

Moxibustion as an Adjuvant Therapy for Cancer Pain: A Systematic Review and Meta-Analysis

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Purpose: Pain is one of the most common and feared symptoms among cancer patients. Unrelieved pain denies patients comfort and greatly affects their overall quality of life. Moxibustion is commonly used to manage chronic pain. However, its efficacy on cancer pain remains inconclusive. This study aimed to evaluate the efficacy of moxibustion for cancer pain.

Methods: We searched seven databases to obtain articles about moxibustion combined with pharmacotherapy for cancer pain published before November 2022. All data extraction was carried out independently by two investigators. RevMan 5.4 software was used for data analysis.

Results: A total of ten trials involving 999 cases were included. The results of the meta-analysis revealed that moxibustion combined with pharmacotherapy was significantly better than drug therapy alone in improving pain relief rate (RR = 1.16, 95% CI = [1.04, 1.30], $P = 0.01$), reducing pain scores (SMD = -1.43, 95% CI = [-2.09, -0.77], $P < 0.0001$), Shortening the onset of analgesia (MD = -12.07, 95% CI = [-12.91, -11.22], $P < 0.00001$), prolonging the duration of analgesia (MD = 3.69, 95% CI = [3.21, 4.18], $P < 0.00001$), and improving quality of life (SMD = 2.48, 95% CI = [0.67, 4.29], $P = 0.007$). In addition, moxibustion combined with pharmacotherapy can effectively reduce adverse reactions of drugs (RR = 0.35, 95% CI = [0.21, 0.57], $P < 0.0001$).

Conclusion: The evidence in this review supports moxibustion as an effective adjuvant therapy for cancer pain management. However, high-quality RCTs are needed to further confirm these findings.

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Keywords: moxibustion, cancer pain, systematic review, meta-analysis

Introduction

Pain is one of the most distressing and common symptoms of cancer patients. Pain can arise both due to the underlying disease and the treatment the patient has been subjected to.¹ According to statistics, more than 70% of cancer patients have experienced pain symptoms, and nearly 50% of these patients are not adequately controlled.² Untreated pain may sometimes cause cancer patients to commit suicide or unnecessary emergency department visits and hospitalizations.^{3,4} Pain in cancer patients is a growing problem. Pain hinders patient recovery and negatively affects the quality of life, mental health and work prospects of cancer survivors.^{5,6}

Currently, the management of cancer pain faces many challenges due to the multifactorial and complexity of cancer pain,⁷ and the clinical management of cancer pain is mostly based on drugs.⁸ Although the three-step analgesic method is effective and recommended by the World Health Organization (WHO),⁹ side effects of drug treatment are common, such as constipation, nausea, vomiting, dizziness, and altered cognition.^{10,11} Furthermore, certain analgesics, such as opioids, are potential drugs that cause addiction and abuse.¹² Aversion to adverse effects of treatment and fear of developing addiction make many patients seek non-pharmacological treatment.¹³⁻¹⁵

In China, moxibustion and acupuncture are the most widely used forms of non-pharmacological treatment, and acupuncture has been recommended by the National Comprehensive Cancer Network clinical practice guidelines as a comprehensive intervention for the management of cancer pain in adults.¹⁶ In addition, the analgesic effects of acupuncture on cancer pain have also been supported by several recent systematic reviews.^{17–19} In fact, like acupuncture, moxibustion is also an ancient acupoint stimulation therapy. It involves the application of burning mugwort indirectly or directly at acupoints or other specific areas of the body to prevent or treat diseases.²⁰ Among the currently available clinical studies on moxibustion for pain, most of them suggest that moxibustion is beneficial for pain patients.^{21–23} Moreover, the analgesic effects of moxibustion have also been demonstrated by evidence from several systematic reviews and meta-analyses.^{24–26} However, these studies focused on diseases including osteoarthritis, low back pain, and cervical spondylosis, and no studies involving cancer pain. There is insufficient clear evidence to support the effectiveness of moxibustion for cancer pain, and until usable evidence is generated, moxibustion cannot be recommended for the management of cancer pain. Therefore, clarifying whether moxibustion is beneficial and safe for cancer pain is an urgent issue to be addressed.

