

The Effect of Complementary and Alternative Medicines on Quality of Life in Patients with Breast Cancer: A Systematic Review

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Abstract

Background: Breast cancer disease and its classic treatment lead to decrease in patients' quality of life (QOL). This systematic review aimed to compare the effectiveness of complementary and alternative medicines (CAMs) categories on the QOL of women with breast cancer. **Methods:** English clinical trials from PubMed, Emabase, Scupos, and Google Scholar databases were searched electronically by the end of 2018 with the Cochrane Collaboration protocol. Two researchers independently extracted data such as participants' characteristics, CAM methods, QOL assessment tools. CAMs were classified into three categories of dietary supplements, herbal medicine, and mind-body techniques. **Results:** During the initial search, 1186 articles were found. After reviewing titles, abstracts, and full texts based on inclusion and exclusion criteria, 28 clinical trials were included in the systematic review, 18 of which was randomized controlled trial (RCT). Participants included women with breast cancer who were undergoing the first three phases of breast cancer or postcancer rehabilitation. Among CAM interventions, one article used a dietary supplement, and the other 27 articles included a variety of mind-body techniques. Twenty-seven studies showed improved QOL ($P > 0.05$). **Conclusion:** The findings may indicate the potential benefits of CAMs, especially mind-body techniques on QOL in breast cancer patients. Further RCTs or long-term follow-up studies are recommended. Moreover, the use of similar QOL assessment tools allows for more meta-analysis and generalizability of results, especially for the development of clinical guidelines.

Keywords: Breast cancer, complementary therapies, quality of life, systematic review

INTRODUCTION

The increasing prevalence of cancer in recent years and its effects on various physical-psychological and social aspects of human life have made it as a major health problem.^[1] Among all types of cancer, breast cancer is one of the most common and the most important health problem in the world.^[2] The prevalence and incidence of the disease have been increasing over the past 25 years, especially in developing countries.^[3] Despite high mortality rates of breast cancer, the survival rate has also been increased.^[4] However, these patients are exposed to numerous physiological and psychological stressors that affect their quality of life (QOL).^[5]

Although classic treatments for breast cancer, such as surgery, chemotherapy, radiotherapy, and hormone therapy, have beneficial medical consequences, they also result in side effects.^[6] Most of patients suffer from the disease and the side effects of classical treatments, such as fatigue, anxiety, depression, nausea,

pain, and a high risk of developing a secondary tumor.^[7] Many patients have reported feelings of abandonment and isolation following the end of their active treatment, which exacerbates symptoms such as depression and anxiety. These feelings and conditions affect their QOL. Hence, the QOL in these patients has been reported lower than other cancer patients.^[8]

In recent years, the study of QOL as an important issue in health care has been considered, especially in breast

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cancer.^[9] According to the WHO definition, QOL is a subjective concept influenced by psychological, cultural, and social factors. Self-assessment is an important factor in evaluating QOL.^[10] Taking actions to control the complications of breast cancer and improving the QOL of patients is strongly recommended.^[11] In this regard, interventions have been introduced which encompass a wide range of psychosocial, behavioral, and environmental strategies. Mostly, these interventions aimed to complement the classic treatment for enhancing the QOL.^[12] Complementary and alternative medicine (CAM) as one of these interventions has been welcomed by many breast cancer patients and survivors.^[13]

According to the National Center for CAM, CAM is defined as a group of diverse medical and health systems, functions, and products that are not generally part of classical medicine.^[14] Complementary therapies are used in combination with classical medicine, while alternative therapies work instead of classical medicine.^[15] Studies also classify CAM into three categories of dietary supplements, herbal medicines, and mind and body techniques:^[16]

- Dietary supplements: Such as alpha-factor, high-dose Vitamin C, selenium, carnitine, vitamins, enzyme therapy, dietary advice
- Herbal medicines: Such as mistletoe therapy, Chinese herbal medicine
- Mind-body Techniques: Such as acupuncture, hyperthermia, movement therapy (qigong), laser therapy, orthomolecular therapy, osteopathy, phototherapy, healing touch, homeopathy, lymphatic drainage, magnet field therapy, manual therapy, neural therapy, Shiatsu.

