



Ameliorative effects of Tai Chi on cancer-related fatigue: a meta-analysis of randomized controlled trials

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Abstract

Purpose This meta-analysis investigated the effectiveness of Tai Chi on cancer-related fatigue (CRF).

Methods Nine databases (PubMed, Web of Science, Ovid, the Cochrane Library, Embase, and four Chinese databases) were searched to identify randomized controlled trials (RCTs) that evaluated the effects of Tai Chi on CRF. The reference lists given in the identified RCTs were also reviewed to identify potentially relevant studies.

Results Six RCTs involving 373 patients were included. The change in short- and long-term CRF (SCRf and LCRf, respectively) was calculated as the change in the mean score for CRF from baseline to the end of intervention period and to the end of post-intervention follow-up, respectively. Pooled results suggested that Tai Chi had a significant positive effect on standard mean difference (i.e., SCRf; SMD = -0.54; $p < 0.0001$), but the impact on LCRf remained unclear. Subgroup analyses of SCRf indicated positive effects of Tai Chi among patients with breast (SMD = -0.81; $p < 0.00001$) and lung cancer (SMD = -0.50; $p = 0.002$), but not prostate cancer ($p = 0.98$). Tai Chi also had effects on SCRf that were superior to physical exercise and psychological support (SMD = -0.49 and -0.84, respectively; both $p < 0.05$). A longer intervention time (8–12 weeks) benefited SCRf more than a shorter time (SMD = -1.08 and -0.36, respectively; both $p < 0.05$).

Conclusion Tai Chi for more than 8 weeks has short-term ameliorative effects on CRF, especially among patients with breast and lung cancer. Its beneficial effects are superior to physical exercise and psychological support. It remains unclear whether there are long-term benefits, and further study is needed.

Keywords Tai Chi · Fatigue · Neoplasms · Meta-analysis

Introduction

Cancer and its treatments commonly cause fatigue (“cancer-related fatigue”), with an incidence of 80–93% [1]. The National Comprehensive Cancer Network (NCCN) [2] describes cancer-related fatigue (CRF) 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.” CRF is reported to be more distressing than vomiting, nausea, or pain [3]. As the societal burden of cancer is increasing alongside its incidence [4–6], anticancer therapy and the care of patients with cancer are major issues for healthcare providers and researchers. Management of CRF is an important issue that has the potential to substantially improve quality of life in cancer patients.

There is some evidence that the occurrence of CRF correlates with both physical and social-psychological factors [7–9]. However, the precise pathophysiological mechanism(s) underlying its development remain unclear. Standard or specific treatment options for CRF are lacking. The NCCN Clinical Practice Guidelines in Oncology recommends non-pharmacological over pharmacologic interventions for CRF because there is little evidence to support the latter and pharmacotherapy may be accompanied by adverse side effects [2]. Clinical studies of CRF have suggested beneficial effects of physical exercise [10], psychological support [11], and complementary therapies

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such as acupuncture [12], moxibustion [13], massage [14], and yoga [15]. Further, a recent meta-analysis published in *JAMA Oncol* determined that physical exercise and psychological interventions were more effective for reducing CRF than available pharmaceutical therapies [16].

Tai Chi is an ancient traditional Chinese exercise therapy, consisting of methodically slow stretching movements, positions of body balance, breath adjustment, and meditation. Tai Chi has been shown to benefit cardiovascular adaptability and endurance [17], psychological well-being [18], and metabolic diseases [19]. In recent years, it has been shown to improve quality of life in patients with cancer by improving insomnia [20] and physical action ability [21]. It has also been shown to be effective in relieving fatigue in patients with arthritis [22], multiple sclerosis [23], and fibromyalgia syndrome [24]. Studies have evaluated the impact of Tai Chi on CRF, although their conclusions have been inconsistent [21, 25–29]. Hence, the aim of this meta-analysis of randomized controlled trials (RCTs) was to evaluate current evidence and estimate the pooled effects of Tai Chi on CRF.

Methods

This meta-analysis was registered in PROSPERO (register code: CRD42017068930) and was conducted according to the PRISMA statement [30].

Information sources and search strategy

Studies were initially identified by searching nine electronic databases without limits of language or publication date. The databases were the following: PubMed, Web of Science, Ovid, the Cochrane Library, Embase, and four Chinese databases (SinoMed, VIP, CNKI, and Wanfang databases). The references listed in the identified studies were also scanned manually to locate further papers that might be relevant. The last completed database search was undertaken on 3 April 2017, with further limited update searches performed until 30 April 2017. Search terms included “Tai Ji,” “Tai Chi,” “neoplasms,” “cancer or tumor or carcinoma,” and “fatigue.” The search strategy is outlined in [Appendix 1](#), but varied slightly depending on the different databases.

