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REVIEW

Effectiveness of Combination of Thunder Fire Moxibustion with Other Forms of Traditional Chinese Medicine for Osteoarthritis Knee: A Meta-Analysis

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Background: Given the prevalence of osteoarthritis and the growing interest in alternative treatments, there is a need to provide a comprehensive evaluation of this integrated TCM approach. Reviews are required to understand the potential benefits and safety of the combination therapy compared to conventional treatments. Hence, this meta-analysis investigates the effectiveness of combining Thunder Fire Moxibustion with other Traditional Chinese Medicine (TCM) modalities, specifically acupuncture and herbal formulas, in treating knee osteoarthritis.

Methods: A comprehensive literature search across databases like PubMed Central, EMBASE, MEDLINE, and others was conducted. The inclusion criteria focused on randomized controlled trials involving patients with knee osteoarthritis, comparing the effectiveness of Thunder Fire Moxibustion combined with other TCM modalities against standard care. The Cochrane Risk of Bias tool was used for bias assessment, and a random-effects inverse-variance model for meta-analysis.

Results: Out of 1467 records, 7 studies met the inclusion criteria. The pooled Risk Ratio (RR) for total effective rate was 1.119, indicating a significant effect of the combined TCM treatment. Subgroup analysis showed a pooled RR of 1.130 for acupuncture combinations and 1.103 for herbal TCM combinations. The incidence of adverse reactions had a non-significant pooled RR of 0.572. The GRADE assessment indicated a low overall quality of evidence due to risks of bias and publication bias.

Conclusion: The combination of Thunder Fire Moxibustion with other TCM modalities shows potential effectiveness in treating knee osteoarthritis, with minimal adverse reactions. However, the low quality of evidence suggests a need for more rigorous studies to confirm these findings.

Keywords: acupuncture, meta-analysis, moxibustion, osteoarthritis

Introduction

Osteoarthritis (OA) of the knee is a chronic degenerative joint disorder marked by cartilage deterioration, joint lining inflammation, and bone overgrowth, leading to pain, stiffness, and impaired mobility.[1] It represents a significant public health challenge, impacting the quality of life for millions worldwide.[1] The prevalence of OA is escalating, attributed to aging populations and increasing obesity rates.[2] Conventional treatments for OA focus primarily on pain management and maintaining joint function but often have limitations and side effects.[3–5]

Traditional Chinese Medicine (TCM), with its holistic approach, offers alternative or complementary strategies in managing OA.[6] Among these, Thunder Fire Moxibustion, a unique form of heat therapy using herbal preparations, has gained attention. It is believed to enhance local circulation and reduce inflammation, thereby alleviating pain and discomfort associated with OA.[7]

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The integration of Thunder Fire Moxibustion with acupuncture or other forms of specific TCM herbal formulas could potentially offer a synergistic effect, enhancing therapeutic outcomes.[8,9] Acupuncture, known for its efficacy in pain relief and functional improvement in OA, involves inserting fine needles at specific meridians to balance the body's energy flow.[10] TCM herbal formulas, on the other hand, aim to correct internal imbalances and strengthen bodily systems, addressing the root causes of OA symptoms.[11]

Furthermore, the intersection of modern medical research and TCM offers a rich avenue for exploring novel therapeutic approaches. Recent studies have increasingly recognized the potential of TCM in managing chronic conditions like OA.[12–14] Thunder Fire Moxibustion, in particular, is rooted in the principles of Qi and Blood circulation in TCM.[7] It is postulated that the heat and herbal components of this therapy synergistically enhance Qi flow, mitigate dampness and cold in the joints, and promote healing.

The concept of combining various TCM modalities stems from the holistic nature of this medical system. It is believed that acupuncture, with its ability to regulate energy pathways, and herbal medicine, with its systemic healing properties, can complement the localized effects of Thunder Fire Moxibustion.[8,9] This integrative approach aligns with the TCM philosophy that addressing both the symptoms and the root cause of an ailment leads to more effective and enduring outcomes. In the context of OA, this could mean not only alleviating pain and discomfort but also slowing the progression of the disease.

Moreover, the rising interest in non-pharmacological treatments for OA, driven by concerns over long-term side effects and dependencies associated with conventional medications, makes the study of TCM modalities particularly timely. Patients and healthcare providers are increasingly looking towards complementary and alternative medicine (CAM) for safer and more holistic treatment options.[15] As such, validating and understanding the efficacy of TCM treatments through rigorous scientific research is crucial. By evaluating various studies' outcomes, this work seeks to provide a comprehensive understanding of the efficacy, safety, and potential mechanism of action of this combined treatment approach. Such an integrated TCM modality could offer a promising alternative to conventional OA treatments, aligning with the growing global interest in holistic and patient-centered healthcare solutions. Hence, this meta-analysis aims to review and synthesize existing literature on the effectiveness of combining Thunder Fire Moxibustion with other forms of TCM in treating knee OA.

