Review Article

Effects of Aromatherapy on Quality Of Life and Pain In Patients With Cancer: A Meta-Analysis



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Abstract

Context. Cancer has become a chronic disease to which new therapeutic approaches are being applied and many patients are interested in the long-term consequences of these approaches. Aromatherapy is one approach that has been used as a safe and comfortable method to alleviate symptoms in patients with cancer, and its effects on various aspects of life have been reported.

Objectives. A systematic review and meta-analysis were conducted to examine the effects of aromatherapy on quality of life (QoL) and pain in patients with cancer.

Methods. Using a comprehensive search strategy, 11 databases were searched from their inception to July 2023 for randomized controlled trials. In the meta-analysis, the standardized mean difference and 95% confidence interval were calculated as effect measures by applying a random effects model.

Results. Fifteen studies met the inclusion criteria. Aromatherapy was found to have favorable effects in improving QoL (Hedges' $\hat{g} = 0.62$, 95% CI: 0.24–1.00), but no statistically significant effect of aromatherapy on pain was found (Hedges' $\hat{g} = -0.46$, 95% CI: -0.99 to 0.07).

Conclusion. The findings indicate statistically significant improvements in QoL when combining aromatherapy and massage, but it was not possible to disentangle the individual effects of each. Considering the characteristics of cancer patients, aromatherapy has beneficial effects as a non-pharmacological method. Further research is needed to investigate the effect of aromatherapy on symptom management, considering factors such as the duration of cancer development and type of cancer. J Pain Symptom Manage 2024;68:e434—e446. © 2024 American Academy of Hospice and Palliative Medicine. Published by Elsevier Inc. All rights are reserved, including those for text and data mining, Al training, and similar technologies.

Key Words

Cancer, aromatherapy, quality of life, pain, meta-analysis

Key Message

Aromatherapy has been employed as a safe and simple approach to relieve symptoms in patients with cancer. We explored the effects of aromatherapy on QoL and pain in patients with cancer. The results suggest that aromatherapy may improve the QoL for cancer patients when combined with massage.

Introduction

Cancer accounts for nearly one in six deaths worldwide. The International Agency for Research on

Cancer predicts that the number of new cases will increase by 36.1% from 19.3 million in 2020 to 30.2 million by 2040.² However, with the development of new drugs and therapeutic approaches, cancer has become a chronic disease.³ Therefore, many patients living with cancer are interested in the long-term consequences of cancer treatment.⁴

Health professionals value improving patients' quality of life (QoL) during the treatment process and regard it as an important health outcome.⁴ QoL is defined as a subjective and dynamic feeling that involves all aspects of life. Overall, QoL was reduced in cancer survivors compared with those without cancer;

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worse outcomes were observed with increasing recency of diagnosis, more advanced stage, and treatment within the last month. OoL is significantly impacted 2 -26 years after cancer diagnosis. 4 QoL is associated with cancer prognosis and has a wide range of physical, psychological, social, and spiritual effects; therefore, it is important to improve patients' QoL after or during treatment. Pain is one of the most distressing symptoms in patients with cancer, and unrelieved pain affects QoL. A systematic review found that the prevalence of pain in patients with cancer was 39.3% after curative treatment, 55.0% during anticancer treatment, and 66.4% in advanced disease, and moderate-tosevere pain was reported in 38.0% of the patients. Despite various cancer treatments, pain remains a common cancer symptom, and effective pain management is still needed. In particular, pain disturbs patients' concentration and thinking, making it difficult for them to perform daily activities. Therefore, adequate pain management may improve health-related QoL.8

Interest in complementary and alternative therapies for cancer treatment and symptom management has emerged, for example, aromatherapy. Aromatherapy involves the use of essential oils extracted from plants such as lavender, jasmine, and geranium. The main molecules in essential oils are inhaled by various methods or absorbed through the skin by massage. Aromatherapy through inhalation works by stimulating olfactory receptors in the olfactory bulb that transmit signals to the limbic system and hypothalamus, which secrete neurotransmitters such as serotonin and dopamine. These neurotransmitters alleviate psychological problems and pain. 9,10 The limbic system includes the amygdala, which is a region associated with pain processes. Odor molecules entering the limbic system can relieve pain by making slight changes to brain activity associated with the pain. Also, changes in breathing pattern related to the inhalation of aroma oil can relieve pain. 11 Aromatherapy massage works on the nervous and immune systems, resulting in mind-body control and emotional effects^{9,12} Lipophilic components of aroma oil change the function of ion channels, carriers, and nerve receptors in response to cell membranes. This explains the sedative effect of aroma oil absorbed into the bloodstream when applied locally through massage.¹¹

In patients with cancer, the effects of aromatherapy in alleviating various symptoms such as pain, sleep problems, anxiety, depression, nausea, and vomiting have been reported. Recent studies have reported that aromatherapy had a positive effect on QoL. However, there are limitations to presenting the effects of individual studies on scientific evidence.