The main causes of the tendency for CAM have been reported as the possibility for enhancing QOL, physical and mental recovery, strengthening the immune system, and reducing the side effects of classical medicine.^[17,18] However, some studies have shown that patients with breast cancer who use CAM have higher rates of mental disorders and lower QOL.^[19] Although a number of systematic reviews have been made in this area, their emphasis has been only on a specific category of CAM.^[20,21] Some have focused on Chinese medicine,^[7,22] or have included all cancer patients.^[23] Thus, there is a knowledge gap about which of CAM categories has more influence on breast cancer patients' QOL. In addition, new clinical trials are conducting in this field, regardless of the results of previous interventions and their effectiveness. Therefore, CAM interventions have not been presented as clinical guidelines for widespread use in breast cancer patients. Results of a systematic review can be useful to compare the effects of three categories of dietary supplements, herbal medicines, and mind and body techniques. Such a systematic review will allow the development of a clinical guideline for use in these patients. In this systematic review, we aimed to compare the effectiveness of CAM categories on the QOL of women with breast cancer.

METHODS

A systematic review was conducted using the Cochrane Handbook for Systematic Reviewers.^[24] Data were analyzed and reported according to Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) using the PRISMA checklist and PRISMA methodology flowchart.^[25] Search questions and strategies were determined by (F. B) and (Z. N) with the supervision of (N. D. N).

Search question, population, inclusion and exclusion criteria

The research question posed in the systematic review was as follows: How does CAM affect the QOL of women with breast cancer? The study population included women who had been diagnosed with breast cancer. There were no criteria and limitations for the method of the diagnosis and stage of breast cancer in the studies. The primary outcome of this review was the QOL assessment of women with breast cancer after receiving CAM interventions and techniques.

The main inclusion criteria were: (1) Study method as a type of clinical trial. (2) The target population should be only women with breast cancer. (3) Investigate patients' QOL as an outcome. (4) CAM methods have been used as intervention. The QOL assessment should have been performed with validated and reliable instruments. To examine all three categories of CAM methods, all of them were included in this review. Most studies in the field have also used the keywords complementary medicine, alternative medicine, and Chinese medicine. Therefore, these three keywords were included in the search protocol to identify more studies in the initial search. Exclusion criteria included not accessible English full-text articles, and receiving classical treatment (radiotherapy, chemotherapy, hormone therapy, and surgery) concurrent with CAM.

Search strategy

Searches of electronic databases were performed in PubMed, EMBASE, Scopus, and Google Scholar. The time limit was not considered for search to reach the maximum number of eligible articles. Studies were searched by the end of 2018. Conference proceeding abstracts were searched in the Conference Proceeding Citation Index. PICO-based keywords included "Breast Cancer," "Breast Neoplasm," "Complementary medicine," "Alternative medicine," "Chinese medicine," "Complementary therapies," and QOL. For example, the search strategy for PubMed based on MeSH is given in Box 1.

Box 1. Search strategy in PubMed

(["Breast Neoplasms" [Mesh] AND "Complementary Therapies" [Mesh]] AND "Quality of Life"[Mesh])

Study selection

After eliminating duplicates, two researchers (F. B) and (Z. N) independently assessed all the titles and abstracts of the articles found in the initial search based on inclusion criteria. In the second step, the full text of all selected articles was reviewed to ensure they were eligible for the final entry. Any disagreements

between researchers (F. B) and (Z. N) were resolved by a third researcher (N. D. N). During the process of reviewing and filtering the articles, no disagreement was observed between researchers.

Data collection and assessment of potential bias

(F. B) and (A. Kh) performed data extraction and quality assessment of the articles. The following study characteristics were collected from final included full texts: First author, year, country, study design, participants, intervention group (the type of CAM) and comparison group with samples, duration of intervention, instrument and measurement time, and a summary of outcome related to QOL.

The quality and risk of bias assessment for included articles were also independently assessed by both researchers. In case of disagreement, (N. D. N) would help to solve them. For quality assessment, the Cochrane Handbook for Systematic Reviews of Interventions criteria were used to estimate performance, attrition, detection, selection, and reporting biases. The risk of bias evaluation items included random sequence generation, allocation concealment, blinding of patients and personnel, blinding of outcome assessment, incomplete outcome data, and selective reporting.