Eligibility criteria

As per the PICOS principles outlined in the PRISMA statement [30], all included studies met the following criteria:

- (1) Types of studies: RCTs concerning the effects of Tai Chi on CRF were included. Reviews, systematic reviews, case reports, editorials, pilot studies, feasibility studies, and study protocols were excluded.
- (2) Types of participants: Patients with a confirmed diagnosis of cancer and symptoms of CRF were considered. No restriction was placed on gender, age, cancer type, tumor grade, or post-treatment.
- (3) Types of intervention: Tai Chi was the experimental intervention. The comparator group had no limitations and included usual supportive care, health education, pharmacotherapy, psychological therapy, acupuncture, moxibustion, and exercises other than Tai Chi such as walking, stretching, yoga, and dancing. Studies with no intervention for the comparator group were also included.
- (4) Types of outcome measures: Assessments of CRF involved effective and validated scales such as Brief Fatigue Inventory, Functional Assessment of Chronic Illness Therapy-Fatigue Survey, and Functional Assessment of Cancer Therapy-Fatigue [31].

Study selection and data extraction

Eligibility assessments were performed by two reviewers independently, with disagreements. The data extraction sheet was predefined according to the template of the Cochrane Consumers and Communication Review Group. One reviewer extracted that data and a second reviewer verified it. Extracted data contained the characteristics of study (study type, publication year, and first author), participants (sample size, age, gender, ethnicity, diagnosis, and tumor grade), interventions (style, intensity, and duration), control groups, outcome measures (the type of CRF scale, mean \pm standard deviation of CRF scores on baseline, post-intervention, and the end of post-intervention follow-up), and the length of post-intervention follow-up period. If quantitative data were not accessible in the article, the reviewers sought the information from the authors or calculated the necessary value from existing statistics.

Quality assessment

The quality of the methods used in the included studies was independently evaluated by two reviewers according to the Cochrane collaboration's tool for assessing risk of bias [32]. Assessments for risk of bias involved evaluation of sequence generation, allocation of concealment, blinding of participants, personnel and outcome assessment, completeness of reported data, selective reporting, and other sources of bias.

Data synthesis and statistical analysis

The short-term change in CRF (SCRf) was the primary measure of treatment effect. It was calculated as the

change in mean score of CRF from baseline to the end of intervention period. The long-term change in CRF (LCRF) was the second measure and was calculated from baseline to the end of post-intervention follow-up period. Since both SCRF and LCRF were continuous variables, the meta-analysis was performed by computing the mean difference (MD) if qualified studies shared the same CRF scale; otherwise, the standard mean difference (SMD) was adopted. If the direction of the CRF scale among studies were different (e.g., some scales had a positive correlation with CRF while others were negative), the mean values measured by the negatively correlated scale were multiplied by -1 to ensure consistency [32]. Heterogeneity was tested by I^2 test. If low statistical heterogeneity was observed ($I^2 \leq 50\%$), the fixed effects model was adopted; otherwise, the random effects model was used ($I^2 > 50\%$). Subgroup analyses were undertaken based on characteristics of the included studies. Sensitivity analysis was performed by omitting each included study, one by one, so as to explore their influence on the overall estimate. Publication bias was visually examined by funnel plot. The Z test was used to determine the significance of the pooled estimate, where $p < 0.05$ indicated statistical significance. All statistical analyses were calculated in Review Manager 5.3 (The Cochrane Collaboration, Copenhagen, Denmark).

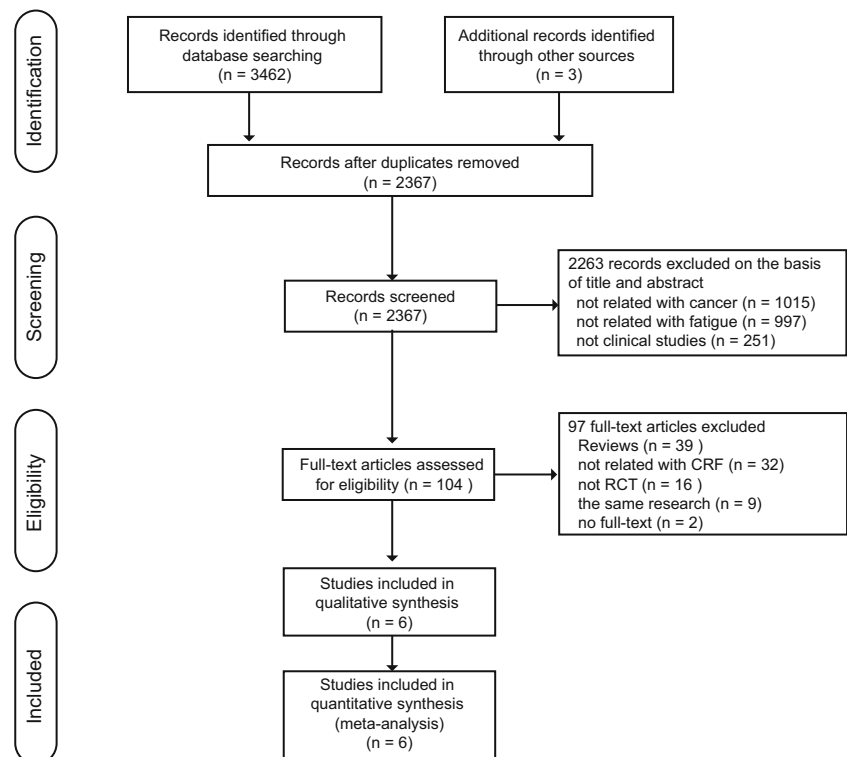
Results

Study characteristics

A total of 3462 records were identified in the initial database search, and further three were located through reference scanning. After excluding duplicates, 2367 records remained. Of these, 2263 were excluded after reviewing titles and abstracts, and 93 were excluded after reviewing the full text against the eligibility criteria. Finally, six articles were included in this meta-analysis. The study selection process is shown in Fig. 1.