Systematic reviews and meta-analyses integrate and analyze existing research results and provide the most scientific evidence for the effects of aromatherapy in

patients with cancer. Systematic reviews and meta-analyses of the effects of aromatherapy on the QoL of patients with cancer are scarce. Previous systematic reviews and meta-analyses regarding the effectiveness of aromatherapy in patients with cancer reported positive effects on sleep quality, ¹⁶ anxiety, and depression.¹⁷ Although many cancer-related symptoms other than pain negatively affect OoL, pain is a major symptom that must not be overlooked. The need for metaanalyses that include more high-quality studies has been suggested because no significant effect on pain was found in aromatherapy through either inhalation or massage. 18,19 Therefore, the present review aimed to identify the overall effects of aromatherapy on the QoL and pain in patients with cancer. A secondary aim was to investigate the moderating factors for the substantial variations in their effects on QoL. The results of this review provide scientific evidence for the application of interventions to enhance QoL among patients with cancer.

Methods

This review and meta-analysis followed the Cochrane Handbook for Systematic Reviews of Interventions²⁰ and the PRISMA guidelines.²¹ The study protocol was registered in PROSPERO (CRD42023440855).

Eligibility Criteria

The inclusion criteria were as follows: 1) participants: adults aged 18 years and older diagnosed with cancer, either undergoing or having completed treatment; 2) interventions: aromatherapy performed using essential oils through various application methods; 3) comparisons: placebo, no intervention, routine care, usual care, and standard care; 4) outcomes: QOL and pain; and 5) study design: randomized controlled trial. The exclusion criteria were as follows: 1) studies with essential missing data necessary for meta-analysis; 2) studies without a control group; and 3) studies combining aromatherapy interventions with other interventions in the experimental group.

Information Sources and Search Strategies

We conducted a comprehensive database search from their inception until July 31, 2023. International databases included PubMed, MEDLINE, Web of Science, Embase, CINAHL, Cochrane Library, and PsycINFO. Domestic (Korean) databases included the National Digital Science Library (NDSL), Research Information Sharing Service (RISS), KoreaMed, and Korean Studies Information Service System (KISS).

The main search terms were "cancer," "aromatherapy," "pain," and "quality of life." The search strategy was developed using various terms, including MeSH

(Medical Subject Headings), synonyms, Emtree (Embase subject headings), and free-text terms. Boolean logical operators ("AND," "OR") were employed. The search strategy is provided in Appendix A. Additionally, we checked relevant previous studies' references and conducted searches on Google Scholar and grey literature without restricting publication year and language, aiming to retrieve all relevant papers.

Study Selection

Duplicate studies were removed from the retrieved data. Two reviewers (M.K. & Y.L.) independently examined the titles and abstracts, selected studies that met the inclusion criteria, and then thoroughly reviewed the full texts of the selected studies to determine which studies to include in the final analysis. Where opinions conflicted, a consensus was reached through discussion. If agreement could not be reached, a third researcher (H.K.) joined the discussion to reach a consensus.

Data Extraction

A data extraction table was developed and two reviewers independently performed the data extraction. The extracted data included the following: general characteristics (first author, publication year, country, study design, participants, and sample size); intervention characteristics (route of administration, type of essential oils, sessions, session length, duration, and follow-up); control group; and outcome (instrument).

Risk of Bias Assessment

Two reviewers (M.K. & Y.L.) independently assessed the risk of bias in the selected studies using the Cochrane risk-of-bias tool 2.0 (RoB2) for randomized controlled trials.²² Five domains (randomization process, deviations from intended interventions, missing outcome data, measurement of the outcome, and selection of the reported results) were evaluated based on predefined criteria. The overall bias was assessed as "low risk," "some concerns," or "high risk" based on evaluations in each domain. In the case of disagreements between the reviewers, discussions were held to reach a consensus. If no consensus was reached, a third researcher (H.K.) joined the discussion to resolve any disagreements.