In recent years, many clinical trials have investigated the efficacy of moxibustion for cancer pain. However, the clinical evidence regarding the efficacy of moxibustion in the treatment of cancer pain remains controversial. Therefore, we performed a meta-analysis of currently available RCTs to assess the efficacy of moxibustion for cancer pain.

Methods

The systematic review protocol has been registered in the PROSPERO database (<https://www.crd.york.ac.uk/PROSPERO/>; registration number CRD42022370942). This review was carried out in compliance with the PRISMA statement.

Literature Search

Two investigators were assigned to independently search all citations in seven electronic databases, including Embase, PubMed, the Cochrane Library, CNKI, WanFang, VIP and the Chinese SinoMed Database. The search time for each database is up to November 2022. The terms used for search were “moxibustion” OR “wormwood” OR “mugwort” OR “moxa” AND “cancer” OR “tumor” OR “neoplasm” OR “carcinoma” AND “pain”. References of included RCTs were also checked to determine potential trials.

Eligibility Criteria

(1) Study types: We considered all RCTs that assessed moxibustion combination drugs compared with drugs alone for cancer pain. (2) Participants: Subjects were patients with malignancy confirmed by cytology or histopathology, all of whom had cancer-related pain not due to a pre-existing pathologies or related to treatments. Patients with various types of cancer will be included, with no restrictions on age, gender, race or degree of pain. (3) Interventions: The intervention methods of the experimental group only included studies of moxibustion combined with western medicine, and the drugs used were the same as those in the control group. Moxibustion here is defined as traditional moxibustion therapy, which is performed by burning moxa material. There are no restrictions on the moxa material or the frequency and duration of moxibustion treatment. (4) Control Interventions: The control group should be treated with conventional western medicine. (5) Outcomes: primary outcomes were pain score, analgesic onset time and duration of analgesia, quality of life and clinical efficacy (percentage of patients with improvement in pain symptoms, evaluated based on Chinese efficacy criteria with comparable definitions), the secondary outcome was adverse events.

Study Selection

Two investigators independently reviewed titles and abstracts based on the inclusion criteria and screened all potentially eligible trials. After that, we carefully evaluated the full text of these studies and performed the final eligibility screening. Disagreements were resolved through discussion.

Data Extraction

Two researchers independently extracted data from the included RCTs and any discrepancies were resolved through consensus. For each RCT, the following data were extracted: study author and location, publication year, sample size, the average age of patients, gender ratio of patients, intervention and its duration, outcomes, and adverse events.

Quality Assessment

Two researchers independently assessed the methodological quality of each included RCT based on the evaluation criteria recommended by the Cochrane Handbook.²⁷ The content includes the implementation of randomization, allocation concealment, blinding, the integrity of data, outcome reporting and other biases.

Statistical Analysis

Statistical analysis was performed by using RevMan 5.4 software. Dichotomous data (effective rate of pain relief and adverse events) were expressed as risk ratio (RR) with 95% confidence intervals (CIs). For continuous data, when results were measured by different scales, outcomes (pain score and quality of life) were reported as standardized mean differences (SMDs) with 95% CIs; otherwise, outcomes (analgesic onset time and duration of analgesia) were reported as MDs with 95% CIs. Heterogeneity was assessed by Cochran's Q statistic and I^2 test. When $P \geq 0.10$ and $I^2 \leq 50\%$, a fixed effects model was applied; otherwise, a random effects model was used. Sensitivity analysis was used to assess the robustness of the results. If more than 10 RCTs were available in the primary outcome, funnel plots were performed to evaluate publication bias.

Results

Literature Search Results

A total of 541 potentially relevant studies were identified during the initial search. It remained 259 studies after removing the duplicates. Then, after the titles, abstracts, and full texts of the articles were read, 10 articles^{28–37} met the inclusion criteria. A flowchart of the literature search process was shown in [Figure 1](#).

Study Characteristics

In 10 RCTs, all trials were published between 2014 and 2021. Only one of the articles³¹ was published in English, the rest were in Chinese. All studies were conducted in China. The sample size ranged from 60 to 308. This study involved a total of 999 cancer pain patients (512 in the experimental group and 487 in the control group). The basic characteristics of all included trials were provided in [Table 1](#).

