

Massage therapy can effectively relieve cancer pain

A meta-analysis

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Abstract

Background: To critically evaluate the effects of massage therapy on cancer pain.

Methods: Nine Chinese and English databases (PubMed, Cochrane Library, Embase, SCOPUS, Web of Science core, China Biomedical Literature Database, China National Knowledge Infrastructure, Wanfang, and VIP) were systematically searched from the inception of databases to November 2022 for randomized controlled trials. According to Cochrane Collaboration, 2 reviewers independently assessed the risk of bias and extracted data from the included studies. All analyses were performed with Review Manager 5.4.

Results: Thirteen randomized controlled trials were included in the meta-analysis, containing 1000 patients (498 in the massage therapy group and 502 in the control group). Massage therapy could significantly relieve cancer pain in patients (standardized mean difference = -1.16 , 95% confidence interval [-1.39 , -0.93], $P < .00001$), especially those in the perioperative period and those with hematological malignancies. Foot reflexology and hand acupressure had a moderate effect on cancer pain relief, with hand acupressure being more effective. Massage duration of 10 to 30 minutes and a program length of ≥ 1 week had a better effect and could significantly relieve pain. The occurrence of adverse events was reported in 4 of the 13 studies, all of which were no adverse events.

Conclusions: Massage therapy can be used as a complementary alternative therapy to relieve cancer pain in patients with hematological malignancies, breast cancer, and cancers of the digestive system. It is suggested that chemotherapy patients use foot reflexology, and perioperative period patients use hand acupressure. A massage duration of 10 to 30 minutes and a program length of ≥ 1 week is recommended to achieve better effects.

Abbreviations: CI = confidence interval, RCTs = randomized controlled trials, SMD = standardized mean difference.

Keywords: cancer pain, cancer patients, massage therapy, meta-analysis

1. Introduction

According to the data released by the International Agency for Research on Cancer of the World Health Organization, approximately 19.293 million new cancer cases were reported globally in 2020.^[1] With the development of diagnosis and treatment modalities, rehabilitation nursing, and scientific research, the survival rate of cancer patients has improved year by year. However, the quality of life of cancer patients has not significantly improved with the development of technology.^[2] As the fifth vital sign of human beings, pain is one of the most common

and intolerable symptoms of cancer patients, which seriously affects the quality of life of cancer patients.^[3] Studies showed that the incidence of cancer pain was 39% in cancer survivors after treatment, 55% in patients receiving anticancer treatment, and 66% in patients with metastatic cancer or at the end of life.^[4] 40% of patients with cancer pain reported moderate to severe pain, and 69% reported that cancer pain had prevented them from carrying out daily activities.^[5] About 1/3 of patients suffering from cancer pain will develop psychological disorders, such as depression and generalized anxiety disorder.^[6] If cancer pain cannot be controlled timely and effectively, patients'

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comfort will be greatly reduced, which may cause or aggravate anxiety, depression, insomnia, and other symptoms in patients. Moreover, this may significantly affect their daily activities, self-care ability, social interaction, and overall quality of life.^[3] How to manage cancer pain has become a common concern of researchers and clinicians.

The treatment of cancer pain includes etiological, pharmacological, and nonpharmacological approaches. Etiological treatment refers to anticancer treatment targeting the causes of cancer pain, including surgery, radiotherapy, chemotherapy, molecular targeted therapy, and so on, which may reduce or relieve cancer pain to some extent, and these treatments themselves can also cause pain in patients. Pharmacological therapy mainly includes nonsteroidal antiinflammatory drugs, opioids, and adjuvant analgesics. However, these drugs may cause a range of side effects, such as peptic ulcers, platelet dysfunction, impaired liver and kidney function, nausea, vomiting, lethargy, dizziness, and respiratory depression.^[7-9] Therefore, as a noninvasive and relatively nontoxic adjunctive therapy, nonpharmacological treatment is of increasing interest to researchers and clinicians.

Nonpharmacologic treatments in cancer pain management include physical therapies (massage therapy, aromatherapy, transcutaneous electrical nerve stimulation, and acupuncture) and cognitive behavior therapies (relaxation, distraction, and imagery exercises).^[10] Among them, massage therapy can promote relaxation, relieve tension and improve blood circulation by applying physical force to muscles, tendons, and connective tissues at specific sites, thus relieving patients' pain. It has the advantages of easy operation and high safety.^[11-14] It has been hypothesized that the mechanism of massage therapy as analgesia is by inducing local biochemical changes in the soft tissues through descending modulatory circuits, improving oxygenation and blood flow as well as increasing the release of certain hormones associated with analgesia that act as pain receptors, such as oxytocin, vasopressin, adenosine, endorphins, and serotonin (Supplementary Table 1, Supplemental Digital Content, <http://links.lww.com/MD/J91>).^[15] At present, studies on massage therapy intervention for cancer pain have reached a certain number, but some of them have small sample sizes and conflicting findings.^[16-18] In addition, the relationship between the positive effects of massage therapy and factors such as type of cancer, stages of cancer, massage modality, and massage sessions remains unclear. Therefore, the purpose of this study was to critically evaluate the effect of massage therapy on relieving cancer pain and to provide evidence and reference for the application of massage therapy in clinical cancer nursing.

2. Methods

The meta-analysis was performed following the PRISMA 2020 guideline for systematic reviews and meta-analyses.^[19]

2.1. Protocol and registration

This review was registered in the international prospective register of systematic reviews (PROSPERO), the registration number was CRD42023403518.