Synthesis and Statistical Analysis

Data analysis was conducted using the R package Meta version 4.0.3 (R Foundation for Statistical Computing, Vienna, Austria).²³ Given the methodological heterogeneity anticipated owing to the inclusion of various studies, DerSimonian-Laird random-effect models²⁴ were chosen. The standardized mean difference (SMD; Hedges' ĝ) was calculated to estimate the

average effect size, and statistical significance was confirmed through a 95% confidence interval. Effect sizes were interpreted as follows: small, $0.2 \le SMD < 0.5$; moderate, $0.5 \le SMD < 0.8$; large, $SMD \ge 0.8$. Heterogeneity was assessed using I2 statistics, where I2 values were interpreted as follows: 0%-40% (might not be important), 30%-60% (may represent moderate heterogeneity), 50%–90% (may represent substantial heterogeneity), and 75%-100% (considerable heterogeneity).²¹ A preplanned subgroup analysis was conducted to explore the sources of heterogeneity. The route of administration and type of essential oil were subjected to subgroup analysis and meta-analysis of variance (ANOVA). The sessions and duration of the intervention were subjected to meta-regression. Additionally, publication bias was assessed through the visual inspection of funnel plots and Egger's regression test, and a sensitivity analysis was performed.

Results

Study Selection

A total of 2320 articles were initially identified; after removing 635 duplicate articles, 1,685 articles remained. Following primary screening of titles and abstracts, 1643 articles were excluded, leaving 42. After excluding two reports that could not be retrieved, the full texts of the remaining 40 articles were reviewed. Among these, 31 articles were excluded for various reasons (see Fig. 1). Thus, nine articles were included in the analysis. A subsequent manual search identified a further 11 articles, six of which were included in the analysis. A total of 15 articles (nine from the database search and six from the manual search) were included in the final analysis (Fig. 1).

Study Characteristics

This systematic review and meta-analysis included 15 studies (see Table 1). QoL was analyzed in 13 comparisons from 12 studies, and pain was analyzed in eight studies involving nine RCTs. Except for one study, all the others were published after 2000. The countries of origin included the United Kingdom (n = 5), Korea (n = 2), Malaysia (n = 2), the United States (n = 2), China (n = 2), Turkey (n = 1), and Egypt (n = 1). The participants in the eight pain-related studies were predominantly patients with breast cancer. The sample size of QoL-related studies included 444 participants in the experimental groups and 466 in the control groups, totaling 910 individuals. The sample size of the pain-related studies included 374 participants in the experimental groups and 379 in the control group, totaling 753 individuals.

In terms of QoL, massage aromatherapy was the most common route of administration (eight studies)

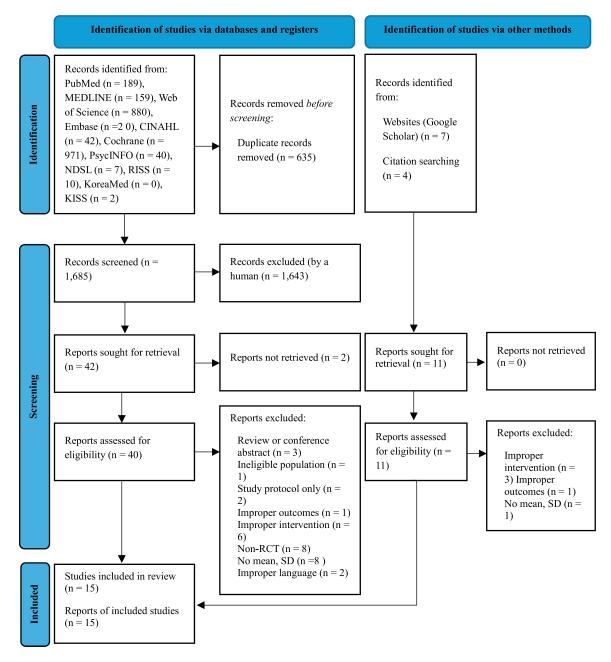


Fig. 1. Flowchart summarizing the process of study selection.

followed by inhalation aromatherapy (three studies), while oral administration or topical application were used in the remaining two studies. Seven studies used single oils. The remaining six studies combined various oils. Intervention sessions varied from 1 to 210 sessions, with session lengths ranging from 1 to 60 minutes per session; three studies did not report the session length. The total duration of the sessions ranged from one day to 10 weeks, with the majority lasting more than three weeks. The control groups included four studies that used a placebo, and four studies with no intervention. Other control groups included standard, routine, conventional, or usual care. The European Organization for Research and Treatment of Cancer quality of life

questionnaire-30 (EORTC QLQ-C30) was the most commonly used measurement tool (three studies).