Materials and Methods

Eligibility Criteria

The review inclusion criteria is as follows: 1) study design such as individual or cluster randomized controlled trials with a parallel arm structure; 2) published full-text articles, excluding case reports, series, conference abstracts, and unpublished grey literature; 3) study targeting the individuals diagnosed with knee OA, without limitations based on age, gender, or the presence of comorbidities; 4) Studies that compare the effectiveness of combination of Thunder Fire Moxibustion with any other form of Traditional Chinese Medicine modalities (predominantly acupuncture and herbal formulas) against standard care or other interventions; 5) study should be reporting any of the following outcomes: the rate of clinical or therapeutic effectiveness, recovery rate, and the incidence of adverse events.

Search Strategy

A thorough and detailed literature search was conducted across multiple databases, including Scopus, MEDLINE, Chinese biomedical literature database, China National Knowledge Infrastructure, Cochrane Library, and search engines like Google Scholar and ScienceDirect. We utilized both medical subject headings (MeSH) and free-text terms, employing Boolean operators to refine the search. Key terms related to knee osteoarthritis and randomized controlled trials were used. The search was limited to articles published from January 1964 to December 2023 and in English and Chinese languages. Additionally, we examined the references of the retrieved studies to capture any potentially overlooked articles.

The search strategy utilized for the review is as follows: ((Thunder Fire Moxibustion [Title/Abstract] OR Moxibustion [Title/Abstract]) AND (Acupuncture [Title/Abstract] OR Herbal Medicine [Title/Abstract] OR Traditional Chinese Medicine

[Title/Abstract])) AND (Osteoarthritis, knee [MeSH Terms] OR knee osteoarthritis [Title/Abstract]) AND (Randomized Controlled Trial [Publication Type] OR RCT [Title/Abstract] OR "Randomized Controlled Trials as Topic"[MeSH]).

This strategy incorporates terms specific to Thunder Fire Moxibustion, acupuncture, and TCM herbal treatments, alongside the knee osteoarthritis aspect, ensuring that the retrieved studies are highly relevant to the research focus (Supplementary file).

Study Screening

In the first phase of study selection, two independent researchers screened titles, keywords, and abstracts. They then acquired and evaluated the full texts of potentially relevant studies against the eligibility criteria for further consideration. Any differences in the initial screening were resolved through mutual agreement between the investigators. In the second phase, these researchers conducted a detailed review of the full texts, selecting those that met the criteria for inclusion in the review. This systematic review adheres to the "Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement 2020" guidelines, detailed in the Supplementary Appendix.[16]

Data Extraction

Upon selecting the eligible full-text articles for the review, both investigators engaged in manual data extraction using a predefined semi-structured form established during the protocol phase. This form helped in gathering key details like author names, study title, publication and study years, study duration and design, setting, location, sample size, outcome assessment tools, mean age of participants, and specifics of interventions and comparators. The first author entered this data, and the second author verified it for accuracy.

Risk of Bias Assessment

The primary and secondary authors were tasked with assessing the risk of bias in the included studies. They used the Cochrane Risk of Bias tool for Randomized Controlled Trials (RoB 2)[17] to evaluate five specific domains: the risk of bias from randomization, deviations from the intended intervention, missing outcome data, measurement of the outcome, and selection of the reported result. Based on these assessments, each study was categorized as having a low, high, or some concerns regarding bias risk, thereby determining the quality of evidence.

Statistical Analysis

The meta-analysis was conducted using STATA version 14.2. For dichotomous outcomes like effective or recovery rates, risk ratios were calculated using the number of events and participants. The pooled estimate was reported as risk ratio with 95% confidence interval (CI). A random effects model with the inverse variance method was employed for weighting studies. Forest plots visually represented study-specific and pooled estimates. Heterogeneity was assessed using the chi-square test and I^2 statistics, with sensitivity analysis conducted to test result robustness.[18]

Regarding publication bias, due to the smaller number of studies (less than 10), traditional methods like Egger's test and funnel plots were not feasible. These methods generally require a larger number of studies to produce reliable results. Instead, we used the Doi plot and the Luis Furuya Kanamori (LFK) index as alternative approaches to explore and quantify potential publication bias.[19] The LFK index ranges from −1 to +1, indicating no publication bias (perfect symmetry). Values between −1 to −2 or +1 to +2 suggest minor asymmetry, while values less than −2 or greater than +2 indicate major asymmetry.

Quality of Evidence Assessment

The GRADE approach is pivotal for evaluating evidence quality in health research. It involves five domains: Risk of Bias, assessing biases in study design and execution; Inconsistency, examining variations in study results; Indirectness, determining the relevance to the research question; Imprecision, evaluating confidence in effect estimates; and Publication Bias, identifying selective reporting.[20] Each domain critically analyzes different aspects of studies, ensuring the evidence's reliability and relevance. This systematic evaluation underpins robust healthcare recommendations.