2.2. Searching strategies

Nine databases, namely PubMed, Cochrane Library, Embase, SCOPUS, Web of Science core, China Biomedical Literature Database, China National Knowledge Infrastructure, Wanfang, and VIP were systematically searched from their inception to November 18, 2022, and relevant randomized controlled trials (RCTs) were retrieved according to the inclusion and exclusion criteria without language restriction. These searches were performed using the following keywords: "neoplasms,"

"cancer," "pain," "massage," and "reflexology." Two reviewers first screened the literature by scanning the titles and abstracts and then read the full texts of potentially eligible trials to decide whether they should be included in the meta-analysis. A third party was invited to render a verdict in the event of a disagreement. The search strategy for the database PubMed is shown in Supplementary Appendix S1, Supplemental Digital Content, <http://links.lww.com/MD/J92> as an example. Additionally, the reference lists of the identified articles were used to further search for potentially relevant studies.

2.3. Inclusion criteria

2.3.1. Participants. Studies on adult patients (≥ 18 years) who were diagnosed with cancer, regardless of gender, race, type of cancer, and stages of cancer.

2.3.2. Interventions and controls. Trials that compared massage therapy intervention with usual care/placebo were included.

2.3.3. Outcomes. Trials that used pain as a primary or secondary outcome and contained extractable pain scores were included.

2.3.4. Study design. Only RCTs were eligible.

2.4. Data extraction

Two reviewers used a predesigned information sheet to extract a range of data independently, including basic study information (authors, year of publication), patient characteristics (sample size, age, gender, type of cancer, stages of cancer, and current treatment), characteristics of the intervention and the control (form, site, duration, frequency, and length of intervention), outcome measures, and adverse events. A third party was invited to make judgement in case of disagreement.

2.5. Risk of bias assessment

Two reviewers independently assessed the risk of bias in the included RCTs using the Cochrane risk of bias assessment tool, which consists of the following 7 domains: adequate sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective reporting, and other bias. Each question can be rated as follows: yes (+), low risk of bias; unclear (?), unclear risk of bias; no (-), high risk of bias.^[19]

2.6. Data analysis

The meta-analysis was conducted by the Review Manager Software (version 5.4). Heterogeneity (variability in the participants, interventions, outcomes, study design, and risk of bias) was assessed first. If moderate clinical heterogeneity was found, subgroup analysis was performed on the pain-related factors in the study. If $P > .1$ and $I^2 < 50\%$, a fixed-effects model was adopted for the analysis due to the homogeneity of the studies; if $P < .1$ and $I^2 \geq 50\%$, then a random-effects model was adopted; if $P < .1$ and the sources of heterogeneity were unknown, a descriptive analysis was conducted without a meta-analysis. For continuous data, the weighted mean difference was determined for the individual trials. The standardized mean difference (SMD) was used if the outcome assessment tools were different.^[19] The effect size between 0.20 and 0.50 was considered a small effect size, 0.50 to 0.80 a medium effect size, and >0.80 a large effect size.^[20] The corresponding point estimates and 95% confidence intervals (CIs) were given for each effect size at $\alpha = 0.05$. 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. Reporting and publication bias were investigated by visually examining the degree of asymmetry of a funnel plot. Use the GRADE system to appraise the quality of evidence in included studies.

3. Results

3.1. Literature search

A total of 2550 records (2547 from database search and 3 from other sources) were identified in the literature search, 1836 of which were left after removing duplicates, and 85 were retrieved by repeatedly reading the title and abstract of the articles. After reading the full texts, 13 RCTs were finally included in the meta-analysis.^[21–33] The process of literature identification and selection is shown in Figure 1.

3.2. Characteristics of the included trials

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

3.2.1. Participants. The 13 trials included a total of 1000 participants whose mean age ranged from 41.47 to 61.40 years. Among the 13 RCTs, 4 were conducted in breast cancer patients,^[23,24,29,32] 3 in patients with hematological malignancies,^[25,28,30] 3 in patients with cancers of the digestive system,^[21,26,31] 2 involving multiple cancer types,^[22,33] and one not mentioning the specific cancer type.^[27] Three of these trials reported the stages of cancer.^[23,26,31] Five trials had participants in the perioperative period,^[21,24,26,27,31] 3 had a treatment status of undergoing chemotherapy,^[22,29,32] while the others had multiple treatment statuses or unreported treatment statuses.

3.2.2. Interventions. All trials used massage therapy, of which 6 adopted foot reflexology,^[21–23,28,30,33] 3 acupuncture