A total of 373 participants were included, with 179 in the Tai Chi group and 194 in the control group. Ages ranged from 40 to 75 years old; ethnicities included both Asian and non-Asian populations and cancer diagnoses comprised breast, lung, and prostate cancer. The intensity of Tai Chi intervention varied from 120 to 420 min per week, with the duration ranging from 4 to 12 weeks. Comparative interventions comprised physical exercise, usual supportive care, and psychological-social support (psychological support therapy or health education). The CRF scale varied between the studies and included the Brief Fatigue Inventory (BFI), Functional Assessment of Chronic Illness Therapy-Fatigue Survey (FACIT-F), Multidimensional Fatigue Symptom Inventory-Short Form (MFSI-SF), and Fatigue Symptom Inventory (FSI).

Fig. 1 Literature search and inclusion process



There was one three-armed parallel group study [28], while the remainders were all two-armed. Blinding is difficult due to the nature of the Tai Chi; therefore, nearly all included studies had a high risk of bias due to inability to blind participants. One study was an exception [27] as it adopted sham qigong (a physical exercise with similar movements to Tai Chi but without breath regulation and mediation) as comparator. No high risks were observed for randomization, allocation, and detection bias, with low risks for reporting bias. One study [21] had high risk of attribution bias. The characteristics and methodological quality of the included studies are summarized in Table 1 and Fig. 2, respectively.

Synthesis of results

SCRF

All included studies reported SCRF, but the scale for CRF varied leading to adoption of SMD for measurement. Since heterogeneity was low ($I^2 = 32\%$), the fixed effects model was used. Pooled analysis (Fig. 3) showed that Tai Chi significantly improved SCRF compared with comparative interventions (SMD = -0.54 ; 95% CI [$-0.75, -0.33$]; $Z = 5.06$; $p < 0.0001$). Sensitivity analyses revealed that no individual studies significantly affected the pooled SMD (all $p < 0.01$), which indicated statistically robust results (Table 2).

To explore potential effect differences, subgroup analyses were performed. As shown in Fig. 3a, subgroup analysis by cancer types indicated that there were significant differences in SCRF between Tai Chi intervention and control groups in patients with breast (SMD = -0.81 ; 95% CI [$-1.13, -0.48$]; $Z = 4.82$; $p < 0.00001$) and lung (SMD = -0.50 ; 95% CI [$-0.83, -0.18$]; $Z = 3.03$; $p = 0.002$) cancer. However, there was no difference for patients with prostate cancer ($p = 0.98$). The test for subgroup difference ($I^2 = 70.8\%$) indicated that cancer type may contribute to heterogeneity.

Subgroup analysis based on comparative intervention (Fig. 3b) showed that Tai Chi intervention had significant beneficial effects on SCRF when compared with physical exercise (SMD = -0.49 ; 95% CI [$-0.76, -0.22$]; $Z = 3.59$; $p = 0.0003$) and psychological support (SMD = -0.84 ; 95% CI [$-1.34, -0.35$]; $Z = 3.33$; $p = 0.0009$), but no significant difference compared to the usual care ($p = 0.12$). As implied in the test for subgroup difference ($I^2 = 28.3\%$), the variable comparative intervention may not be a contributor to heterogeneity.

Further subgroup analysis by duration (Fig. 3c) showed that Tai Chi intervention for ≤ 8 weeks (SMD = -0.36 ; 95% CI [$-0.63, -0.08$]; $Z = 2.56$; $p = 0.01$) and > 8 weeks (SMD = -0.81 ; 95% CI [$-1.13, -0.48$]; $Z = 4.82$;

$p < 0.00001$) improved SCRF. The longer duration (> 8 weeks) had superiority (SMD = -0.81) over shorter duration (SMD = -0.36), with a significant difference in the test for subgroup differences ($I^2 = 74.1\%$). The test for subgroup difference by intensity of Tai Chi (Fig. 3d) implied no significant difference between subgroups ($I^2 = 0\%$), although performing Tai Chi for at least 180 min/week could benefit SCRF (SMD = -0.52 ; 95% CI [$-0.83, -0.22$]; $Z = 3.36$; $p = 0.0008$) while less than 180 min/week may not ($p = 0.05$).

LCRF

Only two studies, conducted by Larkey et al. [27] and McQuade et al. [28], reported LCRF. The former studied LCRF for 3 months of post-intervention follow-up, while the latter reported both 1- and 3-month LCRF. The pooled estimate for the 3-month post-intervention LCRF showed no significant difference between the Tai Chi and control groups ($p = 0.91$). However, the result data reported by McQuade et al. implied a significant difference for 1-month post-intervention LCRF ($p = 0.003$). Subgroup and sensitivity analyses were not conducted due to the small number of studies. The statistics are presented in Fig. 4.