RESULTS

Study selection and data extraction

The results of the search strategy are summarized in Figure 1. A total of 1186 references were identified in the initial search. A total of 385 were deleted due to duplication and 801 references remained. With regard to the main inclusion

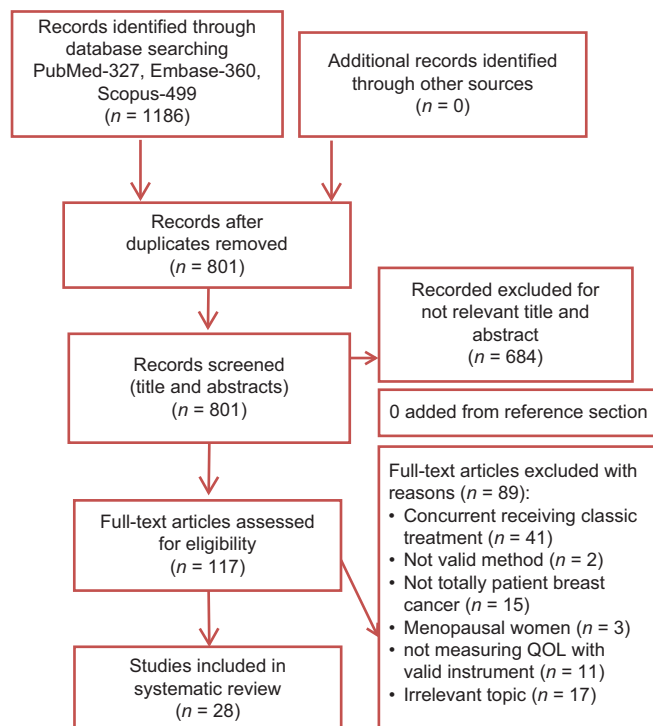


Figure 1: Preferred Reporting Items for Systematic Reviews and Meta-analyses flow diagram

criteria in the titles and abstracts, as well as English full text, 117 remained. Next, the full text of 117 articles was carefully reviewed for inclusion and exclusion criteria. During this phase, 89 articles were deleted. Finally, 28 articles were included in this systematic review. Then, the data were systematically extracted from 28 articles which are shown in Table 1.

Bias assessment results

Figure 2 presents a summary of the risk of bias for all included studies according to the six main criteria in the Cochrane risk of bias tool. In general, the highest risk of bias among articles was related to allocation concealment, random sequence generation, and blinding of outcome assessment, respectively. Nearly 80% of articles had a lower risk of blindness in the area of blinding patients and personnel.

Study characteristics

The studies differed in geographical location, design, and type of clinical trial [Table 1]. Sixteen articles was conducted in the United States,^[27,28,31,33,35-37,39,40,42-46,48,51] three in Canada,^[30,34,47] two in South Korea^[32,53] and one in China,^[41] Germany,^[38] Iran,^[26] Sweden,^[29] England,^[52] Turkey,^[50] and India.^[49] Eighteen studies from 28 included articles were randomized controlled trial (RCT).^[28,30,33-39,41-43,45,49-53] Study design in one study was non-RCT,^[29] and two studies were quasi-experimental.^[31,40] Another six articles benefited from other clinical trial designs. Moreover, 9 of the articles reported that they were pilot studies.^[27,28,33,34,39,40,44,47,48] The total sample size of each study varied from 21 to 271 individuals. Fifteen studies had a sample size of 21–50, and 4 studies had a sample size of 51–100. The sample size in 9 articles was in the range of 271–100. Control group conditions were not accurately described by all authors. However, in clinical trial studies, especially RCT, the control group should be matched with the overall structure of the intervention group,^[54] as the control group’s conditions affect the internal validity of the articles.^[55] Among RCT-designed articles, only five articles used a matched structured control group with equal sample size as the intervention group.^[29,41,49,51,53]

Participants

Patients in 19 included studies were in stages 0–III of breast cancer diagnose and treatment. Four articles assessed breast cancer survivors.^[27,33,34,39] Receiving concurrent classical