Quality Assessment

Seven RCTs^{30,31,33–37} used a random number table to generate random sequences, while one study³² used a computer program, and the rest only mentioned “random”. Two studies^{31,32} mentioned the details of using allocation concealment. Due to the properties of moxibustion therapy, implementing a blind method is difficult. Only one study³² mentioned the details of blinding, which implemented blinding for outcome evaluation. One study³¹ reported the number and reasons for dropouts, and five trials^{28,32,35–37} reported details of adverse events. The Cochrane ROB assessment is shown in [Figure 2](#).

Pain Relief Rate

Seven RCTs^{28,30,32–36} reported the efficacy of moxibustion combined with drugs to relieve pain. Pooled data showed that moxibustion combined with drugs could further relieve the pain associated with cancer compared with the drug group (RR = 1.16, 95% CI = [1.04, 1.30], $P = 0.01$) ([Figure 3](#)).

Pain Score

Seven studies^{29,31–35,37} evaluated pain intensity, six of which were evaluated by NRS and one was assessed by VAS. The random-effects model showed that moxibustion combined with drugs could further relieve pain compared with the drug

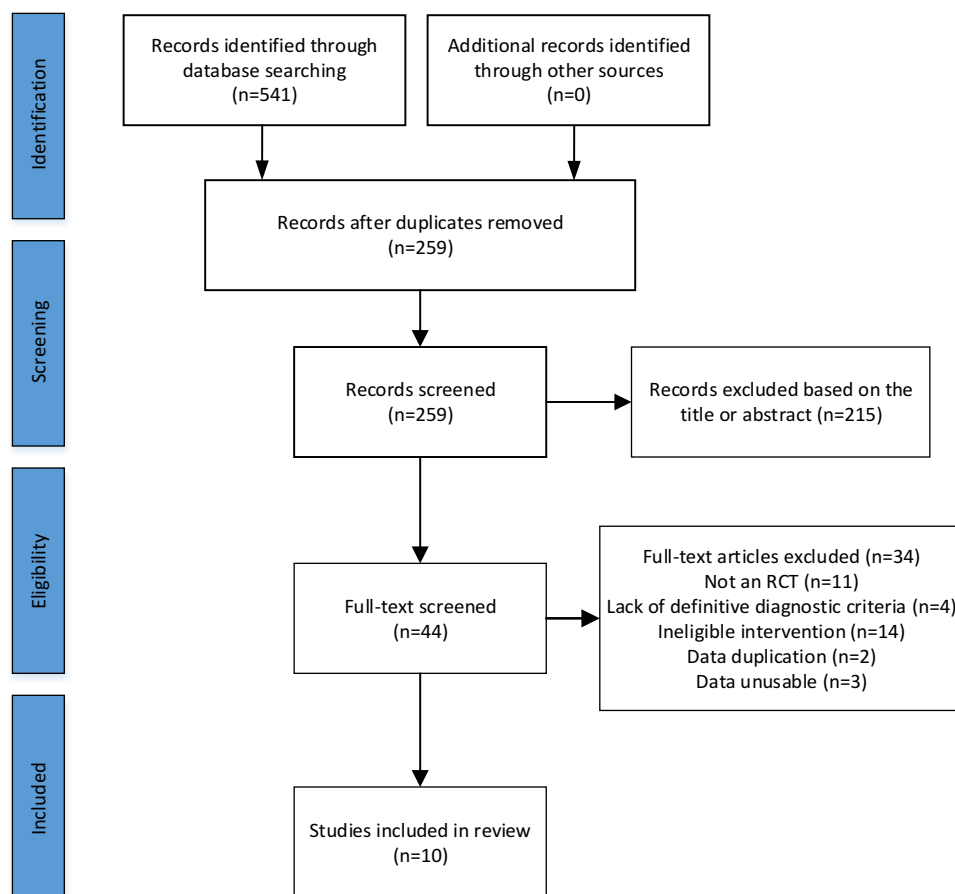


Figure 1 Study flow chart.

group (SMD = -1.43, 95% CI = [-2.09, -0.77], $P < 0.0001$). In addition, as far as NRS and VAS were used for separate evaluation, the results of the two scales were consistent with the aggregated result (Figure 4).