Publication bias

The funnel plot was performed to assess potential publication bias in the included SCRF studies, but was not undertaken for LCRF because of the small sample size ($n = 2$). The shape of the funnel plot appeared asymmetric, which implied potential publication bias (Fig. 5). However, the fail-safety number (Nfs_α) suggested at least 56 RCTs with negative effect were needed to reverse the synthesized results. This indicated low potential for publication bias. The calculation formula for the fail-safety number is as follows [33]:

$$Nfs_\alpha = \frac{(\sum_{i=1}^k t_i)^2}{t_\alpha} - k, \text{ where } \alpha \text{ is the significance level, } t_i \text{ is the } t \text{ value in each of the included studies for Tai Chi versus comparative groups, and } k \text{ is the number of included studies.}$$

In this study, $\alpha = 0.05$ and $k = 6$ so $Nfs_\alpha = 56.366$.

Discussion

Tai Chi is a type of traditional Chinese exercise that combines regular physical exercise with meditation and focused breathing. Regular physical exercise, especially of moderate to vigorous intensity [34–36], has been reported to produce physiological adaptive changes including reduction in fatigue. Tai Chi involves low to moderate intensity physical exercise, which may partially explain its

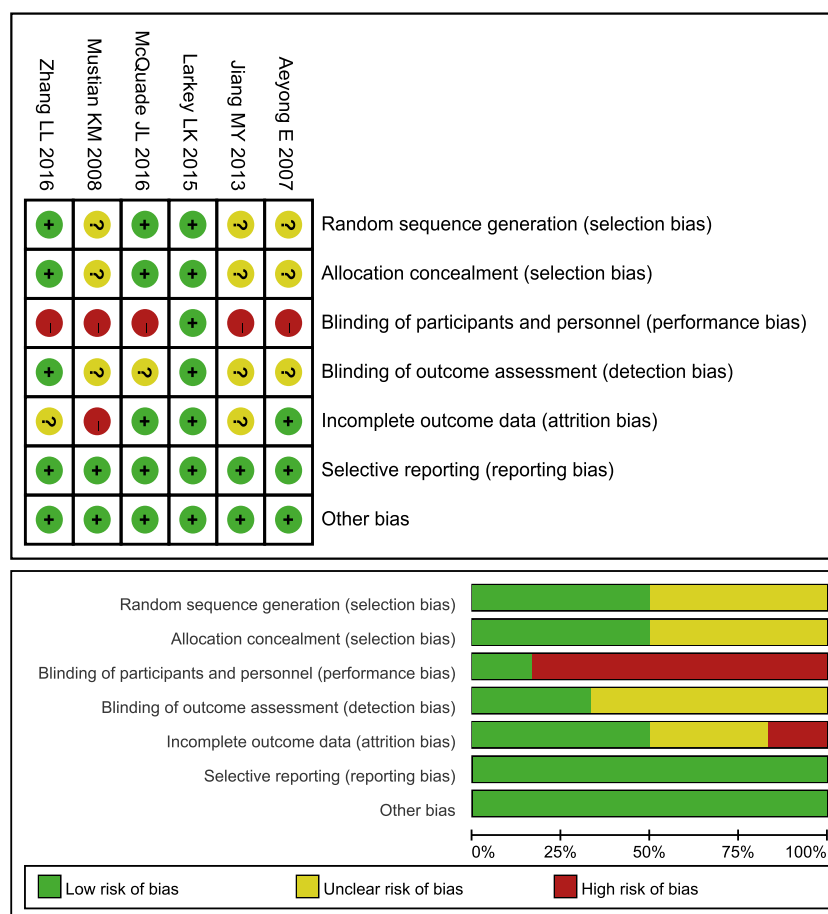
Table 1 Main characteristics of the included studies