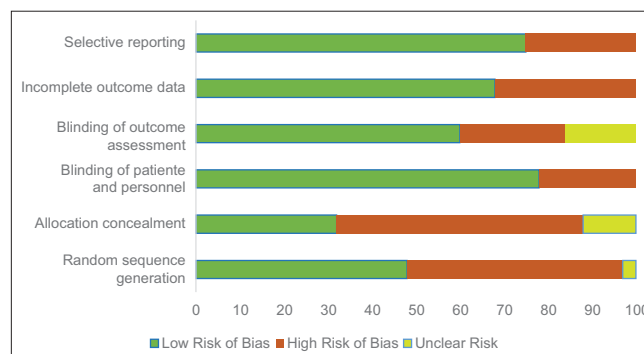


Figure 2: Risk of bias summary

Table 1: Characteristics of included studies

ID	First author, years, Country	Study design	Participants Total =Enrolled	Intervention n =Completed	Comparison n =Completed	Duration	Instrument measurement time	Summary of outcome (P)
1	Aghamoohammadi, 2017, Iran ^[26]	Clinical trial study	Newly diagnosed with breast cancer Total=119	Honey and cinnamon mixture: Three times daily for 1 week n=117	No comparison	1 week	EORTC QLQ-C30: One week before and 1 week after intervention	Significant effect of honey and cinnamon mixture program on QOL after intervention (<0.05)
2	Argenbright, 2016, USA ^[27]	A pilot clinical trial study	Breast cancer survivors with lymphedema Total=21	Bowen work intervention: 5-10, 45 min sessions	No comparison	6 weeks	SF-36/FACT-B: At baseline and postintervention	Significant change in mental health domain of SF-36 and total score of FACT-B, indicating of improvement in QOL of participants (<0.05)
3	Bao, 2014, USA ^[28]	Dual-center, double-blind, randomized controlled trial	Breast cancer, receiving an adjuvant AI Total=n=59	RA n=23	SA n=24	8 weeks	EORTC QLQ-C30: At baseline and at 4, 8 and 12 weeks	QOL significantly improved in SA group (<0.05)
4	Carlsson, 2004, Sweden ^[29]	Nonrandomized controlled trial	Newly diagnosed with breast cancer Total=120	ABCW: 5-29 days n=60	CBCW: Regional care program for all patients n=60	1-4 weeks	EORTC QLQ-C30: At baseline, 4 weeks, 3 months, 6 months, 1 year	Improvements in some subscales for QOL between baseline and different follow-up periods in ABCW group (<0.05)
5	Carlson, 2013, Canada ^[30]	A multi-site randomized controlled trial	Breast cancer with stage I, II, or III Total=271	MBCR: Eight weekly group sessions of 90 min each plus a 6 h workshop n=113 or SET: 12 weekly group sessions of 90 min each n=104	Control group; SMS: 1 day n=54	1 day to 12 weeks (depends on intervention)	FACT-B: At baseline and immediately postintervention	More improvement in QOL at MBCR group compared with control group (<0.05)
6	Charlson, 2014, USA ^[31]	A pilot study Quasi-experimental	Stage I-III breast cancer who had completed initial treatment: 8 weekly group sessions focus on teaching meditation skills/12-session cognitive-affective-behavioral learning program Total=46	Guided meditation and cognitive-affective-behavioral learning n=46	No comparison	20 weeks	FACT-G: At baseline and immediately after intervention	Intervention had clinically significant impact on improving QOL (<0.05)
7	Cho, 2016, South Korea ^[32]	Randomized trial	Breast cancer patients with AWS Total=41	PT combined with MLD 3 times/week n=21	MLD 5 times/week n=20	4 weeks	EORTC QLQ-C30: At baseline and after 4 weeks of treatment	QOL has been improved in both groups (<0.05)
8	Crane-Okada, 2012, USA ^[33]	Randomized controlled pilot feasibility study	Breast cancer survivors Total=39	MMP n=20	Usual care n=19	12 weeks	QOL breast cancer questionnaire: At baseline, after intervention (12 weeks), after 18 weeks	MMP group showed improvement in QOL, after intervention compared to control group (<0.05)
9	Culos-Reed, 2006, Canada ^[34]	A pilot randomized controlled trial study	Primary breast cancer survivors Total=38	Yoga program: 75 min in a quiet and dimly lit yoga studio n=20	Usual care n=18	7 weeks	EORTC QLQ-C30: At baseline and immediately after the yoga program	Significant effect of yoga program on QOL after intervention (<0.05)

Contd...

Table 1: Contd...