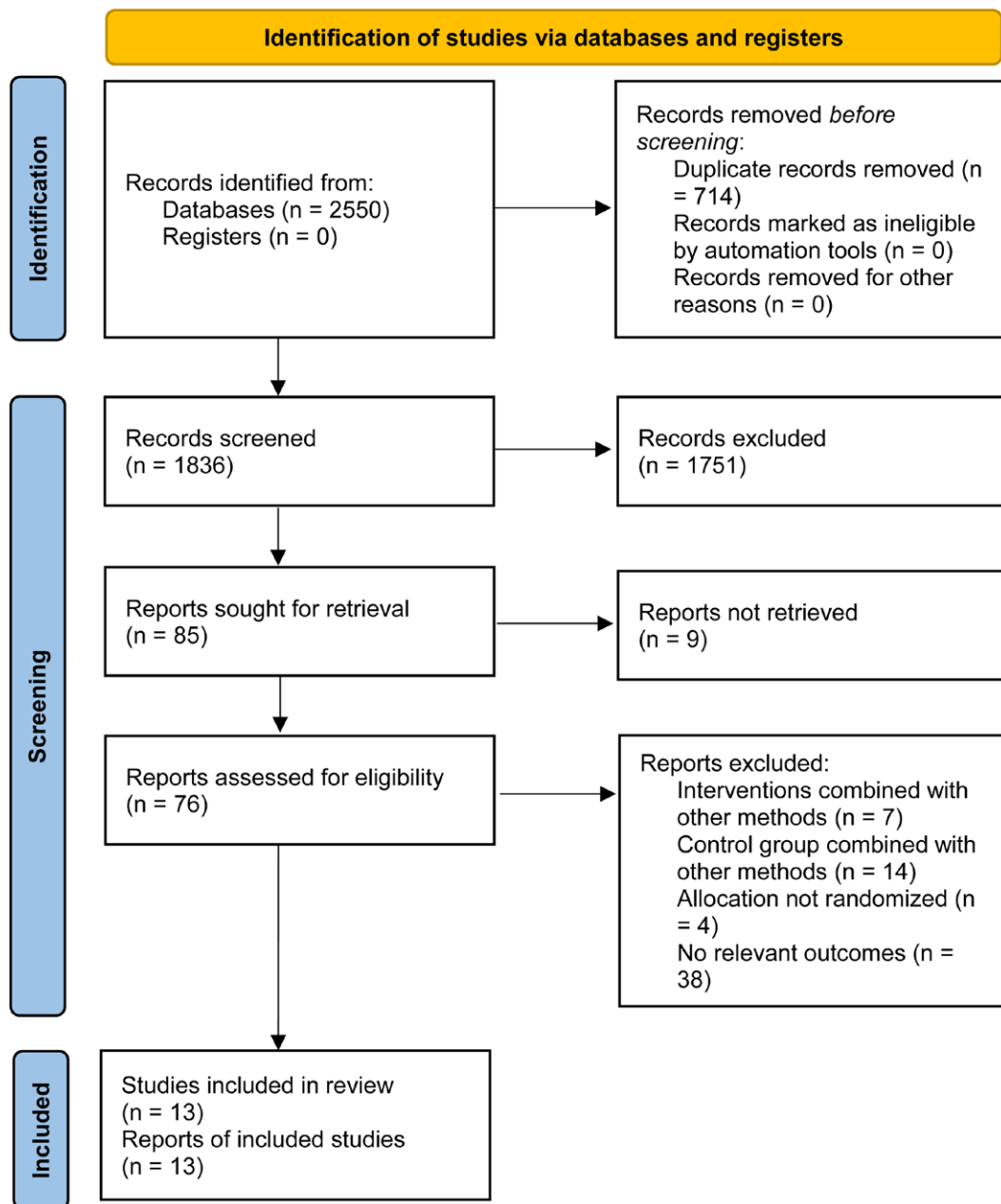


Figure 1. Flow chart of study identification and selection.

Table 1**Studies included in the meta-analysis.**

Author, year	Sample (MG/CG)	Mean age (\pm SD) gender	Cancer type	Cancer stage	Current treatment	Treatment group (intervention form, massage area, duration, frequency, program length)	Control group	Pain scale	Adverse events
Tsay, 2008 ^[21]	30/31	59.80 \pm 14.70 Male 29, female 32	Mixed	NR	Perioperative period	Foot reflexology; digestive reflex zones of upper and lower abdomen, liver, spleen, gall bladder, duodenal, intestine, and colon; 20 minutes; 1 time/day; 3 days	Usual care	SF-MPQ	NR
Tian, 2011 ^[22]	30/30	MG: 58.54 \pm 9.48 Male 21, female 9 CG: 58.50 \pm 7.87 Male 23, female 7	Mixed	NR	Chemotherapy	Foot reflexology; basic reflex area (kidney, superior renal gland, ureter, bladder, celiac plexus) and reflex areas corresponding to a diseased organ or system; 30 minutes; 3 times/day; 6 days	Usual care + take a comfortable position for bed rest; 30 minutes; 3 times/day; 6 days	Changhai Pain Measuring Scale	NR
Gwen, 2012 ^[23]	95/96	MG: 55.30 \pm 9.40 CG: 57.30 \pm 11.80 Female	Breast cancer	III–IV, or I–II with recurrence or metastasis	Chemotherapy, hormone therapy	Foot reflexology; the 9 essential breast cancer-specific reflex areas; 30 minutes; 1 time/week; 4 weeks	Usual care	BPI-SF	None
Zheng, 2015 ^[24]	35/35	NR Female	Breast cancer	NR	Perioperative period	Acupressure massage; Quze, Chize, Neiguan, Shangyang, Jianjing acupoint; 13 minutes; 2 times/day; until the patient is discharged (>7 days)	Usual care	VAS	NR
Hamid, 2017 ^[25]	50/50	MG: 45.80 \pm 6.16 Male 25, female 25 CG: 44.10 \pm 6.33 Male 23, female 27	Leukemia	NR	NR	Acupressure massage; Taichong, Zusanli, Quchi, Hegu; 8 minutes; 3 times/week; 4 weeks	Usual care	VAS	NR
Huang, 2017 ^[26]	30/30	MG: 61.40 \pm 11.32 Male 18, female 12 CG: 59.17 \pm 14.40 Male 16, female 14	Colorectal cancer	I–IV	Perioperative period	Hand acupressure; palmar acupoints (gastrointestinal pain points, spleen points, large intestine points); 54 minutes; 3 times/day; 5 days	Usual care	Abdominal Distension Pain Grading	NR
Moloud, 2017 ^[27]	30/30	56.67 \pm 10.90 NR	NR	NR	Perioperative period	Hand acupressure; LI4 point, HT7 point; 4 minutes; 2 times/day; 1 day	Usual care	VAS	None
Simin, 2018 ^[28]	42/42	MG: 2.500 \pm 15.139 Male 23, female 19 CG: 42.100 \pm 15.766 Male 23, female 19	Hematological malignancies	NR	NR	Foot reflexology; NR; 30 minutes; 1 time/day; 3 days	The placebo method: sole touching	VAS	NR
Nur, 2019 ^[29]	19/21	MG: 44.50 \pm 10.70 CG: 47.00 \pm 9.60 Female	Breast cancer	NR	Chemotherapy	Classical massage sessions; NR; 30 minutes; 1 time/week; 12 weeks	Usual care	S-LANSS	None
Masoume, 2019 ^[30]	36/36	MG: 41.47 \pm 13.70 Male 25, female 11 CG: 46.90 \pm 15.40 Male 27, female 9	Lymphoma	NR	Peri-chemotherapy	Foot reflexology; the thumb toe, under the ball of the foot in the center, the inner and outer edges of the foot, the inner edge of the sole, heel of the ankle; 30 minutes; 1 time/day; 5 days	Usual care	NRS	None
Li, 2020 ^[31]	40/40	MG: 59.63 Male 26, female 14 CG: 61.18 Male 28, female 12	Primary liver cancer	Middle and terminal stage	Perioperative period	Acupressure massage; Taichong, Zusanli, Neiguan; 9 minutes; 2 times/day; 3 days	Usual care	NRS	NR
Zhao, 2021 ^[32]	41/41	MG: 44.15 \pm 1.06 CG: 44.21 \pm 1.08 Female	Breast cancer	NR	Chemotherapy	Tuina therapy; Zhongchong, Jianshi, Neiguan, Tianquan, Daling, Laogong; 20–25 minutes; 1 times/day; 4 weeks	Usual care	Likert-4	NR