Regarding pain, there were four studies on massage aromatherapy, three on inhalation aromatherapy, and one on dietary administration. Mixed oils were used in four studies and the other four used single oils (lavender in two studies, coconut, and ginger). The intervention sessions ranged from 2 to 56 sessions; one study reported this information imprecisely. The length of a single session varied from 1 to 60 minutes, with one study not reporting this information. The total duration of the sessions ranged from one day to six weeks. The control groups included three studies with placebo, three with usual care, and three with no

 ${\it Table~1} \\ {\it Characteristics~of~the~Included~Studies}$

No.	First author	Study Design	Participants /Sample Size R = E:C; A = E:C	Intervention (Route of Administration/ Essential oils)	Comparator	Outcome (Instrument)	Sessions (Length)	Duration	Follow Up
1	Clemo-Crosby ²⁶	RCT, single blind	Patients with breast cancer/ R = 135:149; A = 110:106	Massage (lavender and bergamot)	Usual care	Pain (EORTC QLQ-C30)	6 (60 min)	6 weeks	6 weeks
2	Halm ²⁷	RCT	Patients undergoing radiotherapy for breast cancer	Topical application (helichrysum, frankincense, lavender, Geranium)	Standard care	QOL (QLI)	210 (NR)	10 weeks	10 weeks
3	Deng ²⁸	RCT	Breast cancer during perioperative periods/ R = 40:40 A = 40:40	Inhalation (3 drops of essential oil (lavender: bergamot: geranium=1:2:3) on sterile sponge)	Usual care	Pain (VAS)	2 (30 min)	1 day	4 hours after tracheal extubation
4	Khamis ¹⁴	RCT	Participants with second or third stage cancer	Massage (5 mL of lavender oil)	No intervention	QOL (RSCL)	6 (30 min)	2 weeks	2 months
5	Lai ²⁹	RCT	Patients suffering with advanced cancer	Massage (bitter orange, black pepper, rosemary, majoram and patchouli in olive)	No intervention	QOL (MQOL-HK)	5 (15–20 min)	5 days	5 days
6	Law ³⁰	RCT	Patients with breast cancer/ R = 30:30 A = 30:30	Dietary (virgin coconut oil 10 ml)	No intervention	►QOL (EORTC QLQ-C30) ►Pain (EORTC QLQ-C30)	56 (NR)	4 weeks	6th chemotherapy cycle
7	Lua ³¹	RCT, single blind cross over	Patients with breast cancer undergoing chemotherapy/ R = 38:37; A = 30:30	Inhalation (two drops of ginger oil)	Placebo (Fragrance matched artificial placebo)	PQOL (EORTC QLQ-C30) Pain (EORTC QLQ-C30)	15 (2 min)	5 days	8 days
8	Ovayolu ¹⁵	RCT	Patient with breast cancer/ R = 70:70 A = 70:70	1) Inhalation (lavender, mint, chamomile, jasmine, violet, rosemary, and eucalyptus blended in proportions of 2:2:2:1:1:1:1)	Routine care	QOL (Quality of life scale)	12 (5 min)	4 weeks	6weeks
				2) Massage (same oils in inhalation)			12 (35 min)	4 weeks	6 weeks