ID	First author, years, Country	Study design	Participants Total =Enrolled	Intervention n =Completed	Comparison n =Completed	Duration	Instrument measurement time	Summary of outcome (P)
10	Garlick, 2011, USA ⁽³⁵⁾	A phase II randomized controlled trial	Breast cancer in stages 0-III Total=30	PSIT: 3 h sessions over 8 weeks for a total of 24 h n=20	No comparison	8 weeks	FACT-B: At baseline, postintervention, and follow-up 4 weeks after treatment	Significant improvement in QOL between pre- and post-test of PSIT has been found (<0.05)
11	Gudenkauf, 2015, USA ⁽³⁶⁾	Randomized controlled dismantling trial	Stage 0-III breast cancer Total=138	CBT n=55 or RT n=70	HE control group n=58	5 weeks	FACT-B: At baseline and postintervention	The CBT group reported improved QOL compared to RT and HE groups (<0.05)
12	Henderson, 2012, USA ⁽³⁷⁾	RCT	Early-stage breast cancer Total=172	MBSR: Seven weekly 2.5-3.5 h sessions MBSR n=53	NEP or usual n=52 Supportive care (UC) n=58	8 weeks	FACT-B: After interventions, at 4 months, at 12 months	Significant improvement in QOL of MBSR group versus NEP and UC groups (<0.05)
13	Koch, 2017, Germany ⁽³⁸⁾	Open-label, RCT	Nonmetastatic breast cancer Total=40	Yoga and meditation: 90 min sessions n=21	Usual care: Offered the same yoga classes as the intervention group after 24 weeks n=19	12 weeks	FACT-B: At baseline, week 12, and week 24	Significant improvement in QOL subscales except physical wellbeing in yoga and meditation group (<0.05)
14	Larkey, 2016, USA ⁽³⁹⁾	Double-blind, randomized controlled pilot study	Breast cancer survivors Total=101	QG/TCE: n=42	SQG: n=45	12 weeks	SF-36: At baseline, after 12 weeks intervention, at 12 weeks postintervention	No statistical significant change between QG/TCE and SQG on breast cancer patients QOL (>0.05)
15	Levine, 2012, USA ⁽⁴⁰⁾	A pilot/ feasibility study Quasi-experimental	Previously treated for breast cancer Total=25	Yoga program n=25	No control group	6 weeks	FACT-B: Pre- and post-intervention and after 6 months	Significant improvement was found in all categories except social well-being (<0.05)
16	Liu, 2017, China ⁽⁴¹⁾	Randomized controlled trial	Primary breast cancer stage 0-IIIb Total=158	Guolin-Qigong (two 60 min sessions per week) n=79	Physical stretching program (260 min sessions per week) n=79	24 weeks	FACT-B: At baseline, after 12 weeks, immediately after 24 weeks, and at 48 weeks follow-up visit	GLQC was more effective in terms of QOL improvements than physical stretching (<0.05)
17	Milbury, 2013, USA ⁽⁴²⁾	Randomized controlled trial	Stages I-III breast cancer Total=47	TSM program: Two weekly meditation classes (60 min) n=18	Wait list control group received usual care n=24	6 weeks	SF-36: At baseline, the last week of the meditation program and 1 month after intervention	Meditation programs have significant improvement on mental health aspect of QOL (<0.05) There was no statistical difference on physical aspect of QOL after TSM
18	Monti, 2013, USA ⁽⁴³⁾	Randomized controlled trial	Newly diagnosed with breast cancer Total=191	MBAT n=98	BCSG n=93	8 weeks	SF-36: At baseline, immediately postintervention, at 6 months and extended follow-up (week 36)	No significant difference between MBAT and BCSG in QOL after 36 weeks (<0.05), QOL in both groups has been improved

Contd...

Table 1: Contd...