Analgesic Onset Time and Duration of Analgesia

Three studies^{28,36,37} reported the mean analgesic onset time and duration of analgesia. The combined data showed that the mean analgesic onset time in the moxibustion group was shorter than the control group (MD = -12.07, 95% CI = [-12.91, -11.22], $P < 0.00001$) and the mean duration of analgesia in moxibustion group was longer than the control group (MD = 3.69, 95% CI = [3.21, 4.18], $P < 0.00001$) (Figures 5 and 6).

Quality of Life

Three studies used FACT-G,²⁹ KPS³⁴ and QOL-LC³⁵ to assess the quality of life. Our pooled results showed that moxibustion combined with drugs could further improve the quality of life of cancer patients compared with the control group (SMD = 2.48, 95% CI = [0.67, 4.29], $P = 0.007$). In addition, as far as FACT-G, KPS and QOL were used for separate assessments, the results of the three scales were consistent with the aggregated result (Figure 7).

Adverse Events of Drugs

Five studies^{28,32,35-37} reported adverse events of drugs, such as constipation, nausea, dizziness, and vomiting. The fixed-effects model showed that moxibustion combined with drug therapy can reduce adverse reactions of drugs (RR = 0.35, 95% CI = [0.21, 0.57], $P < 0.0001$) (Figure 8).

Table I Characteristics of Included Studies

Study	Study Location	Sample Size (Male/Female)	Mean Age (SD)	Interventions Group	Control Group	Treatment Period	Outcomes
Huang (2014) ²⁸	Guangxi, China	T: 24 /26 C: 23 /27	T: 42.60±13.79 C: 42.62±12.73	Moxibustion+ C	Drugs (three-step analgesic ladder)	T: once a day for a week, 20–30 min, plus (C) C: twice a day for a week	CE, AE, AOT, DOA
Li (2016) ²⁹	Henan, China	T: 91 /75 C: 75 /67	NR	Moxibustion+ C	Drugs (three-step analgesic ladder)	T: twice a day for 4 weeks, 20 min, plus (C) C: twice a day for 4 weeks	NRS, FACT-G
Zou (2017) ³⁰	Hubei, China	T: 26 /22 C: 24 /24	T: 58.26±4.38 C: 58.19±4.35	Moxibustion+ C	Drugs (three-step analgesic ladder)	T: twice a day for 2 weeks, 30 min, plus (C) C: 2 weeks	CE
Bao (2019) ³¹	Zhejiang, China	T: 19 /19 C: 20 /17	T: 58.1±7.9 C: 58.7±9.9	Moxibustion+ C	Drugs (three-step analgesic ladder)	T: once a day, five times per week for 2 weeks, plus (C) C: 2 weeks	NRS
Pang (2019) ³²	Guangdong, China	T: 19 /11 C: 16 /14	T: 57.27±8.395 C: 58.83±11.561	Moxibustion+ C	Drugs (three-step analgesic ladder)	T: once every two days for 40 days, plus (C) C: once every two days for 40 days	CE, VAS, AE
Chen (2020) ³³	Shaanxi, China	T: 36 /24 C: 35 /25	T: 64.26 ± 7.83 C: 63.57±7.25	Moxibustion+ C	Drugs (three-step analgesic ladder)	T: once a day for 6 days, 25 min, plus (C) C: twice a day for 6 days	CE, NRS
Liu B (2020) ³⁴	Hebei, China	T: 16 /14 C: 18 /12	T: 49.13±9.48 C: 50.20±10.56	Moxibustion+ C	Drugs (three-step analgesic ladder)	T: once every two days for 2 weeks, plus (C) C: twice a day for 2 weeks	CE, NRS, KPS
Liu LX (2020) ³⁵	Zhejiang, China	T: 16/14 C: 13/17	T: 53±9 C: 53±9	Moxibustion+ C	Drugs (three-step analgesic ladder)	T: once a day for 2 weeks, plus (C) C: twice a day for 2 weeks	CE, NRS, QOL-LC, AE
Xu (2021) ³⁶	Shanghai, China	T: 15/15 C: 16/14	T: 65.8±4.1 C: 66.4±4.2	Moxibustion+ C	Drugs (three-step analgesic ladder)	T: once a day for 10 days, 20–30 min, plus (C) C: 10 days	CE, AE, AOT, DOA
Lv (2021) ³⁷	Guangdong, China	T: 16/14 C: 18/12	T: 53.19±4.68 C: 52.36±5.12	Moxibustion+ C	Drugs (three-step analgesic ladder)	T: once a day for a week, 30 min, plus (C) C: twice a day for a week	NRS, AE, AOT, DOA

Abbreviations: AE, adverse events; AOT, Analgesic onset time; C, control group; CE, clinical effect; DOA, Duration of analgesia; FACT-G, functional assessment of cancer therapy-general; KPS, the Karnofsky performance score; NR, not reported; NRS, numeric rating scale; QOL-LC, quality of life scale for liver cancer; T, therapy group.