Table 1
Continued

No.	First author	Study Design	Participants /Sample Size R = E:C; A = E:C	Intervention (Route of Administration/ Essential oils)	Comparator	Outcome (Instrument)	Sessions (Length)	Duration	Follow Up
9	Shammas ³²	RCT, single blind	Patients with breast cancer/ R = 29:29 A = 27:22	Inhalation (4 drops of lavender oil)	Placebo (coconut oil)	Pain (VAS)	NR (one min before operation, every two hours during operation and every four hours during 12 hours)	5 days	5 days
10	Soden ³³	RCT	Patients with various type of cancer/ R = 16:13 A = 10:13	Massage (lavender oil in sweet almond oil)	Placebo (carrier oil) No intervention	►QOL (RSCL) ►Pain (VAS)	4 (30 min)	4 weeks	4 weeks
11	Sohn ³⁴	RCT	Patients with breast cancer/ R = 15:17 R = 15:17	Massage (0.7 mL of 4% blended oils) (frankincense: bergamot: lavender = 1:1:2)	No intervention	Pain (KCPAT)	28 (1 min)	2 weeks	2 weeks
12	Wilcock ³⁵	RCT	Cancer patients with palliative care R = 23:23 A = 11:18	Massage (1% lavender and chamomile in sweet almond carrier oil)	Conventional day care	QOL (MYMOP)	4 (30 min)	4 weeks	4 weeks
13	Wilkinson ³⁶	RCT	Patients with various type of cancer/ R = 46:57 A = 43:44	Massage (Roman chamomile oils)	Placebo (sweet almond carrier oil)	QOL (RSCL)	3 (NR)	3 weeks	3 weeks
14	Wilkinson ³⁷	RCT	Patients with various type of cancer/ R = 144:144 A = 106:115	Massage (20 essential oils)	Usual supportive care alone	►QOL (EORTC QLQ-C30) ►Pain (EORTC QLQ-C30)	4 (60 min)	4 weeks	6 weeks post randomization 10 weeks post randomization
15	Yu ³⁸	RCT	Patients with colorectal cancer/ R = 22:22 A = 18:19	Inhalation (1 ml 1% lavender)	Placebo (almond oil)	QOL (6-point scale)	1 (20 min)	1 day	Post intervention

Note. A = analyzed; C = control group; E = experimental group; EORTC QLQ-30 = european organization for research and treatment of cancer quality of life questionnaire; KCPAT = Korean cancer pain assessment tool; MQOL-HK = McGill quality of life for Hong Kong Chinese; MYMOP = measure yourself medical outcome profile; NR-not reported; QLI = quality of life index; R = randomized; RCT = randomized controlled trial; RSCL = rotterdam symptom checklist; UK = United Kingdom; USA = United States of America; VAS = visual analog scale.

Study	Randomization process	Deviations from intended interventions	Missing outcome data	Measurement of the outcome	Selection of the reported result	Overall
Clemo-Crosby (2018)	+	•	+	?	•	?
Deng (2022)	•	•	+	?	•	?
Halm (2014)	•	•	+	?	•	?
Khamis (2023)	?	•	+	?	•	?
Lai (2011)	?	1	2	?	•	(2)
Law (2014)	•	•	+	?	•	?
Lua (2015	•	•	•	•	•	•
Ovayolu (2014)	2	•	+	?	•	(2)
Shammas (2021)	?	•	+	•	•	?
Soden (2004)	•	•	•	?	•	?
Son (2005)	2	•	•	?	•	1
Wilcock (2004)	•	•	2	?	•	(1)
Wilkinson (1999)	•	-	•	•	•	•
Wilkinson (2007)	•	•	+	?	•	?
Yu (2017)	•	•	+	•	•	•
+ Low risk	? Some con	cerns	High risk			

Fig. 2. Risk-of-bias summary according to the revised Cochrane risk-of-bias tool for randomized trials (ROB 2).

intervention. The most commonly used measurement tool was the EORTC QLQ-C30 (four studies).

Risk of Bias

Regarding overall risk of bias, three of the 15 reviewed studies were judged as "low" risk, eight as "some concerns," and four as "high risk." Three studies were rated as having "some concerns" because of insufficient information on the random allocation sequence or concealment of the allocation sequence until the participants were enrolled and assigned to the intervention group. Both issues were present in two studies, leading to a "high risk" rating. Regarding deviations from intended interventions, in two studies, participants and carers delivering the interventions were aware of the intervention group during the trial, and appropriate analysis to estimate the effect of adhering to

intervention was not used, with unanalyzed outcomes having a significant impact, resulting in a "high risk" rating. In terms of missing outcome data, there was no evidence that the results were biased by missing outcome data, and the missingness in the outcome could depend on its true value, leading to a "high risk" rating in the two studies. In terms of outcome measurement, 11 studies had outcome assessors who were aware of the interventions received by participants, but this was not likely to have a substantial impact, resulting in a rating of "some concerns." Selection of the reported result was assessed as "low" for all studies (Fig. 2).

Effects of Aromatherapy on QoL

The evaluation of the effect of aromatherapy on QoL in patients with cancer revealed a moderate effect size (SMD = 0.62, 95% CI: 0.24–1.00) (Fig. 3). There

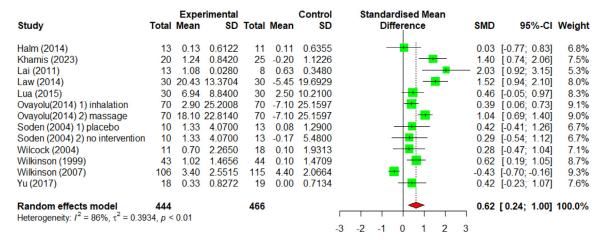


Fig. 3. Forest plots: effect of aromatherapy on QoL.

