervention, but no serious events occurred.

Table 2 Subgroup and sensitivity analyses of yoga on fatigue score changes in breast cancer patients

Outcome type	K	ES	Sample size		Random-effects analysis				Fixed-effects analysis			
					SMD	95% CI		*P*	SMD	95% CI		*P*
			YG	CG		*L*	*U*			*L*	*U*	
Status of treatment												
Post-treatment	4	5	79	74	−0.80	−1.52	−0.09	0.03	−0.52	−0.86	−0.19	0.002
Intra- treatment	13	29	1033	997	−0.25	−0.47	−0.03	0.03	−0.16	−0.25	−0.07	0.0003
Type of yoga												
Hatha yoga	2	3	122	86	0.35	−0.13	0.83	0.15	0.24	−0.04	0.52	0.1
Iyengar yoga	3	7	219	225	−0.17	−0.55	0.21	0.37	0.02	−0.17	0.20	0.87
Form of intervention												
Yoga class	7	11	214	216	−0.92	−1.53	−0.32	0.003	−0.77	−0.98	−0.57	<0.00001
Yoga class + home-based yoga	6	14	579	593	0.14	0.02	0.25	0.02	0.14	0.02	0.25	0.02
Duration of yoga class												
60 min	2	5	128	132	−1.20	−2.28	−0.12	0.03	−0.94	−1.21	−0.66	<0.00001
90 min	2	3	39	37	−0.98	−1.46	−0.49	< 0.0001	−0.98	−1.46	−0.49	<0.0001
Length of program												
4 weeks	2	2	34	33	−0.81	−1.86	0.24	0.13	−0.62	−1.12	−0.12	0.02
6 weeks	2	3	80	75	−0.68	−1.07	−0.29	0.0006	−0.68	−1.01	−0.35	<0.0001
8 weeks	3	5	88	88	−1.32	−2.48	−0.16	0.03	−1.41	−1.77	−1.05	<0.00001
12 weeks	6	15	531	449	−0.09	−0.30	0.13	0.43	−0.04	−0.17	0.09	0.51
Dimension of fatigue												
Physical fatigue	4	8	295	272	−0.83	−1.34	−0.32	0.001	−0.91	−1.08	−0.73	<0.00001
Emotional fatigue	3	6	216	216	−0.16	−0.35	0.03	0.10	−0.16	−0.35	0.03	0.09
Cognitive fatigue	2	4	180	184	−0.63	−0.90	−0.35	< 0.00001	−0.63	−0.84	−0.41	<0.00001
Mental fatigue	2	4	115	88	−0.47	−0.75	−0.19	0.001	−0.47	−0.75	−0.19	0.001

K number of studies, *ES* number of effect size, *YG* yoga group, *CG* control group, *SMD* standardized mean difference effect size, *L* lower, *U* upper, *Yoga class* supervised yoga class, excluding studies that encouraged home-based yoga or exercise, self-practice in the hospital and used intensive intervention/decentralized intervention

Discussion

The meta-analysis including 2183 participants demonstrated that yoga had a slight but statistically significant effect on mitigating fatigue in breast cancer patients. A former meta-analysis also indicated that yoga had a beneficial impact on fatigue in breast cancer patients [27], but it did not conduct subgroup analysis according to status of treatment, frequency and duration of intervention, type of yoga, length of program, and dimension of fatigue.

The included studies did not provide estimates of the effect size that could be pooled for subgroups of age, ethnicity, or cancer stage. Therefore, no subgroup analysis was made according to these stratification factors. The frequency and duration of home-based yoga and the frequency of supervised yoga class could not be integrated, so we did not conduct a subgroup analysis according to these factors.