(Continued)

Table 1
(Continued)

Author, year	Sample (MG/CG)	Mean age (±SD) gender	Cancer type	Cancer stage	Current treatment	Treatment group (intervention form, massage area, duration, frequency, program length)	Control group	Pain scale	Adverse events
Kristen, 2021 ^[33]	20/20	NR MG: male 9, female 11 CG: male 6, female 14	Mixed	NR	Chemotherapy, radiation therapy, other treatments	Foot reflexology; solar plexus, diaphragm, chest, lungs, esophagus, thyroid, helper to thyroid, pituitary gland, stomach, liver, adrenals and gallbladder; 20–25 minutes; 1 time/day; 1 day	Usual care	VAS	NR

BPI-SF = The Brief Pain Inventory-Short Form, CG = control group, MG = massage group, NR = not reported, NRS = Numerical Rating Scale, SF-MPQ = Short Form of McGill Pain Questionnaire, S-LANSS = Self-Leeds Assessment of Neuropathic Symptoms and Signs, TACE = transcatheter arterial chemoembolization, VAS = visual analog scale.

massage,^[24,25,31] 2 hand acupressure,^[26,27] 1 classical massage therapy,^[29] and 1 Tuina therapy.^[32] The duration of the massage therapy in 3 trials was ≤10 minutes,^[25,27,31] in 4 trials was 10 to 30 minutes,^[21,24,32,33] and in 6 trials was ≥30 minutes.^[22,23,26–28,30,31,33] The length of the massage therapy of 8 trials was < 1 week,^[21,22,26–28,30,31,33] and that of the other 5 trials was ≥ 1 week.^[23–25,29,32]

3.2.3. Controls. Among the 13 studies included in the meta-analysis, the control group in 12 studies received usual care,^[21–27,29–33] and only 1 study used the placebo method.^[28]

3.2.4. Risk of bias in individual studies. The overall and individual risks of bias of the meta-analysis are shown in Figure 2. Nine studies reported the method of random sequence generation and were rated as low-risk,^[21,23–30] 3 unclear risk,^[31–33] and 1 high-risk.^[22] Five studies reported the allocation concealment method^[21,23,26,29,30] while 8 did not.^[22,24,25,27,28,31–33] Because the intervention measures were difficult to conceal, the blinding of participants and personnel was at high risk.^[21–33] Seven studies reported the blinding of outcome assessment,^[21,23,26,27,29,30,33] and the rest were unclear. For other sources of bias, 2 were high-risk,^[25,26] 7 were unclear,^[21,22,24,28,31–33] and the rest were low-risk.

3.3. Analysis of overall effects

Thirteen RCTs^[21–33] reported the pain scores of cancer patients before and after the intervention. The analysis of the changes in pain scores in 13 studies showed that massage therapy intervention could significantly alleviate cancer pain in patients (SMD = -1.16, 95% CI [-1.39, -0.93], *P* < .00001) (Fig. 3), thereby proving the effectiveness of massage therapy as a complementary and alternative therapy for cancer pain. The funnel plot indicated that the publication bias was mild, and the sensitivity analysis revealed that the model was relatively stable. The GRADE system appraised the quality of the outcome indicator “cancer pain” as moderate (Fig. 4).