ID	First author, years, Country	Study design	Participants Total =Enrolled	Intervention n =Completed	Comparison n =Completed	Duration	Instrument measurement time	Summary of outcome (P)
19	Mustian, 2004, USA ⁽⁴⁴⁾	A pilot study	Primary breast cancer stage 0-IIIb Total=21	TCC: Three times a week for 60 min n=11	PST program: Three times a week for 60 min n=10	12 weeks	FACT-F: At baseline, 6 weeks, and 12 weeks	TCC group showed improvements in QOL and PST group showed decline in QOL (<0.05)
20	Nidich, 2009, USA ⁽⁴⁵⁾	Single-blind, randomized controlled trial	Newly diagnosed with breast cancer Total=130	TM: 7-step course lasted 1-1.5 h n=64	Usual care n=66	18 months	FACT-B: At baseline and every 6 months during intervention	Significant improvements were found in the TM group compared with controls in overall QOL (<0.05)
21	Richardson, 1997, USA ⁽⁴⁶⁾	Clinical trial methodology	Primary breast cancer (excluding IV) Total=47	Standard care with 1 h support or imagery/relaxation Support (n=16) Imagery (n=16)	Standard care n=15	6 weeks	FACT-B: In the week before and the week after a 6 week intervention	Imagery group participants had greater QOL than the support group participants. Both interventions improved QLO compared standard care (<0.05)
22	Speed-Andrews, 2010, Canada ⁽⁴⁷⁾	A pilot evaluation	Newly diagnosis of breast cancer Total=24	Iyengar yoga program: Before and after n=24	No comparison	12 weeks	SF-36/FACT-B: At baseline and postprogram	Improvements in QOL and psychosocial functioning after yoga program (<0.05)
23	Sprod, 2012, USA ⁽⁴⁸⁾	A pilot study	Breast cancer survivors Total=21	TCC: Three times/week; 60 min/session n=9	SST: Offered 4 weeks of TCC following the 12 weeks intervention n=10	12 weeks	SF-36: At baseline, mid-intervention (6 weeks) and postintervention (12 weeks)	Statistical significant change between TCC and SST at postintervention on QOL of breast cancer patients
24	Vadrajaja, 2009, India ⁽⁴⁹⁾	Randomized controlled trial	Stage II and III breast cancer Total=88	Yoga program: 18-24 sessions lasting 60 min daily n=44	Brief supportive therapy: Once in 10 days n=44	6 weeks	EORTC QLQ-C30: At baseline, after 6 weeks	Improvements in some subscales for QOL between baseline and postintervention follow-up in yoga group (<0.05)
25	Vardar Yağlı, 2015, Turkey ⁽⁵⁰⁾	Randomized controlled trial	Newly diagnosed with breast cancer Total=52	Yoga combined with aerobic exercise training: Submaximal exercise 30 min/day, 3 days/week and 1 h yoga program n=19	Aerobic exercise training: Submaximal exercise 30 min/week, 3 days/week n=21	6 weeks	EORTC QLQ-C30: At baseline and posttraining	The group with aerobic exercise and yoga showed marked improvement compared with the aerobic exercise group in fatigue perception (<0.05)
26	Walker, 2010, USA ⁽⁵¹⁾	Randomized controlled trial	Stage 0-III pre- or post-menopausal breast cancer Total=50	Acupuncture twice per week for the first 4 weeks then once for the first rest 8 weeks n=25	Venlafaxine 37.5 mg orally at night for 1 week, then 75 mg at night for the remaining 11 weeks n=25	12 weeks	Men QOL: At baseline; at the end of treatment; and at 3, 6, 9, and 12 months follow-ups	Acupuncture was as effective as venlafaxine for QOL (<0.05)

Contd...

Table 1: Contd...

ID	First author, years, Country	Study design	Participants Total =Enrolled	Intervention n = Completed	Comparison n = Completed	Duration	Instrument measurement time	Summary of outcome (P)
27	Williams, 2002, UK ^[52]	Randomized controlled crossover Study	Breast cancer with unilateral - related lymphedema Total=31	MLD 45 min session, performed Monday-Friday, over 3 weeks period n=29	SLD 20 min each day, over a 3 weeks period n=31	12 weeks (6 weeks nontreatment during interventions)	EORTC QLQ-C30: At baseline, after interventions, at 3, 9, and 12 postintervention	MLD improved emotional function, dyspnea, and reduced sleep disturbance (<0.05). SLD did not result in significant changes for QOL
28	Yao, 2016, South Korea ^[51]	Randomized controlled trial	Newly diagnosed with breast cancer Total=30	Combined acupuncture and moxibustion (warm acupuncture) with 3 of the needles each being topped by a 3 cm moxa stick n=15	Diosmin: 900 mg 3 times daily n=15	30 days period	EORTC QLQ-C30: At baseline, after treatment	Self-reported QOL was significantly better with warm acupuncture than with diosmin (<0.05)

SF-36=Medical outcomes study short-form health survey, QOL: Quality of life, EORTC QLQ-C30: European organization for research in the treatment of cancer-QOL, MenQOL: The menopause specific QOL questionnaire, FACT-B: The functional assessment of cancer treatment-breast, FACT-G: The General Functional Assessment of Cancer Therapy Scale, RCT: Randomized controlled clinical trial, AI: Aromatase inhibitor, AWS: Axillary web syndrome, RA: Real acupuncture, ABCW: Anthroposophic medicine, MBCR: Mindfulness-based cancer recovery, PT: Physical therapy, MMP: Mindful movement program, PST: Psycho - spiritual integrative therapy, CBT: Cognitive-behavioral training, RT: Relaxation training, MBSR: Mindfulness-based stress-reduction, QG/TCE: Qigong/Tai Chi Easy, TSM: Tibetan sound meditation, MBAT: Mindfulness-based art therapy, TCC: Tai Chi Chuan, TM: Transcendental meditation program, MLD: Manual lymphatic drainage, SA: Sham acupuncture, CBCW: Conventional medicine, SMS: Stress management seminar, HE: Health education, NEP: Nutrition education program, SQG: Sham Qigong, BCSCG: Breast cancer support group, PST: Psychosocial support, SST: Standard support therapy, SLD: Simple lymphatic drainage, UC: Usual care, QLO: Quality of life

treatment was considered as exclusion criterion. In a study co-administered with CAM, an aromatase inhibitor was used but because it was part of medication therapy, the study remained in review.^[28]