Table 2
Moderator Analysis

Categorical Moderators	Number of Trials	SMD (Hedges' ĝ)	95% CI	I^2	Between Groups	
					Q _b (df)	P
Route of administration						
Massage	8	0.65	0.12; 1.87	89.7	6.88(2)	0.032
Inhalation	3	0.42	-0.40; 1.25	0.0		
Others	2	1.00	-0.24; 1.89	88.5		
Type of essential oil						
Single oil	7	0.74	0.23; 1.25	59.5	0.52(1)	0.469
Mixed oils	6	0.46	-0.07; 1.10	90.9		
Continuous moderators	k	QM (df)	P	b	Z	\mathbb{R}^2
Total intervention session	13	0.17 (1)	0.675	-0.001	2.985	8.82
Duration of intervention	13	78.55 (1)	0.233	-0.105	2.679	0.02

Note. CI = confidence interval; df = degree of freedom; Q_b = between groups; QM = Q moderator.

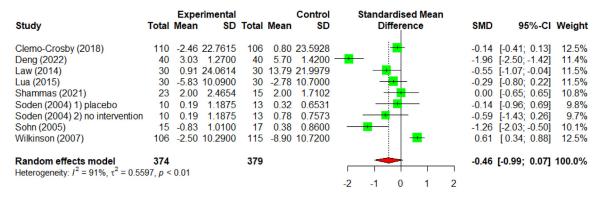


Fig. 4. Forest plots: effect of aromatherapy on pain.

was considerable heterogeneity, with an I^2 of 86% (P < 0.01).

In the route of administration subgroup analysis, massage aromatherapy (SMD = 0.65, 95% CI: 0.12 to 1.87, $I^2 = 89.7\%$) was effective in improving the QoL of patients with cancer, while inhalation aromatherapy and other methods were not statistically significant. The meta-ANOVA also indicated a statistically significant difference between groups (P = 0.032) (Table 2).

In the type of essential oil subgroup analysis, single oils (SMD = 0.74, 95% CI: 0.23, 1.25, I^2 = 59.5%) were effective in improving the QoL of patients with cancer, whereas mixed oils were not statistically significant (SMD = 0.46, 95% CI: -0.07, 1.10). The meta-ANOVA results also indicated no statistically significant differences between groups (P= 0.049).

To explore possible sources of heterogeneity, a moderator analysis was conducted on the continuous moderator, the total sessions. The total number of intervention sessions (QM = 0.17, df = 1, P = 0.675) and intervention duration (QM = 78.655, df = 1, P = 0.233) did not appear to be statistically significant moderators.

Effects of Aromatherapy on Pain

The additional outcome of our study, the effect of aromatherapy on pain, showed no statistically significant effect (SMD = -0.46, 95% CI: -0.99 to 0.07) (Fig. 4).

Publication Bias

To assess publication bias in the QoL studies, we initially conducted a visual inspection of asymmetry using a funnel plot (Fig. 5). Although there was no apparent visual asymmetry, Egger's regression test was performed for a more precise analysis, and the results indicated no statistically significant differences (t = 1.753, P = 0.107). Owing to the limited number of pain studies, a publication bias analysis was not conducted.

Sensitivity Analysis

Prior to conducting a sensitivity analysis for the QoL studies, we identified the studies that had the greatest influence on the overall effect size through a Baujat plot (Fig. 6A). The results indicated that Wilkinson et al. The had the most significant impact on the overall effect size. After removing this study, the SMD was 0.72 (95% CI: 0.44–1.00) (Fig. 6B). However, this did not substantially differ from the overall effect size. After systematically removing other studies, the overall effect size remained relatively stable. Therefore, the effect of aromatherapy on the QoL of patients with cancer can be considered reliable.

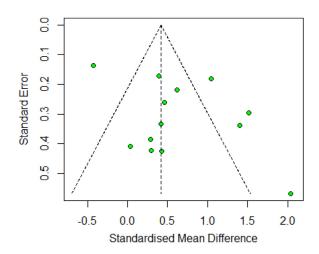


Fig. 5. Funnel plot for the relationship between aromatherapy and QoL.