Sensitivity Analysis and Publication Bias

Sensitivity analysis showed that the results of the meta-analysis were stable. Since the cumulative number of RCTs included in each outcome was less than 10, we did not analyze publication bias.

Discussion

Main Findings

In our current study, we included 10 RCTs that compared moxibustion plus drugs with drugs alone. In terms of the pain relief rate, the results of the meta-analysis showed that the moxibustion group was significantly better than the drug group. Concerning reducing pain score, the NRS and VAS score was used to report the intensity of pain. Our pooled analysis indicated that moxibustion plus drugs were more effective than drugs alone in reducing pain scores. In terms of analgesic onset and duration, the moxibustion group had the advantage of shorter onset and longer duration of analgesia compared with drug treatment alone. For improving quality of life, the FACT-G, KPS, and QOL-LC score was used to assess the quality of life of cancer pain patients. Our research results show that moxibustion plus drugs were more effective than drugs alone in improving the quality of life. In this meta-analysis, five RCTs reported details of adverse events. The combined data show that moxibustion combined with pharmacotherapy can effectively reduce the incidence of adverse reactions to drugs. In addition, although one study reported adverse events of moxibustion, such as fainting during moxibustion and burns, the symptoms were mild. Thus, moxibustion seems to be an effective and safe adjuvant treatment for cancer pain.

Advantages of Moxibustion for Analgesia

Moxibustion is an ancient external therapy with a history of about 2500 years of application in China. It is widely used for the management of various health conditions and has the benefits of non-invasive, painless, safe and convenient.^{38,39}

	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and personnel (performance bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Other bias
Bao 2019	+	+	-	?	+	?	?
Chen 2020	+	?	-	?	+	?	?
Huang 2014	-	?	-	?	+	?	?
Li 2016	-	?	-	?	+	?	?
Liu B 2020	+	?	-	?	+	?	?
Liu LX 2020	+	?	-	?	+	?	?
Lv 2021	+	?	-	?	+	?	?
Pang 2019	+	+	-	+	+	?	?
Xu 2021	+	?	-	?	+	?	?
Zou 2017	+	?	-	?	+	?	?

Figure 2 Risk of bias summary.

Unlike acupuncture, the characteristics of moxibustion in terms of material and using fire determine its function toward warming and nourishing.⁴⁰ According to the description in ancient Chinese literature, moxibustion has the functions of warming channels and collateral, dispelling cold and relieving pain, preventing and treating diseases.⁴⁰ This makes moxibustion adopted as a treatment for many diseases, including cancer pain.⁴¹⁻⁴³ In China, moxibustion has been widely used in the management of cancer patients, and related studies have confirmed the positive effects of moxibustion in improving immune function, relieving fatigue, and alleviating side effects associated with chemotherapy (eg, myelosuppression and gastrointestinal reactions).⁴³⁻⁴⁶ The potential mechanism of moxibustion efficacy may be related to the combination of thermal, pharmacological, and radiation effects of moxa combustion.⁴⁰ Therefore, moxibustion