3.4. Subgroup and sensitivity analysis

3.4.1. Status of treatment. Massage therapy significantly relieved the pain of perioperative patients (SMD = -1.19, 95% CI [-1.67, -0.71], *P* < .00001),^[21,24,26,27,31] and also had a significant effect on patients undergoing chemotherapy (SMD = -0.93, 95% CI [-1.27, -0.60], *P* = .04) (Table 2).^[21,29,32]

3.4.2. Type of cancer. Massage therapy had a significant effect on relieving pain in patients with breast cancer (SMD = -1.01, 95% CI [-1.50, 0.51], *P* < .00001),^[23,24,29,32] a greater effect on pain relief in patients with hematological malignancies (SMD = -1.37, 95% CI [-1.64, -1.10], *P* < .00001),^[25,28,30] and a

moderate effect on patients with cancers of the digestive system (SMD = -0.68, 95% CI [-1.12, -0.25], *P* = .006) (Table 2).^[21,26,31]

3.4.3. Massage modality. There was no statistical difference between acupressure massage and the control group in relieving cancer pain (SMD = -1.69, 95% CI [-1.81, -1.56], *P* = .41),^[24,25,31] foot reflexology had a moderate effect on pain relief in cancer patients (SMD = -0.61, 95% CI [-0.91, -0.32], *P* < .00001),^[21–23,28,30,33] and hand acupressure also had a moderate effect on pain relief in cancer patients with better results (SMD = -0.64, 95% CI [-1.11, -0.17], *P* = .02) (Table 2).^[26,27]

3.4.4. Massage duration. There was no statistical difference between the control group and the massage group in relieving cancer pain when the massage duration was <10 minutes (SMD = -1.62, 95% CI [-1.74, -1.49], *P* = .53),^[25,27,31] while massage with a duration of 10 to 30 minutes could significantly alleviate the pain^[21,24,32,33] (SMD = -1.45, 95% CI [-1.98, -0.91], *P* ≤ .0001) and that with a duration of ≥ 30 minutes had a moderate effect on pain relief in patients (SMD = -0.57, 95% CI [-0.79, -0.35], *P* < .0001) (Table 2).^[22,23,26,28–30]

3.4.5. Program length. Massage therapy with a treatment course of <1 week had a moderate effect on pain relief in cancer patients (SMD = -0.79, 95% CI [-1.04, -0.53], *P* < .0001),^[21,22,26–28,30,31,33] and a treatment course of ≥ 1 week could significantly alleviate the pain in cancer patients (SMD = -1.37, 95% CI [-1.68, -1.06], *P* < .00001) (Table 2).^[23–25,29,32]

3.5. Adverse events

Four studies reported that no adverse events occurred,^[23,27,29,30] while the remaining 9 did not report adverse events (Table 1).

4. Discussions

This meta-analysis of 13 trials showed that massage therapy had a significant effect on relieving cancer pain in patients, which is consistent with previous research findings.^[34,35] However, Pan’s study^[34] only focused on breast cancer patients and did not cover a variety of cancer types, and thus this study could not fully explain the effect of massage therapy on pain in cancer patients. Although the trials included in Boyd’s^[35] study covered a variety of cancer types, it did not conduct subgroup analyses according to the status of treatment, type of cancer, massage modality, massage duration, and program length. After subgroup analyses as per the above variables, the results showed that massage therapy could significantly relieve pain in the perioperative period and in patients undergoing chemotherapy. In terms of cancer type, massage therapy had the best pain relief effect on patients with hematological malignancies, a significant effect on patients with breast cancer, and a moderate effect on

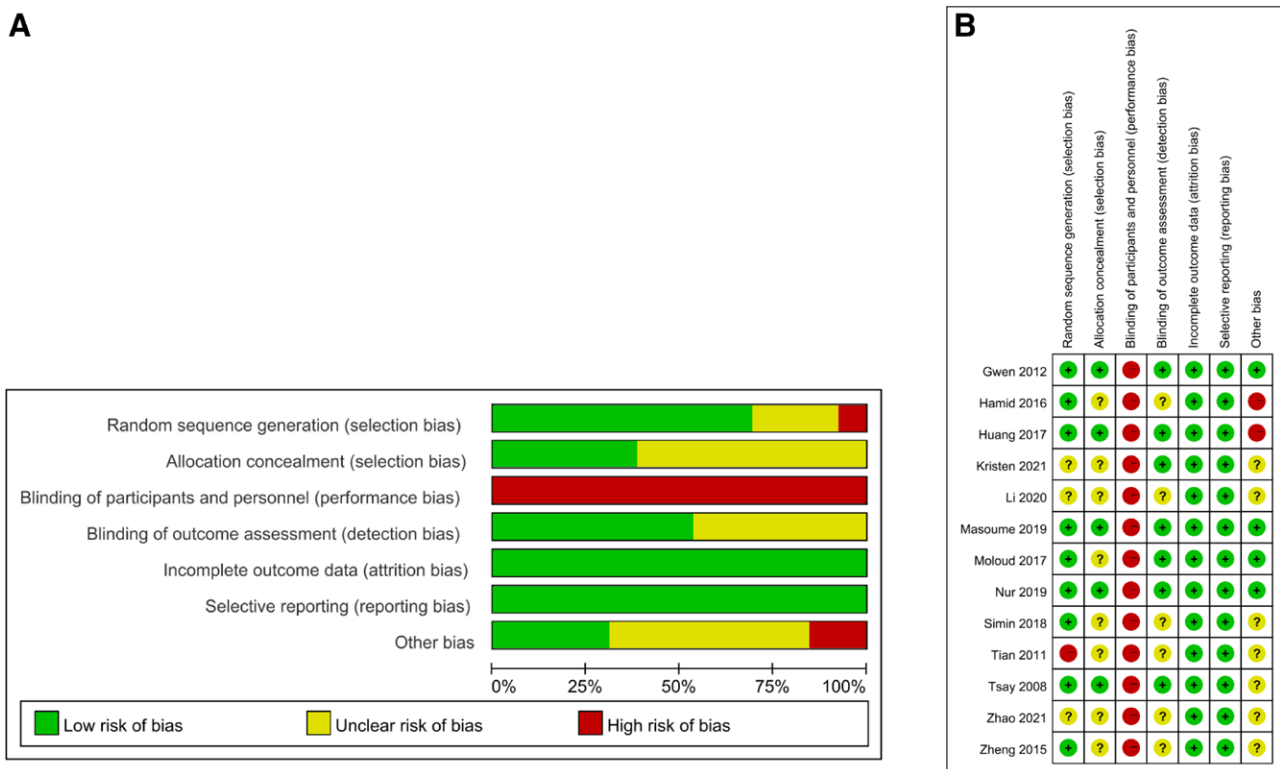


Figure 2. Risk of bias assessment using the Cochrane tool: (A) overall trials; (B) individual trials.

patients with cancers of the digestive system. Foot reflexology had a moderate effect on pain relief in cancer patients, and hand acupressure also had a moderate but better effect. A massage duration of 10 to 30 minutes and a program length of ≥ 1 week could significantly relieve cancer pain.