Source	Design	Diagnosis and tumor grade	Cancer treatment	Ethnicity (T/C)	Mean age \pm SD (years)	Sample size (male/female)	Intervention	Control	Outcomes
Aeyong E 2007 [25]	RCT	Breast cancer (I–II)	Mastectomy	Korean (25/23)	44.2 \pm 6.65 (30–60)	T: 25 (0/25) C: 23 (0/23)	T = Tai Chi Duration = 60 min/session Frequency = 2 sessions/week Length = 12 weeks T = Tai Chi Duration = 60 min/session Frequency = 1 session/2 days (10–21th day/CTC) Length = 4 CTCs	C = Education Duration = 60 min/session Frequency = 1 session/2 weeks Length = 12 weeks C = Low-impact exercise Duration = 60 min/session Frequency = 1 session/2 days (10–21th day/CTC) Length = 4 CTCs C _a = Light exercise; C _b = Waiting list control (usual care) Duration _a = 40 min/session Frequency _a = 3 sessions/week Length _a = 1 RTC (6 or 8 weeks) C _b = Waiting list control (usual care) Length _b = 1 RTC (6 or 8 weeks)	BFI
Zhang LL 2016 [29]	RCT	Lung cancer (I–IV)	Chemotherapy	Chinese (47/44)	62.8	T: 47 (37/10) C: 44 (31/13)	T = Tai Chi Duration = 60 min/session Frequency = 1 session/2 days (10–21th day/CTC) Length = 4 CTCs T = Tai Chi Duration = 40 min/session Frequency = 3 sessions/week Length = 1 RTC (6 or 8 weeks)	C = Education Duration = 60 min/session Frequency = 1 session/2 weeks Length = 12 weeks C = Low-impact exercise Duration = 60 min/session Frequency = 1 session/2 days (10–21th day/CTC) Length = 4 CTCs C _a = Light exercise; C _b = Waiting list control (usual care) Duration _a = 40 min/session Frequency _a = 3 sessions/week Length _a = 1 RTC (6 or 8 weeks) C _b = Waiting list control (usual care) Length _b = 1 RTC (6 or 8 weeks)	MFSI-SF
McQuade JL 2016 [28]	RCT	Prostate cancer (I–III)	Radiotherapy	White (20/18/23) Hispanic (1/2/0) Asian (0/1/0) Black (0/0/1)	T: 62.2 \pm 7.4 C _a : 65.0 \pm 5.9 C _b : 66.0 \pm 8.4	T: 21 (21/0) C _a : 21 (21/0) C _b : 24 (24/0)	T = Tai Chi Duration = 60 min/session Frequency = 1 session/2 days (10–21th day/CTC) Length = 4 CTCs T = Tai Chi Duration = 40 min/session Frequency = 3 sessions/week Length = 1 RTC (6 or 8 weeks)	C = Education Duration = 60 min/session Frequency = 1 session/2 weeks Length = 12 weeks C = Low-impact exercise Duration = 60 min/session Frequency = 1 session/2 days (10–21th day/CTC) Length = 4 CTCs C _a = Light exercise; C _b = Waiting list control (usual care) Duration _a = 40 min/session Frequency _a = 3 sessions/week Length _a = 1 RTC (6 or 8 weeks) C _b = Waiting list control (usual care) Length _b = 1 RTC (6 or 8 weeks)	BFI
Larkey LK 2015 [27]	RCT	Breast cancer (0–III)	Combination (surgery/chemotherapy/radiotherapy)	Latino (1/1) Non-Latino (40/35)	58.8 \pm 8.94 (40–75)	T: 45 (0/45) C: 42 (0/42)	T = Tai Chi Duration = 30 min/session Frequency = 5 sessions/week Length = 12 weeks T = Tai Chi Duration = 60 min/session Frequency = 3 sessions/week Length = 12 weeks	C = Sham qigong Duration = 30 min/session Frequency = 5 sessions/week Length = 12 weeks C = Psychosocial support therapy Duration = 60 min/session Frequency = 3 sessions/week Length = 12 weeks	FSI
Mustian KM 2008 [21]	RCT	Breast cancer (0–IIIb)	Not mentioned	90% Caucasian 10% other	52 \pm 9 (33–78)	T: 11 (0/11) C: 10 (0/10)	T = Tai Chi Duration = 60 min/session Frequency = 3 sessions/week Length = 12 weeks	C = Psychosocial support therapy Duration = 60 min/session Frequency = 3 sessions/week Length = 12 weeks	FACIT-F
Jiang MY 2013 [26]	RCT	Advanced lung cancer	Not mentioned	Chinese (30/30)	T: 64.4 \pm 2.8 (46–75) C: 65.6 \pm 2.0 (48–75)	T: 30 (14/16) C: 30 (16/14)	T = Tai Chi Duration = 30 min/session Frequency = 2 sessions/day Length = 30 days	C = Routine care Length = 30 days	BFI

Subscript letters a and b represent the first control group and the second control group, respectively

RCT randomized controlled trial, SD standard deviation, T Tai Chi group (intervention group), C control group, CTC chemotherapy cycle, RCT radiotherapy cycle, BFI Brief-Fatigue Inventory, MFSI-SF Multidimensional Fatigue Symptom Inventory-Short Form, FSI Fatigue Symptom Inventory, FACIT-F Functional Assessment of Chronic Illness Therapy-Fatigue Survey

Fig. 2 Methodological qualities of all eligible studies



beneficial effects on CRF, while other non-physical components like meditation and breathing adjustment may also add to the favorable effects against CRF [37]. Slow deep breathing has been associated with a more balanced autonomic nervous system and may contribute to reduced fatigue [38]. Meditation alone has been found to reduce somatic symptoms like anxiety, depression, and fatigue [39–42]. Thus, even though Tai Chi may theoretically be categorized as a physical exercise in a broad sense, it should not be classified solely as this. It is also not appropriate to consider Tai Chi the same as other complementary exercise practices, such as yoga or qigong (another kind of traditional Chinese exercise reliant on meditation), as the intensity of physical exercise and amount of non-physical exercise components vary. Tai Chi can produce greater improvement in physical function than either yoga or qigong. Further, it potentially has greater psychological advantages than “standard” physical exercise approaches. Thus, Tai Chi may be a better intervention for CRF management [21, 27, 43, 44]. This background information leads us to conduct a meta-analysis focused on the effect of Tai Chi alone on CRF, rather than on other forms of exercise.