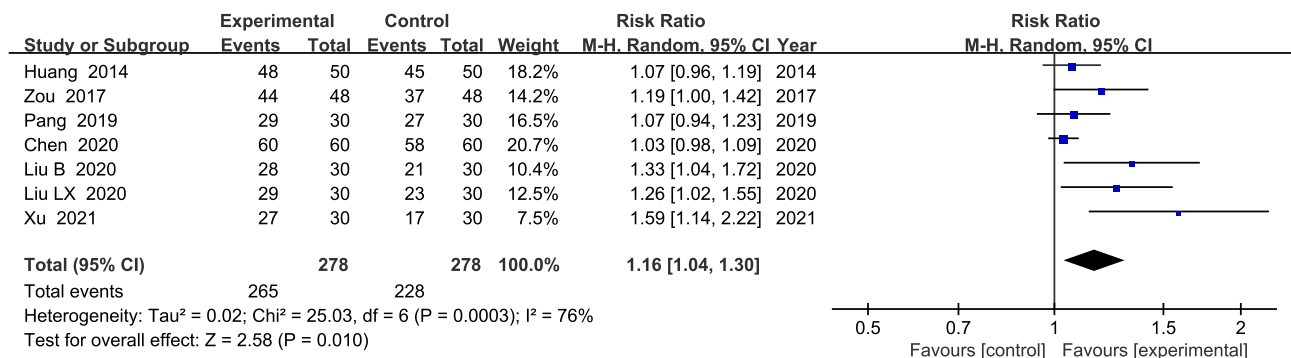


Figure 3 Meta-analysis of pain relief rate.

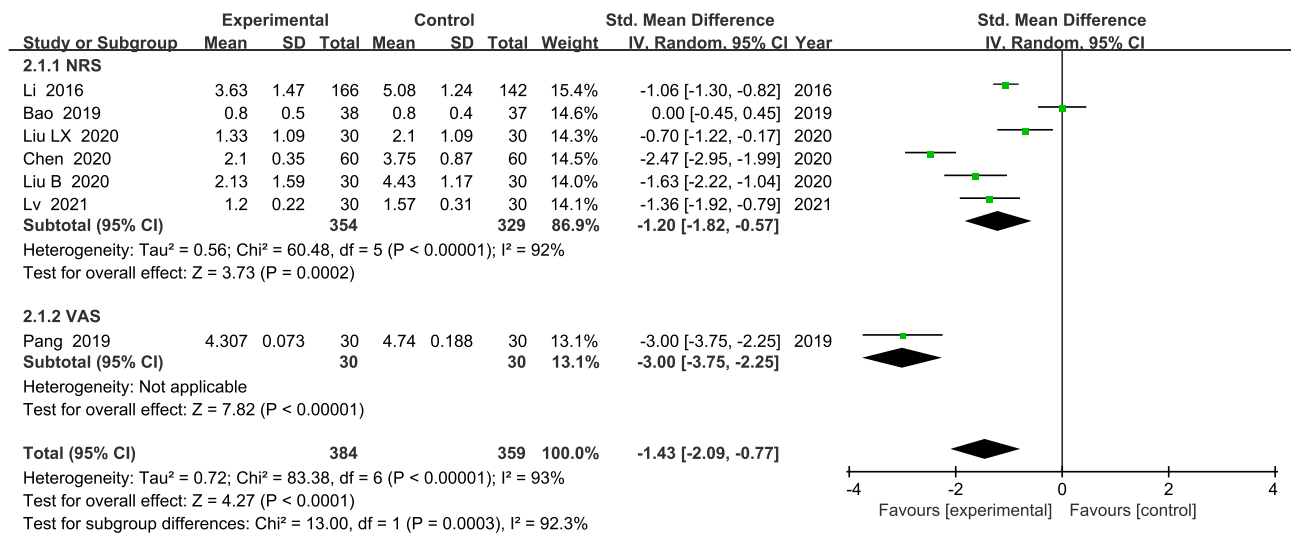


Figure 4 Meta-analysis of pain Score.

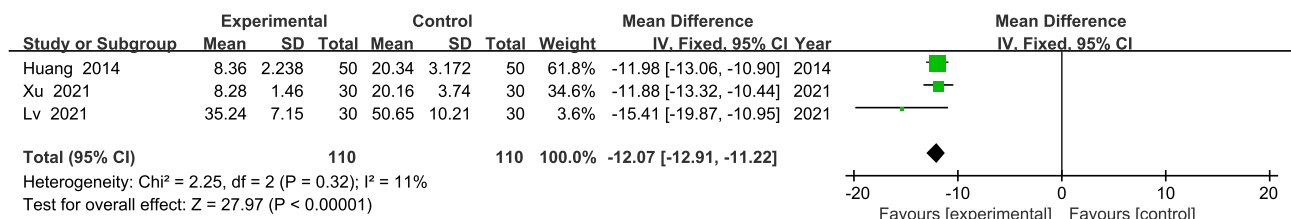


Figure 5 Meta-analysis of analgesic onset time.