Difference in the status of treatment and type of cancer may affect the effectiveness of massage therapy in relieving cancer pain. In this meta-analysis, we grouped different cancer treatment statuses in subgroup analysis, and the results showed that massage therapy significantly alleviated the pain in patients undergoing chemotherapy as well as perioperative patients with an even better effect. As a common symptom cluster of adverse reactions in patients undergoing chemotherapy, fatigue, sleep disturbance, and pain are interrelated and affect one another.^[36,37] Studies suggested that massage therapy could stimulate vasoconstrictive nerves, improve systemic venous and lymphatic blood flow, increase local blood micro-circulation, promote body relaxation, and improve patients' sleep quality, thus relieving patients' fatigue and reducing the body's sensitivity to pain,^[38,39] which may be one of the reasons why massage therapy has achieved significant effect in relieving pain in chemotherapy patients. According to Traditional Chinese Medicine, surgery would increase the degree of damage to the patient's blood vessels and cause endogenous stagnation, which is not conducive to the movement of the body's qi, hence the Traditional Chinese Medicine theory "Stagnation results in pain." Massage therapy can dredge the body meridians,^[40] effectively relieving the pain in cancer patients after surgery. Subgroup analysis of cancer types in this meta-analysis showed that massage therapy had a moderate effect on pain relief in patients with cancers of the digestive system, a significant effect on patients with breast cancer, and a greater effect on patients with hematological malignancies. Compared with patients with other cancer types, patients with hematological malignancies have more frequent chemotherapy and longer treatment cycles.^[41-44] Li Xueping^[45] investigated the pain-related symptom clusters in 77 leukemia patients, among which numbness and tingling of hands and feet were reported

most. According to the subgroup analysis conducted in this study, of the 3^[25,28,30] trials in which the subjects were patients with hematological malignancies, 2^[28,30] received foot reflexology therapy. Foot reflexology could reduce tension and stagnation and improve body circulation by stimulating the receptors on the feet, which may help to eliminate neurotoxic compounds in the peripheral nervous system and reduce numbness and tingling of hands and feet.^[30,39] This may be one of the reasons for the obvious pain relief in patients with hematological malignancies. The significant relief of pain in patients with breast cancer might be related to the fact that the included patients were all women, who, due to their own physiological and psychological characteristics, experience greater fluctuations in their perception of stimuli than men during massage,^[46] and may therefore have better massage effects. The application of massage therapy in patients with cancers of the digestive system can dredge collaterals with stomach strength and warm meridians, enabling the spleen qi to be transported and the stomach qi to fall, reducing nausea, vomiting, diarrhea, and insomnia in patients, thus relieving their pain to a certain extent.^[47,48] The above results indicate that, massage therapy, as a complementary alternative treatment to adjuvant pharmacological therapy, can alleviate the pain in patients with hematological malignancies, breast cancer, and cancers of the digestive system.

Massage therapy is a scientific and systematic operation of soft tissues, which increases lymphatic drainage, promotes circulation, and improves muscle metabolism. By increasing parasympathetic activity and reducing sympathetic activity, massage therapy can alleviate patients' pain.^[49,50] An important factor affecting its effectiveness is the massage modality. In this study, the subgroup analysis of different massage modalities showed that foot reflexology had a moderate effect on pain relief in cancer patients, and hand acupressure also had a moderate effect on pain relief with better results, while the effect of acupressure massage on cancer pain showed no statistical difference compared with the control group. According to the trials in subgroup analyses, of the 6 studies on foot reflexology, all 5