The pooled results of this meta-analysis showed an overall benefit for Tai Chi in SCRF (SMD = -0.54; $p < 0.0001$). This suggested potential clinical value in the short-term control of CRF. To further evaluate discrepancies in the effectiveness of CRF, we undertook subgroup analyses. These analyses suggested that Tai Chi improved SCRF in patients with breast or lung cancer. There was no effect in prostate cancer, but further investigation of this is needed as only one study of prostate cancer was included in the meta-analysis. The mechanism for the favorable effects of Tai Chi on CRF is currently unclear. Another recent meta-analysis indicated that Tai Chi produces a positive impact on immune system function and cortisol concentrations in patients with cancer [45]. Tai Chi has also been reported to enhance vagal modulation and alter sympathovagal balance [46], to effectively regulate the hypothalamic-pituitary-adrenal (HPA) axis by decreasing cortisol concentrations [47] and fluctuation [48], and to reduce interleukin-6 and tumor necrosis factor concentrations [49] among CRF patients. Collectively, these findings suggest that the ameliorative effect of Tai Chi on CRF may relate to its function in enhancing vagal

Fig. 3 Subgroup analysis by cancer types (a), comparative intervention (b), intervention time (c), and intervention intensity (d) for the difference in SCRF. The data of the three-armed parallel group study conducted by McQuade JL 2016 was presented independently for physical exercise and usual care group as McQuade JL 2016 a and McQuade JL 2016 b, respectively

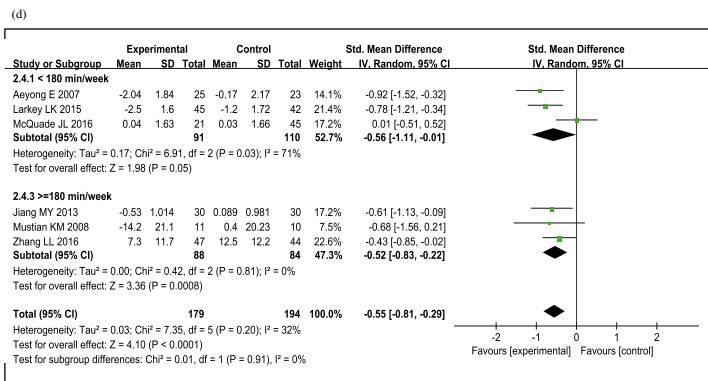
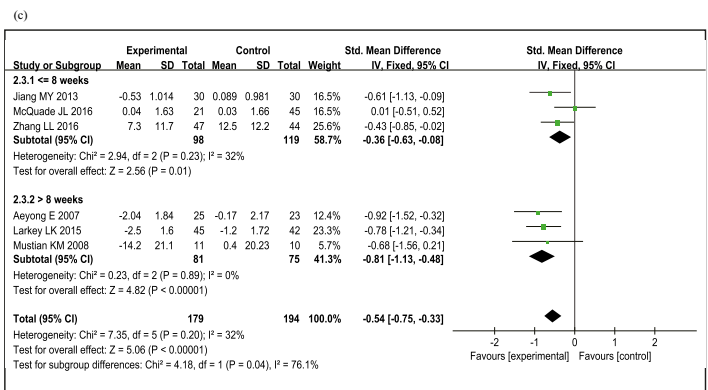
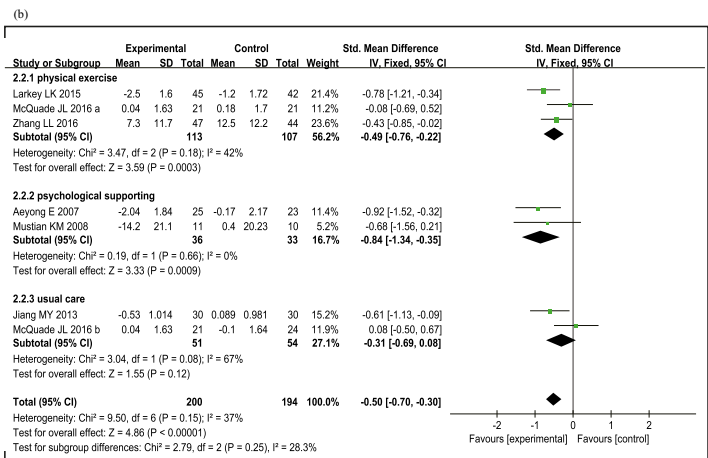
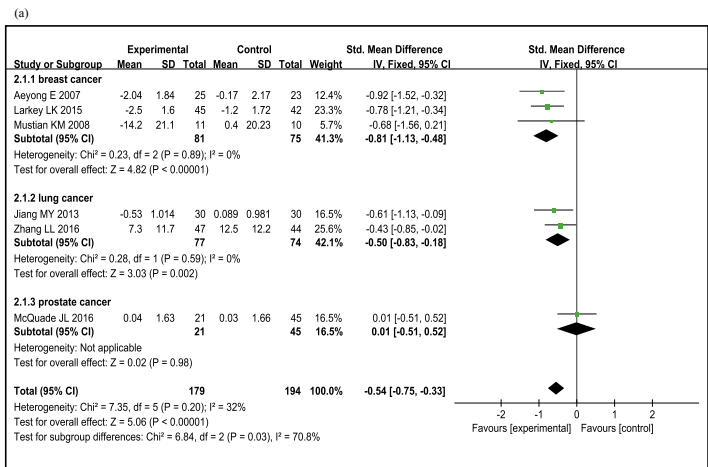