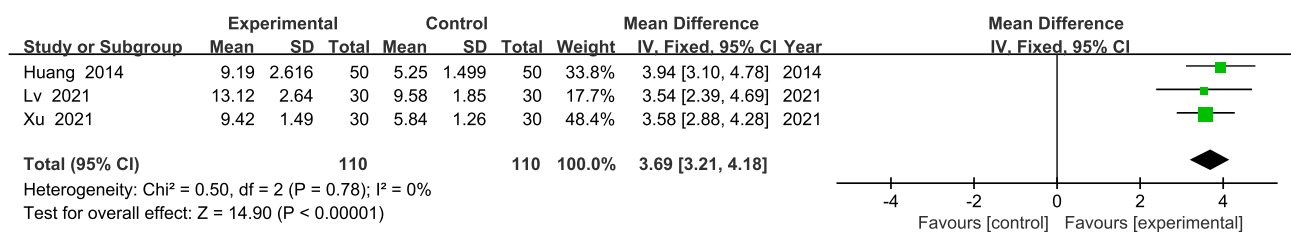


Figure 6 Meta-analysis of duration of analgesia.

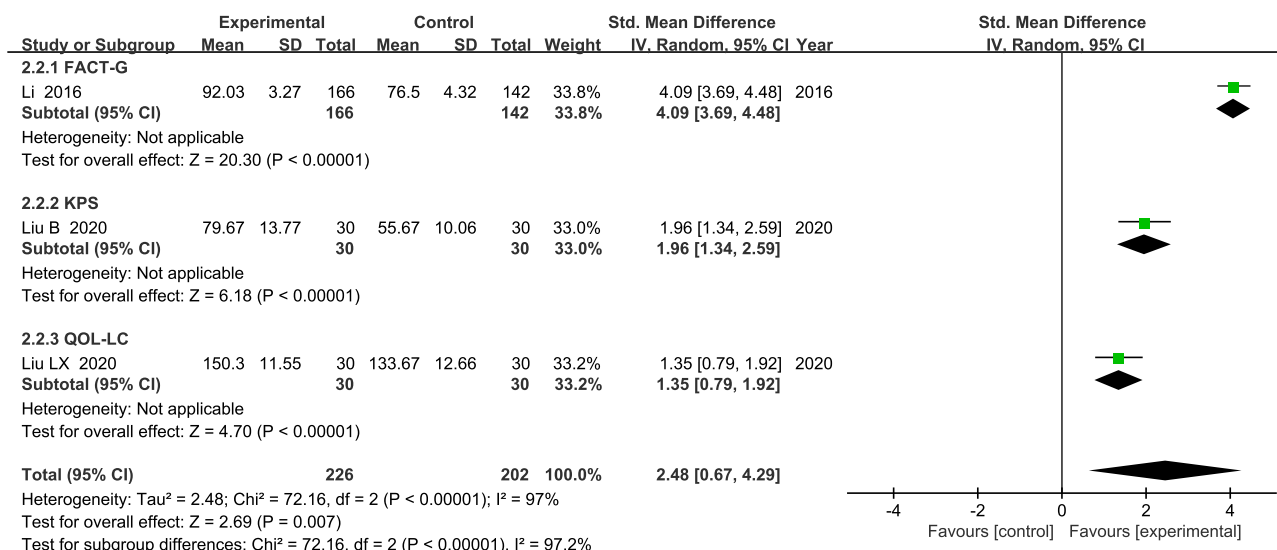


Figure 7 Meta-analysis of quality of life.