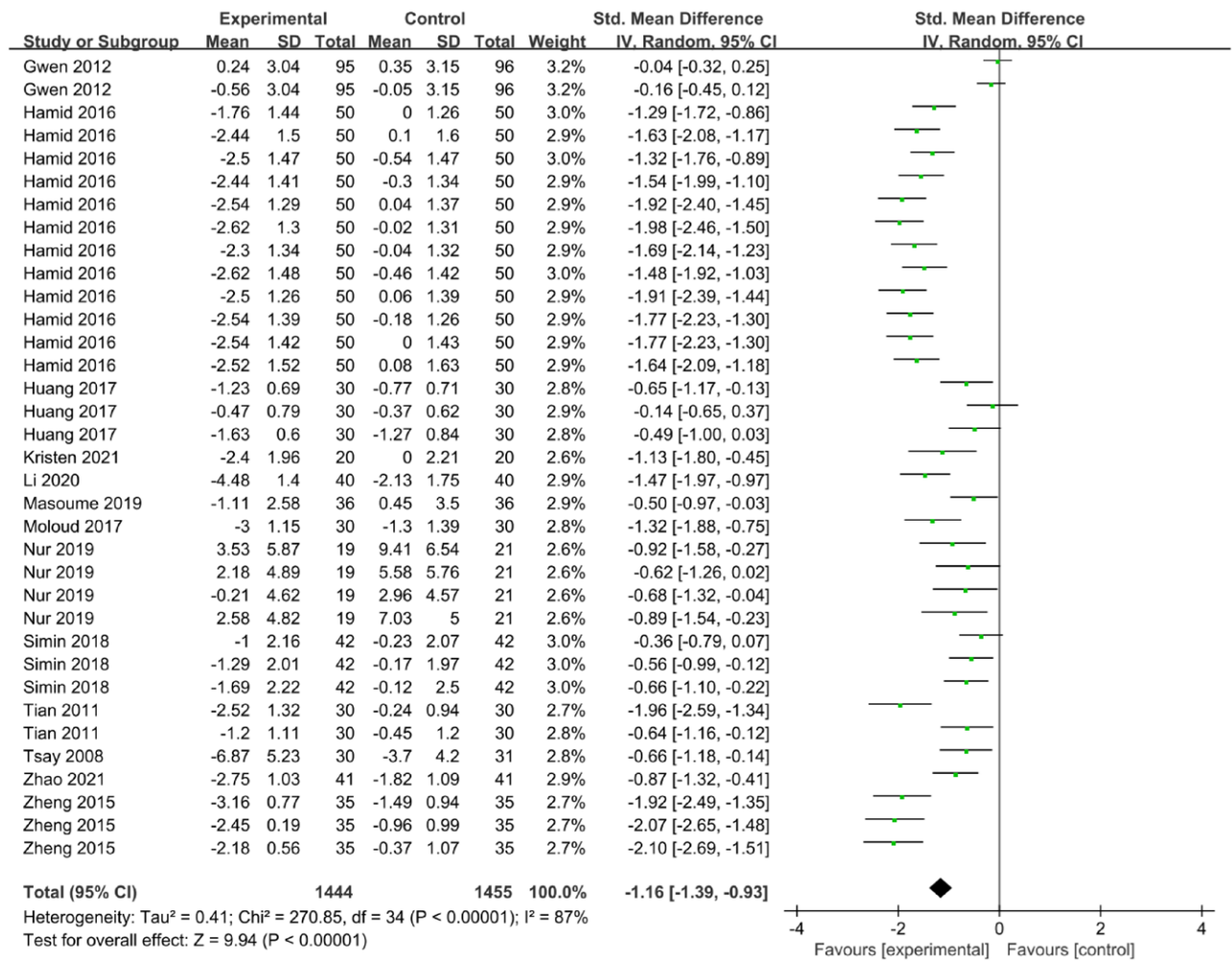


Figure 3. Overall effect of massage therapy on cancer pain.

No of studies	Quality assessment						No of patients		Effect		Quality	Importance
	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Massage therapy	Usual care/placebo method	Relative (95% CI)	Absolute		
13	randomised trials	serious ¹	no serious inconsistency	no serious indirectness	no serious imprecision	none	498	502	-	SMD 1.16 lower (1.39 to 0.93 lower)	⊕⊕⊕O MODERATE	CRITICAL

¹ There are biases in random sequence generation, allocation concealment and blinding of participants and personnel in included studies.

Figure 4. Results of GRADE quality evaluation of evidence in included studies. GRADE = .

studies^[21–23,30,33] selected targeted reflex zones related to cancer pain in the study participants, with the exception of Simin,^[28] who did not specify which foot reflex zones were massaged. In addition, 4^[22,23,30,33] of the 6 studies^[21–23,28,30,33] that used foot reflexology had patients undergoing treatment such as chemotherapy or radiotherapy,^[22,23,30,33] when invasive procedures were generally performed on the patient’s arm or chest wall. Foot reflexology did not involve invasive procedures and did not interfere with the treatment the patient was receiving. The patients were relaxed when receiving the massage, so foot reflexology had a relatively better effect on relieving pain in chemotherapy patients. In the 2 studies on hand acupressure, for patients with gastrointestinal dysfunction after colorectal cancer surgery, Huang^[26] selected the gastrointestinal pain points, spleen points, large intestine points and massaged them. Moloud^[27] massaged Hegu and Shenmen when patients received bone marrow biopsy and aspiration, which not only alleviated pain,^[51] but also relieved tachycardia and hypertension that might be associated with bone marrow biopsy and aspiration.^[52–54] In the 3 acupressure massage trials, Hamid^[25] massaged the Taichong,

Zusanli, Quchi, and Hegu points of leukemia patients. Taichong is mainly used to treat liver qi stagnation and reduce pain transmission in the liver meridian.^[55] Zusanli is mainly used to treat nausea and vomiting.^[56] The combination of Quchi and Hegu is mainly used to treat colds and flu. The above acupressure points were not targeted for relieving pain in leukemia patients. Li^[31] selected 3 acupressure points for massage in patients with liver cancer, of which Taichong could alleviate pain in the liver region, while Zusanli and Neiguan were mainly used to treat nausea and vomiting,^[56,57] and the combined use of the 3 points may have overshadowed the analgesic effect of Taichong to some extent. In Zheng’s^[24] study, researchers selected the Chize, Shangyang, Quze, Neiguan, and Jianjing points for massage. The combination of these points can dredge the meridians in the upper limbs, shoulders, and back, regulate tendons, and relieve pain. However, for postoperative breast cancer patients, the chest incision pain might be more severe than the pain in the arms, shoulders, and back. The acupressure points selected in the above trials on acupressure massage were not well targeted, which might be responsible for the negative results. The

Table 2

Subgroup analyses of massage therapy on cancer pain changes.