Table 2 Sensitivity analysis of pooled effects in short-term cancer-related fatigue changes

Excluded study	SMD [CI]	Z	p	I ² (%)
Jiang MY 2013 [26]	-0.53 [-0.76, -0.30]	4.51	0.0001	45
Larkey LK 2015 [27]	-0.47 [-0.71, -0.23]	3.85	0.0001	33
McQuade JL 2016 [28]	-0.65 [-0.88, -0.42]	5.55	<0.00001	0
Mustian KM 2008 [21]	-0.54 [-0.75, -0.32]	4.84	<0.00001	45
Zhang LL 2016 [29]	-0.58 [-0.83, -0.34]	4.67	<0.00001	43
Aeyong E 2007 [25]	-0.49 [-0.72, -0.27]	4.27	0.0001	29
None	-0.54 [-0.75, -0.33]	5.06	<0.0001	32

SMD standard mean difference, CI confidence interval

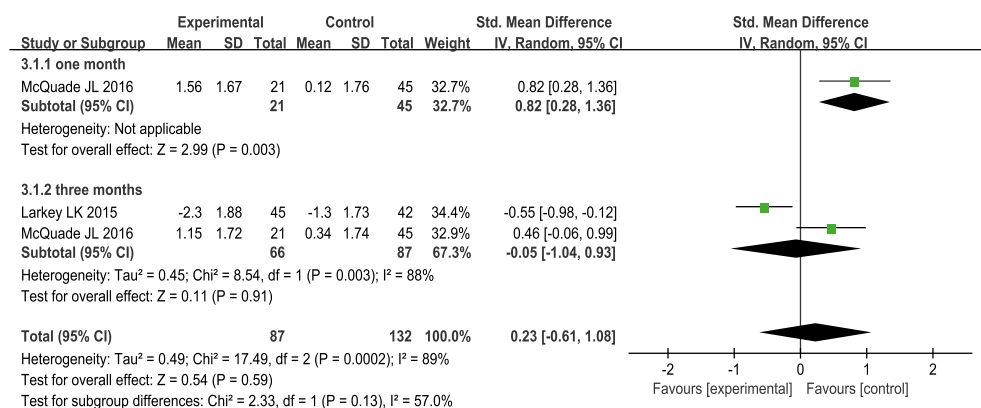
modulation, regulating the HPA axis and reducing some cytokines. This may partially explain the positive results observed among breast and lung cancer patients. However, the single RCT of prostate cancer included in this meta-analysis did not support a benefit for Tai Chi in CRF. In this study, all patients underwent radiotherapy simultaneously with Tai Chi, which may potentiate the existing level of fatigue [50], potentially mitigating the benefit expected with Tai Chi.

The results of the meta-analysis implied that Tai Chi was superior to physical exercise and psychological support in SCRF (SMD = -0.49 and -0.84, respectively; both $p < 0.05$). This is consistent with the theory that Tai Chi can exert both physical and psychological benefits [51, 52]. Tai Chi was not demonstrated to be superior to usual care (SMD = -0.31, $p > 0.05$, $I^2 > 50\%$), which may be ascribed to several factors. The medical treatments used in the usual care arms of the RCTs varied. They were consistent in that they did not adopt Tai Chi, physical exercise, or psychological support, but detailed information on what constituted “usual care” was not disclosed. CRF was scored on a subjective scale, with some of the drugs used (e.g., interferon [53] and modafinil [54]) potentially interfering with a subjective feeling of fatigue. Any drug-related effects that promote “usual care” as favorable in terms of relief from CRF cannot be excluded due to the absence of detail in the

included studies. Potential disease- or symptom-related confounders for CRF such as pain, anemia, nutritional deficits, and sleep disturbance [1] were also seldom assessed in the included studies. Thus, it is unclear whether the patient groups were similar at baseline, which potentially impacts on study findings.

The results suggested that a longer intervention time (> 8 weeks) benefited SCRF more than a shorter intervention time (≤ 8 weeks), with SMD of -0.81 and -0.36, respectively (both $p < 0.05$). However, there was no difference in effect between the subgroups of intervention intensity, classified as the total intervention time per week (test for subgroup differences showed $I^2 = 0\%$). The reason for this may be that both the frequency and duration have an influence on the effect of Tai Chi for SCRF, which is unable to be analyzed as subgroups due to limited sample size. The effect of Tai Chi on LCRF was inconclusive due to the limited sample size ($n = 2$) and inconsistent findings, which meant we were unable to ascertain if a difference in effectiveness existed between 1 and 3 months post-intervention.