Complementary and alternative interventions

Table 2 shows the category of CAM interventions in the included studies and their impact on QOL. None of included articles used herbal medicine as a CAM intervention. Only one article used dietary supplements^[26] and the other 27 articles used a variety of mind-body CAM techniques for intervention. Except one article in the mind-body category,^[39] all other 27 papers reported a significant effect of CAM interventions on improving QOL of patients. Most articles that showed significant CAM effect had only reported P value and did not mention the confidence interval. There was a great deal of variation in mind-body interventions in this category, but yoga^[34,38,40,47,49,50] and acupuncture^[28,51,53] interventions were more common.

Quality of life outcome

All QOL outcomes were assessed using self-report tools. QOL survey tools were varied. The EORTC QLQ C30 and Functional Assessment of Cancer Therapy-Breast (FACT-B) tools were most commonly used in the studies, and each of them was used nine times in the included articles. The Short Form (SF)-36 tool was also used in four articles to measure QOL. Two studies used both SF-36 and FACT-B tools. Each of the Functional Assessment of Chronic Illness Therapy-F, FACT-G, men-QOL, and QOL Breast Cancer Questionnaire tools were used in one article. All studies performed QOL measurements at baseline and after the intervention. However, the time intervals for measuring and using the tool for follow-up were different among the articles, and some articles did not measure QOL as follow-up.^[26,27,30,31,34,36,46,47,50,53]

DISCUSSION

This systematic review reports evidence of 28 articles, including 18 RCT articles and 10 articles with other experimental, quasi-experimental, and non-RCT designs. These articles contain data related to the outcome of CAM on QOL in patients with breast cancer. Although no time limit was applied to the articles, 18 articles were published after 2010. This study is the first systematic review that examines the impact of CAM according to its category of dietary supplements, herbal medicine, or mind-body techniques on the QOL of women with breast cancer. Despite the great diversity of studies in the type of CAM, study design, duration of interventions, duration of follow-up, and QOL assessment tools, 27 articles reported improvement in overall or subscales of the QOL. Among 28 included studies, only one was in the dietary supplements category, and none was used herbal medicine. Other studies used a variety of mind-body techniques as CAM.

Using CAM in mind-body techniques such as yoga, acupuncture, art therapy, music therapy, guided imagery, cognitive-behavioral stress management, and mental exercise

Table 2: Categories of complementary and alternative medicine in included studies

Category of CAM	First author	CAM	Outcome on QOL (P)
Dietary supplements	Aghamohammadi, 2017	Honey and cinnamon mixture	Independent <i>t</i> -test (0.001)
Mind-body techniques	Argenbright, 2016	Bowen work	Paired sample <i>t</i> -test (0.003)
	Bao, 2014	RA	Wilcoxon signed-rank test (0.022)
	Carlsson, 2004	ABCW	Paired sample <i>t</i> -tests (<0.05*)
	Carlson, 2013	MBCR or supportive-expressive therapy	Repeated measures ANOVA (0.005)
	Charlson, 2014	Guided meditation and cognitive-affective-behavioral learning	Paired <i>t</i> -test (0.01)
	Cho, 2016	PT combined with MLD	Independent <i>t</i> -test (<0.001)
	Crane-Okada, 2012	MMP	Two-way repeated-measures analysis (0.02)
	Culos-Reed, 2006	Yoga program	Two-way repeated-measures analysis (<0.01)
	Garlick, 2011	Psycho-spiritual integrative therapy	Repeated measures ANOVA (<0.01)
	Gudenkauf, 2015	CBT	Repeated measures ANOVA (<0.001)
	Henderson, 2012	Mindfulness-based stress-reduction	Independent <i>t</i> -test (<0.05*)
	Koch, 2017	Yoga and meditation	Paired sample <i>t</i> -tests (<0.05*)
	Larkey, 2016	QG/TCE	NS**
	Levine, 2012	Yoga program	Independent <i>t</i>-test (<0.001)
	Liu, 2017	Guolin-qigong	A mixed-effect model (0.002)
	Milbury, 2013	TSM	Repeated measures ANOVA, mental health (<0.05)
	Monti, 2013	MBAT	Mixed effects regression analysis (<0.001)
	Mustian, 2004	TCC	ANOVA (<0.001)
	Nidich, 2009	TM	Repeated measures ANOVA (0.037)
	Richardson, 1997	Imagery/relaxation support	<i>F</i> -test (<0.03)
	Speed-Andrews, 2010	Iyengar yogaprogram	Paired sample <i>t</i> -tests (<0.05*)
	Sprod, 2011	TCC exercise	Repeated measures ANOVA (0.045)
	Vadiraja, 2009	Yoga program	Repeated measures ANOVA (<0.05*)
Vardar Yağlı, 2015	Yoga combined with aerobic exercise training	Paired sample <i>t</i> -tests (<0.05)	
Walker, 2010	Acupuncture	Repeated measures ANOVA (<0.002)	
Williams, 2002	MLD	Independent <i>t</i> -test (0.006)	
Yao, 2016	Combined acupuncture and moxibustion	Paired sample <i>t</i> -tests (<0.001)	