Outcome type	k	ES	Sample size		P	Random-effects analysis			
			MC	CG		SMD	95% CI		P
							L	U	
Status of treatment									
Perioperative period	5	9	165	166	86%	-1.19	-1.67	-0.71	<.00001
Chemotherapy	3	7	90	92	55%	-0.93	-1.27	-0.60	.04
Type of cancer									
Breast cancer	4	10	190	193	91%	-1.01	-1.50	-0.51	<.00001
Hematological malignancies	3	16	128	128	82%	-1.37	-1.64	-1.10	<.00001
Cancers of the digestive system	3	5	100	101	73%	-0.68	-1.12	-0.25	.006
Massage modality									
Foot reflexology	6	10	253	255	78%	-0.61	-0.91	-0.32	<.00001
Acupressure massage	3	16	125	125	4%*	-1.68	-1.80	-1.56	.41
Hand acupressure	2	4	60	60	69%	-0.64	-1.11	-0.17	.02
Massage duration									
≤10 min	3	14	120	120	0%*	-1.62	-1.74	-1.49	.53
10–30 min	4	6	126	127	82%	-1.45	-1.98	-0.91	<.0001
≥30 min	6	15	252	255	68%	-0.57	-0.79	-0.35	<.0001
Program length									
<1 week	8	13	258	259	70%	-0.79	-1.04	-0.53	<.0001
≥1 week	5	22	240	243	90%	-1.37	-1.68	-1.06	<.00001

CG = control group, CI = confidence interval, ES = number of effect size, k = number of studies, L = lower, MG = message group, SMD = standardized mean difference effect size, U = upper.

* Applied fixed effect model.

negative effect of acupressure massage on cancer pain may also be related to the small sample size included in this meta-analysis (only 3 studies). Therefore, the results regarding the effect of different massage modalities on relieving cancer pain should be interpreted with caution. In addition, of the 5 studies that used acupressure massage and hand acupressure,^[24–27,31] the participants of 4 studies were in the perioperative period,^[24,26,27,31] whose main source of pain was surgical incision. When acupressure massage was applied at this time, the patients were likely to worry about the massage movements pulling on the surgical incision, which may affect the effect of acupressure massage to some extent. In contrast, hand acupressure was applied far from the surgical incision, and neuroreflexology suggests that stimulation of the corresponding projection points on the hands could produce a direct effect on the cerebral cortex, thereby rapidly regulating the physiological function of the human body.^[26] Therefore, hand acupressure may be more suitable for perioperative cancer patients than acupressure massage.

Massage duration and program length also affected the effect of massage on relieving cancer pain. Subgroup analysis showed that a massage duration of ≤10 minutes had no statistically significant effect on cancer pain relief compared with the control group, while a massage duration of 10 to 30 minutes had a significant effect on cancer pain relief, and a massage duration of ≥30 minutes had a moderate effect. This is consistent with the findings of Hulme,^[58] who found that it was not the case that the longer the massage time, the better the effect but that 17 to 20 minutes of massage can actually produce beneficial results. If the massage duration is too short, the natural analgesics such as endorphins are not yet released, so it is difficult to achieve the desired analgesic effect, which is one of the possible reasons for the negative results in the group with a massage duration of <10 minutes in this study. A subgroup analysis of massage program length showed that a program length of <1 week had a moderate effect on pain relief in cancer patients, and a program length of ≥1 week provided significant cancer pain relief. Therefore, we recommend a massage duration of 10 to 30 minutes and a program length of ≥1 week to achieve better pain relief. In addition, the 4 trials that reported adverse events in this study all reported no occurrence of adverse events,^[23,27,29,30] which may be due to the fact 3 of the 4 trials had excluded high-risk groups

when recruiting study participants.^[27,29,30] Of the other 9 studies that did not report adverse events,^[21,22,24–26,28,31–33] 7 also considered the safety of massage therapy^[21,22,24–26,32,33] when developing their inclusion and exclusion criteria, and included low platelet values, allergies, and the presence of trauma in the massage area in the exclusion criteria for the studies. Although some studies have concluded that massage is a noninvasive operation that is only applied to the body surface and has a low probability of causing complications such as infection or bleeding,^[56] the results regarding the safety of massage therapy should be interpreted with caution in this meta-analysis. In the future, higher-quality studies with larger sample sizes are still needed to verify our findings.

5. Limitations of the current study

Although this meta-analysis provided a comprehensive review of the studies on massage therapy for cancer pain relief, several limitations remain. First of all, the overall quality of the studies included in this meta-analysis was medium, with 3 studies of high quality,^[23,29,30] 7 of medium quality,^[21,24,27,28,31–33] and 3 of low quality,^[22,25,26] and the sample size of 2 studies was <30 cases.^[29,33] The GRADE system appraised the quality of the outcome indicator “cancer pain” as moderate. Secondly, the outcome measurement tools and intervention measures used in the studies were not entirely uniform, which might affect the stability of the results. Thirdly, factors such as the degree of cancer pain and stage of cancer can affect the effect of massage therapy on pain. However, most of the studies included in this meta-analysis^[21–30,32,33] did not report information about these factors, which may also affect the comprehensiveness of the results of this meta-analysis. In future studies, more scientific methodology with larger sample sizes is needed to further elucidate the effects of massage therapy on cancer pain.

6. Conclusions

Massage therapy is effective in relieving cancer pain in patients with hematological malignancies, breast cancer, and cancers of the digestive system. It has significant effects during

chemotherapy and the perioperative period and should be considered as a complementary alternative therapy for pain management in cancer patients. Foot reflexology is recommended for chemotherapy patients and hand acupressure for perioperative patients to achieve better analgesic effects. The massage duration of 10 to 30 minutes has the best effect, and the effect of a massage program length of ≥ 1 week in relieving cancer pain is better than that of < 1 week. More studies with larger sample sizes are needed for future research on the degree of cancer pain, cancer staging, and other aspects.

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