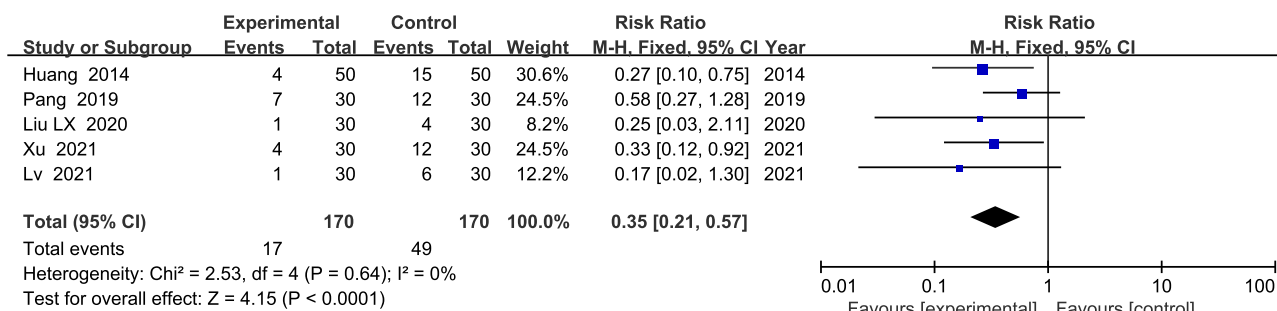


Figure 8 Meta-analysis of adverse events of drugs.

treatment may have the advantage of multiple pathways and targets compared to the single pathway of drug treatment for pain. In addition, several recent meta-analyses have also confirmed the analgesic effect of moxibustion,^{23,24,47} which may be related to the role of moxibustion in regulating pain-related signal pathways, reducing neuroinflammation, and inhibiting the production of pro-inflammatory cytokines (eg, TNF- α , IL-1 β , IL-6).⁴⁸⁻⁵⁴

Relation to Previous Studies

Previously, researchers have systematically evaluated the efficacy of acupuncture for cancer pain. A systematic review involving 17 RCTs found that acupuncture was significantly associated with decreased cancer pain and less analgesic use.¹⁷ In another meta-analysis focusing on acupuncture combined with drugs for cancer pain, the results of this study showed that acupuncture combined with drugs had better analgesic efficacy than drugs alone.¹⁸ Furthermore, in a Cochrane systematic review of moxibustion for cancer, it was found that moxibustion treatment may contribute to reducing the hematological and gastrointestinal toxicity of radiotherapy or chemotherapy and improving the quality of life of cancer patients.⁴³ However, there is no previously available meta-analysis on the efficacy of moxibustion combined with medication for cancer pain. To the best of our knowledge, this is the first meta-analysis to evaluate the efficacy of moxibustion combined with pharmacotherapy for cancer pain. Our study found that the analgesic effect of moxibustion combined with drugs for cancer pain was superior to drugs alone, and the combined treatment also had advantages in improving the quality of life of cancer pain patients and reducing the side effects of drugs. Despite the limited level of evidence, we believe that the findings of this study may provide a better reference for clinicians.

Strengths and Limitations

This review performed a systematic literature search, standardized literature quality assessment, and appropriate statistical analyses, which methodological strengths ensured the objectivity of the study findings and the comprehensiveness of the evidence. In terms of efficacy evaluation, the NRS and VAS scales are currently recognized tools used to assess pain severity. Therefore, using these two scales to evaluate the efficacy of moxibustion for cancer pain has good reliability.

Some limitations exist in the current meta-analysis. First, since this study only included RCTs from English and Chinese databases, this may miss some potentially eligible trials. Second, the methodological quality of most trials is not satisfactory. Only two RCTs mentioned the details of allocation concealment, and only one RCT reported the details of using blinding. Low reporting quality affected the credibility of the evidence in this study. Third, only one RCT was published in English, while the rest were published in Chinese, and all studies were performed in China. Therefore, the evidence from this study may be restricted by the region. Lastly, there was significant heterogeneity in some of the outcomes. Although subgroup analyses were performed based on different assessment scales, heterogeneity was not resolved. We consider that the source of heterogeneity may be related to the clinical design and methodology of the included studies, including differences in the degree of cancer pain, duration of moxibustion treatment, and sample size.

Conclusions

The results of our meta-analysis show that moxibustion combined with pharmacotherapy is more effective than drugs alone in terms of relieving pain or improving the quality of life of cancer pain patients. In addition, moxibustion combined with drugs can effectively reduce the side effects of drugs. But given the limitation in this meta-analysis, high-quality RCTs are still needed to confirm the role of moxibustion combined with pharmacotherapy for cancer pain.

Data Sharing Statement

All the data was shown in the article.

Ethics Approval

Not applicable.

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Disclosure

The authors declare that they have no conflicts of interest in this work.

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