Discussion

Interpretation of results and comparison with previous studies

Complementary therapies such as aromatherapy are becoming increasingly common in palliative care and cancer treatment units.³⁹ Therefore, this study examined the effectiveness of aromatherapy in improving the QoL and reducing pain in patients with cancer.

Regarding the effect of aromatherapy on QoL, the results revealed a moderate effect size that was slightly higher than that reported in previous studies ¹⁸ Many studies now advocate using aromatherapy to enhance QoL among patients with cancer ²⁸ This study's result was consistent with previous research which indicated that aromatherapy improved QoL and patient satisfaction. ³¹ Aromatherapy has been shown to improve various physical and psychological complications ⁴¹ among patients with cancer, indicating its effectiveness in

enhancing QoL. Our study provided evidence for the application of aromatherapy to enhance the QoL of patients with cancer. QoL in cancer patients should also be recognized as an overall health outcome across psychosocial and spiritual aspects. Furthermore, as cancer has recently become a chronic condition,³ efforts to improve the QoL of patients with cancer over extended periods of time are necessary. Therefore, the results of this study are encouraging and suggest aromatherapy's therapeutic potential.

However, the results showed considerable heterogeneity, and we attempted to identify its cause. In the route of administration subgroup analysis, massage was effective in enhancing QoL while other methods showed no significant effects. Therefore, aromatherapy combined with massage has a major effect on the QoL of patients with cancer. Massage therapy is often relaxing and enjoyable for individuals experiencing various types of pain. In addition to the physical benefits of aromatherapy, pleasant scents may contribute substantially to patient satisfaction ⁴⁰ Additionally, massage has been shown to be effective in reducing symptoms and improving the QoL of patients with cancer⁴² A previous study showed that aromatherapy massage had a more pronounced effect on improving QoL among patients with breast cancer than massage alone. 15 However, this result only showed that interventions combining aromatherapy with massage had a significant effect on QoL. It is difficult to determine the individual effects of aromatherapy versus massage and it remains unclear whether the observed results are solely attributable to aromatherapy or if they are the result of the synergistic effects of both massage and aromatherapy. Nevertheless, as aromatherapy massage has been found to be more effective than aromatherapy inhalation, it is necessary to consider this when developing strategies to enhance the QoL of patients with breast cancer.

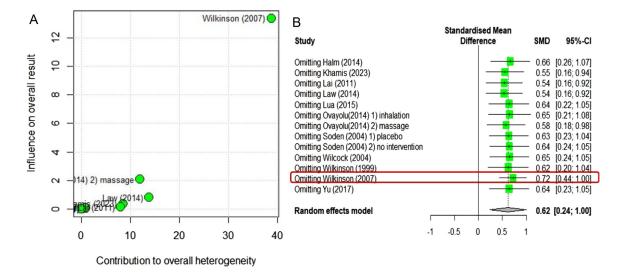


Fig. 6. a) Baujat plot (QoL). b) Forest plot of sensitivity analysis (QoL).

However, since the number of studies involving aromatherapy inhalation was limited in the subgroup analysis, additional analyses with more studies are needed to obtain more reliable results.

Conversely, our review found that the number of sessions and intervention length were not statistically significant moderators. This is consistent with findings from previous meta-analyses on the effects of aromatherapy on anxiety⁴³ and the nausea and vomiting symptoms⁴⁴ of patients with cancer. However, the variation in the number of sessions and length of intervention across each study in our study was substantial. Some studies had shorter interventions with more sessions, ^{31,34} while others had longer interventions with fewer sessions. ^{35,37} Therefore, drawing conclusions that number of sessions and length of intervention did not influence the effect of aromatherapy is challenging. To obtain more reliable results, further research including a larger number of studies is necessary.