Two meta-analyses related to Tai Chi and CRF have already been published. Yu et al. [55] focused on whether Tai Chi could relieve fatigue, with the latter term including CRF as well as fatigue related to age, insomnia, multiple sclerosis, rheumatoid arthritis, and chronic obstructive pulmonary disease. In this meta-analysis, only three

Fig. 4 Comparison of mean LCRF between Tai Chi intervention and control groups

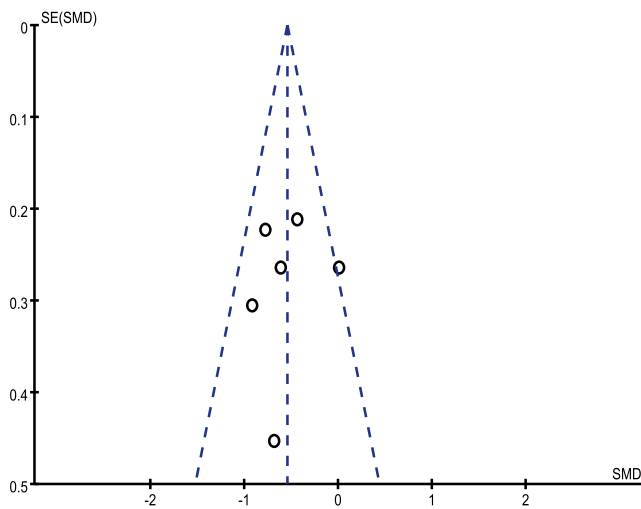


Fig. 5 Funnel plot of short-term cancer-related fatigue changes from the baseline

RCTs [26, 27, 29] of CRF were included. Their results implied a positive effect of Tai Chi on CRF, but subgroup analyses were not conducted. Ma et al. [56] focused on the effect of traditional Chinese exercise on CRF and included two RCTs of Tai Chi [21, 27]. The remaining nine included RCTs involving qigong. The authors did not identify a positive effect of Tai Chi and qigong (synthesized RCT data) on CRF and did not undertake independent analysis of the two Tai Chi RCTs. Therefore, these two meta-analyses only partially investigate the direct effects of Tai Chi on CRF. In our meta-analysis, we narrowed the research theme to the effect of Tai Chi alone on CRF. We also identified more eligible RCTs for conclusion and undertook subgroup analyses to explore efficacy discrepancies in different cancer types and with different Tai Chi duration and intensity. Consequently, our findings are more precise and direct than the two previously published meta-analyses and are more meaningful to clinicians and researchers engaging in CRF management.

Nevertheless, our study has a few limitations. First, the sample size was small, which may impact on the statistical estimates of the effects of Tai Chi on CRF. More RCT studies related to the benefits of Tai Chi for this indication are needed to provide more robust statistical conclusions. There are currently several registered RCTs with a large sample size being underway [57, 58]. The findings of these studies will contribute to a more reliable conclusion about the benefits of Tai Chi in CRF. Also, in our meta-analysis, there was a variation in participant characteristics, tumor grade, and combination therapies between included studies. There may be other unidentified and uncontrolled factors that might have influenced our results.

This meta-analysis was a quantitative summary of former RCTs about the effect of Tai Chi on CRF. This work may

provide a meaningful reference for clinicians because the collated results support the potential clinical applicability of Tai Chi for the short-term management of CRF in breast and lung cancer patients. The findings also suggested that Tai Chi for longer than 8 weeks benefited SCRF more than a briefer intervention period. The long-term effect of Tai Chi is related to patient adherence; thus, appropriate encouragement and supervision are important for follow-up in future studies on long-term benefits. Researchers could also conduct additional evaluations, such as whether Tai Chi alleviates CRF associated with other types of cancer, to establish the optimal intervention intensity and duration.

Conclusions

In conclusion, this meta-analysis demonstrated that Tai Chi has a short-term ameliorative effect on CRF in patients with breast and lung cancer, especially when the intervention is more than 8 weeks. Its beneficial effect may be superior to physical exercise and psychological support. Nevertheless, since the long-term benefits of Tai Chi remain unclear and our meta-analysis has limitations, more detailed studies are needed to confirm our findings. Finally, research is also needed to explore the effectiveness of Tai Chi on CRF in different patient groups including those with other types of cancer and cancers of different severity (tumor grade or cancer stage) and involving different treatment modalities.

Individual author contributions SJ Song and XQ Yue designed this review. SJ Song and JH Yu performed the literature search and data extraction. SJ Song, Y Ruan, and X Liu performed the data analysis. SJ Song, JH Yu, and Y Ruan wrote the initial draft of the paper, and X Liu, LJ Xiu, and XQ Yue contributed to the final draft of the paper and approved the final version of the paper.

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Compliance with ethical standards

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

Appendix 1

Literature search strategy in PubMed:

#1 “Tai Ji” [Mesh]

#2 tai ji or taiji or tai chi or taichi or taijiquan or tai ji quan or tai chi chuan or t'ai chi or tai-ji

#3 #1 or #2
 #4 “Neoplasms” [Mesh]
 #5 cancer or tumor or tumour or carcinoma or neoplasia or neoplasm or malignan*
 #6 #4 or #5
 #7 fatigue or cancer-related fatigue or CRF or chemotherapy-related fatigue or treatment-related fatigue
 #8 “Fatigue” [Mesh]
 #9 apathy or apathetic or lassitude or weakness or lethargy or lethargic or tired or weary or weariness or exhaustion or exhausted or lackluster
 #10 #7 or #8 or #9
 #11 #3 and (#6 or #10)

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