*For subscales, **NS; *P*>0.05. NS: Not significant, ANOVA: Analysis of variance, QOL: Quality of life, CAM: Complementary and alternative medicine, RA: Real acupuncture, ABCW: Anthroposophic medicine, MBCR: Mindfulness-based cancer recovery, PT: Physical therapy, MMP: Mindful movement program, CBT: Cognitive-behavioral training, QG/TCE: Qigong/Tai Chi Easy, TSM: Tibetan sound meditation, MBAT: Mindfulness-based art therapy, TCC: Tai Chi Chuan, TM: Transcendental meditation program, MLD: Manual lymphatic drainage

techniques were more than any other CAM interventions, especially herbal medicine or dietary supplements. Therefore, improvement in QOL was also reported in mind-body techniques more than the other two categories. Previous review studies have also emphasized the impact of CAM in mind-body techniques on improving QOL in cancer patients.^[7,22,56] In addition, Roberts showed little benefit in their systematic review on the effect of herbal medicines on reducing hot flashes in women with breast cancer.^[57] On the other hand, Leggett *et al.* performed a systematic review on the effect of different CAM methods on cancer symptoms, QOL, and side effects of breast cancer treatment. This review, which examined different types of studies, found insufficient evidence to suggest that CAM has an effect on improving QOL in breast cancer patients. Most of the CAM interventions in included studies in this review were dietary supplements and herbal medicines.^[15] However, the effect of yoga as a mind-body technique on QOL improvement in breast cancer patients has been systematically reviewed by Lin *et al.*, but no confirmed findings on the effect of yoga on QOL have been found.^[56]

Overlay, the risk of bias was relatively significant among the reviewed studies. One area with high risk of bias was blinding of outcome assessment in the study of QOL, which is based on self-reporting. Kreutz *et al.* stated that in assessing outcomes that are self-reported, the possibility of blinding of outcome assessment is reduced.^[58]

Despite some notable findings from this systematic review, there are some limitations that must be considered when interpreting the findings. First, there was a great deal of heterogeneity in the study design, type of CAM intervention, and type of clinical trial among the studies. Similar interventions also differed in terms of the implementation plan (frequency of intervention, duration, and characteristics of the research population). Second, articles that examined the impact of CAM on QOL in women with breast cancer were more focused on mind-body techniques. Third, in addition to the variation in the mind-body interventions under study, various QOL assessment tools were used. This variation in the types of interventions and outcome measurements did not allow for a meaningful meta-analysis even among the subgroups. Fourth, only English-language

articles were included in this review that potentially poses a risk of publication and language bias.

CONCLUSION

The findings of the present review indicate the significant effect of most CAM interventions on QOL in women with breast cancer. Given the increasing prevalence of breast cancer worldwide and the increasing life expectancy of these patients, interventions are needed to improve QOL of these patients. The positive impact of various CAM methods on different aspects of breast cancer patients' lives, such as sleep status, life expectancy, and QOL, has been emphasized in many studies. It seems that the promotion of CAM methods can be a cost-effective care approach in breast cancer patients and recommend by health-care providers. However, there is insufficient evidence of the effectiveness of different types of CAM approaches for the development of clinical guidelines. Therefore, further RCT studies are needed for each type of CAM intervention with more similarity in QOL assessment tools to enable meta-analysis.

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Conflicts of interest

There are no conflicts of interest.

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