Aromatherapy had no significant impact on alleviating pain in patients with cancer. This result is similar to some previous studies that found no significant difference between the aromatherapy and control groups, 18,19 whereas Corasaniti et al. 45 demonstrated the effectiveness of aromatherapy in reducing the intensity of cancerrelated pain. Some researchers have proposed that olfactory stimulation through aromatherapy may lead to an immediate reduction in pain.46 Lakhan et al.40 found that aromatherapy can be effective in treating pain in a variety of medical conditions. The reason for these contrasting results is unclear; however, a probable explanation is that cancer-related pain is complex and distinct. Many patients describe cancer-related pain as a distressing or intolerable aspect of their cancer;⁴⁷ in one study, 38.0% of the participants reported moderate to severe pain, and 51.9% had advanced, metastatic, or terminal disease⁷ As such, cancer-related pain is chronic and severe compared with other conditions. However, we did not restrict inclusion criteria to patients meeting a minimum level of pain when selecting studies that measured pain, so it may be inferred that aromatherapy had no statistically significant effect on cancer pain in this metaanalysis. Nevertheless, successful management of diverse types of cancer pain requires an approach that combines both pharmacological and nonpharmacological treatments and includes immediate relief of acute pain to prevent the development of chronic pain. 48 Therefore, it is necessary to investigate the impact of cancer pain on the characteristics related to pain in patients with cancer, such as the duration of cancer development and the type of cancer.

Strengths and limitations

Our results show that aromatherapy is effective in improving the QoL of patients with cancer, providing health professionals with safe additional treatment options that may alleviate cancer-related symptoms without additional medications.

We synthesized only RCTs with a reasonable design and appropriate methods to confirm our findings and ensure study quality, whereas other studies included nonrandomized controlled trials or had a very limited dataset.

This study included RCTs published until 2023 without limiting the scope to specific aromatherapy types. Our study thus differs from previous studies in several respects. This study is significant in that it demonstrates the effects of aromatherapy based on specific intervention methods, types of oils, session durations, and overall intervention periods, providing a basis for future research in aromatherapy interventions.

However, this study has several limitations. First, although the sample size was larger than that of other systematic reviews, there is insufficient literature available to conduct a meta-analysis in which all variables can be adequately controlled for. We believe that meaningful results can be obtained in meta-analyses when a sufficient number of studies are available. Therefore, additional studies would enable a multifaceted analysis of the effects of aromatherapy on various symptoms in patients with cancer.

Second, the critical problem for these primary RCTs of aromatherapy was the low quality and small sample size, and three studies were associated with a high risk of bias. We believe that the evidence levels for each aromatherapy RTC were low or moderate owing to the high risk of bias in primary studies; therefore, large, well-designed RCTs should be conducted in future to confirm the conclusions of the available meta-analyses. Additionally, we only searched Korean and English literature; therefore, we may have missed publications in other languages.

Lastly, owing to the limited number of studies, the generalizability of the results from subgroup analysis is restricted. Therefore, adding high-quality studies in the future for additional analysis would yield more reliable results.

Conclusions

This study indicated that aromatherapy improved the QoL of patients with cancer, which suggests that aromatherapy has beneficial effects as a non-pharmacological treatment. However, the study did not reveal any significant effects on pain alleviation. Aromatherapy is a simple and easily performed intervention suitable for patients with cancer undergoing treatment; however, the mechanism of aromatherapy for pain is yet to be fully understood. Therefore, further research is needed to confirm the effects of aromatherapy on pain management. Furthermore, characteristics related to pain in patients with cancer, such as the duration of cancer development and the specific type of cancer, need to be examined.

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Appendix A. Search strategy

- 1. Synonyms
- 1) Cancer
 - Tumor
 - Neoplasm
 - Tumors
 - Neoplasia
 - Neoplasias
 - Cancer
 - Cancers
 - Malignant Neoplasm
 - Malignancy
 - Malignancies
 - Malignant Neoplasms
 - Neoplasm, Malignant
 - Benign Neoplasms
 - Benign Neoplasm

2) Aromatherapy

- Aromatherapy
- Aromatherapies
- Aroma
- Aroma Therapy
- Aroma Therapies
- Therapies, Aroma
- Therapy, Aroma
- Essential oil
- Oil OR Oils

3) Pain

- Pain
- Pains

4) QOL

- Quality of life
- Life Quality
- Health-Related Quality of Life
- Health Related Quality of Life
- HRQOL OR QOL

2. Search strategy (PubMed)

(Cancer OR Cancer* OR Tumor OR Tumors OR Neoplasm OR Neoplasia* OR Malignant Neoplasm* OR Malignancy OR Malignancies OR Neoplasm* Malignant OR Benign Neoplasm*) AND (Aromatherapy OR Aromatherapies OR Aroma* OR Aroma Therapy OR Aroma Therapies OR Therapies Aroma OR Therapy Aroma OR Essential oil OR Oil OR Oil*) AND (Pain OR Pains OR Quality of life OR Health related quality of life OR Health-related quality of life OR Life quality OR HRQOL OR QOL)

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