The subgroup analysis and the sensitivity analysis indicated that the supervised yoga class plus home-based yoga had no effect on fatigue in breast cancer patients; we also found that the results of subgroup analyses involving the studies implementing home-based yoga were negative, such as the subgroup analyses of Hatha yoga, Iyengar yoga, and 12-week intervention; however, when we removed these studies, the results became valid. Six studies adopted supervised yoga class plus home-based yoga as the form of intervention [8, 12, 14, 17, 20, 24] and one study used home-based yoga only [21]. These seven studies contained certain factors that might affect the analysis results. Moadel's study had a poor adherence-32% of the patients did not participant in the intervention at all, and the low adherence was associated with increased fatigue, radiotherapy, younger age and no antiestrogen therapy [8]. Littman's study also had a low adherence; patients attended an average of 19.6 facility-based classes (range 1–61; median: 20.5) and practiced at home an average of 55.8 times (range 2–102; median: 62) [12]. Loudon's study had a small sample size (intervention group: 12, control group: 11) [14].The sample size of Cramer's study was also small (intervention group: 19, control group: 21) [17]. Lötzke's study had a high dropout rate

and the missing data were imputed using Rubin's multiple imputation MI method; there were 92 participants in this study; at t1, 2 participants dropped out from yoga group and 1 participant dropped out from control group; at t2, 29 and 25 patients dropped out from yoga group and control group, respectively; for breast cancer patients, additional interventions during cancer treatment may be too exhausting; the high dropout rate may reflect a low acceptance for supportive interventions during cancer treatment [20]. Chaoul's study indicated that the patient-instructor encounter time was limited, which might account for the absence of significant effects when comparing yoga to usual care; the study's booster sessions had a low adherence-51% of the participants did not attend any booster sessions [24]. Stan's study also demonstrated a poor adherence to yoga, only 39%; the participants relied on self-discipline and the bi-weekly phone calls as their source of motivation; home-based yoga lacked scheduled sessions or the peer pressure, which might lead to less motivation; the study also had a small sample size (intervention group: 18, control group: 16) [21]. Due to the above-mentioned factors, the results of analysis should be treated with caution. As to what led to the negative results in subgroup analysis, the above-mentioned factors or the home-based yoga, we cannot easily conclude yet. Also, we need to implement home-based yoga with caution, taking into account the safety problem, although no serious events have been reported up to present.

Drawing upon the results of this meta-analysis, the clinical professionals can formulate individualized yoga practice program for breast cancer patients based on patients' individual condition, e.g., supervised yoga class, 60/90 min/session with a duration of 6/8 weeks. However, more high-quality studies with high adherence, low dropout rate and large sample size are still needed to confirm the best yoga type, the most valid form of intervention, the most reasonable frequency and duration of yoga practice, and the most suitable length of program in order to relieve CRF in breast cancer patients.

Limitations of the current study

Despite our comprehensive review of the literature on fatigue in breast cancer patients, the present study still has some limitations. First, among the 17 studies included in the meta-analysis, nine studies had a sample size of less than 30 subjects. Second, the quality of the studies included in this meta-analysis is mediocre, which may influence the results. Third, it is known that various symptoms, such as pain, sleep disturbance, emotional distress, nutrition, and level of activity among others, can impact CRF level; however, several included studies did not report information regarding these factors, which may have significant impacts on study outcomes. Therefore, further studies with more scientific methodology, larger sample sizes, and a multi-center design are needed.

Conclusions

Yoga can be considered as an alternative therapy to relieve fatigue in breast cancer patients who have completed treatment or are undergoing anti-cancer treatment. From this meta-analysis, we find that supervised yoga class can reduce fatigue in breast cancer patients remarkably, a 6-week program had a medium effect on CRF; 60/90-min yoga class and a 8-week program had a significant effect; yoga could markedly reduce the physical fatigue in breast cancer patients, had a medium impact on cognitive fatigue, and a small effect on mental fatigue. In addition, future researchers should address the issue of adherence and strengthen the supervision of yoga intervention to ensure its effect on CRF.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflicts of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Appendix. A detailed search strategy for Medline

#1	"Breast Neoplasms" [Mesh] OR breast tumor [Title/Abstract] OR Breast Cancer [Title/Abstract] OR Breast Carcinoma [Title/Abstract] OR Mammary Cancer [Title/Abstract] OR Mammary Carcinoma [Title/Abstract] OR Mammary Neoplasm [Title/Abstract] OR Mammary tumor [Title/Abstract]
#2	"Fatigue" [Mesh] OR Asthenia [Title/Abstract] OR Lassitude [Title/Abstract]
#3	"Yoga" [Mesh] OR Yogic [Title/Abstract] OR Asana [Title/Abstract]
#4	randomized controlled trial [Publication Type]
#5	#1 AND #2 AND #3 AND #4

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