Results

PRISMA Flow Diagram

Figure 1 presents the PRISMA flowchart detailing the study selection process. Initially, 1467 records were identified, out of which, 97 full-text studies were identified. These, along with two additional studies found via bibliography review, underwent secondary screening. Ultimately, 7 studies met the inclusion criteria and selected for analysis.[8,9,21–25]

Included Study Characteristics

Only RCTs were included and all the studies were from China. The sample size in combination group and comparison group ranges from 33 to 75. The most combination of thunder fire moxibustion was with acupuncture followed by TCM herbal formula. The most common comparison groups were western medicines like celecoxib, diclofenac or glucosamine sulfate (Table 1). Overall, three out of the seven studies had higher risk of bias, while rest of them had some concerns (Table 2).

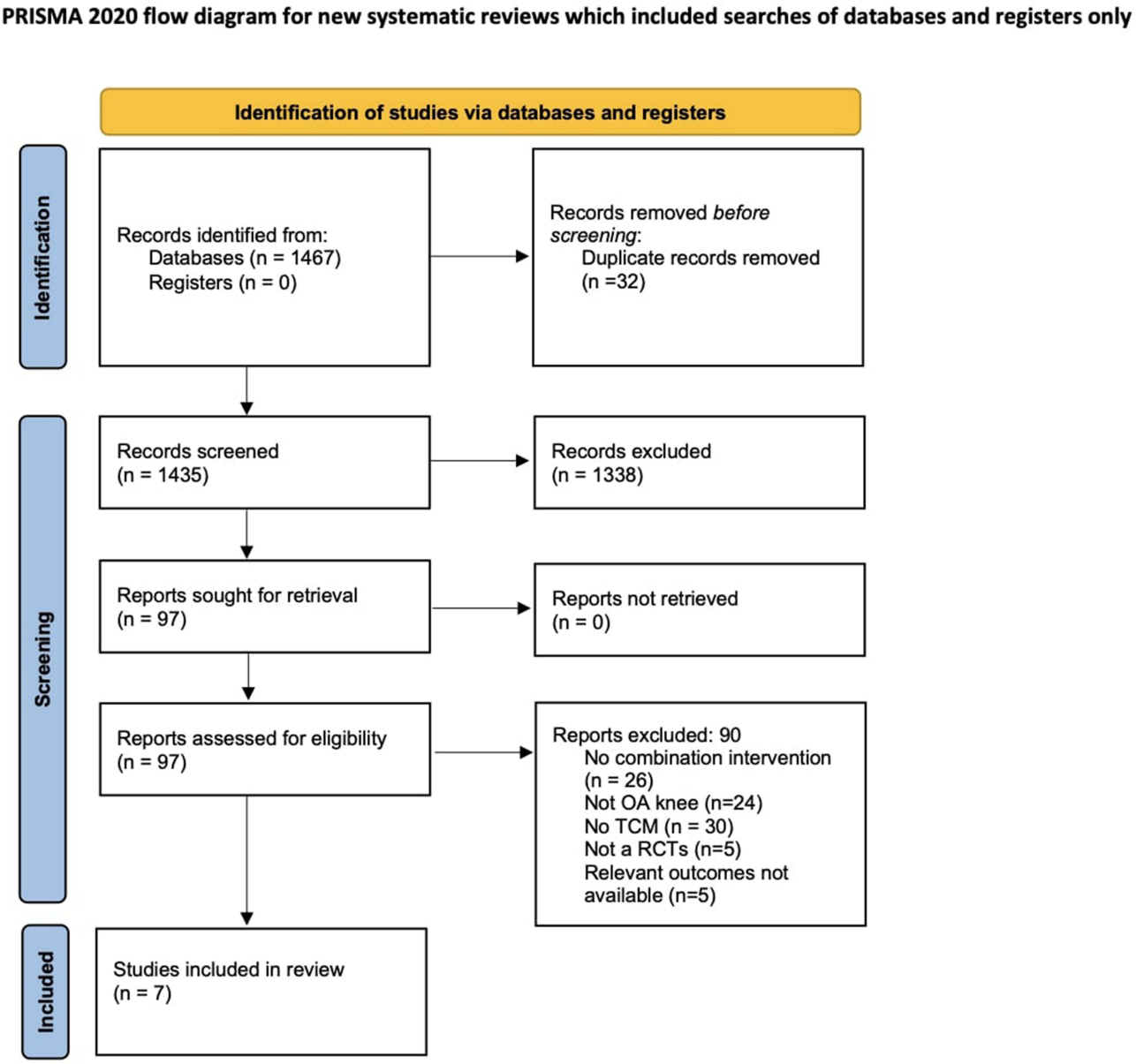

Figure 1 PRISMA flowchart.

Table 1 Characteristics of the included studies (N=7)

Author Identifier	Country	Study design	Intervention Group Details	Comparison Group Details	Sample Size Intervention Group	Sample Size Comparison Group
Deng 2020[8]	China	RCT	Thunder fire moxibustion in combination with electroacupuncture once a day for 30 minutes for 14 days	Oral administration of diclofenac sodium double release enteric coated tablets 75 mg once a day for 14 days	35	33
Hu 2019[9]	China	RCT	Thunder fire moxibustion in combination with Shuangbai powder once a day 7 days course for consecutive four courses	Thunder fire moxibustion alone once a day 7 days course for consecutive four courses	33	34
Lin 2022[24]	China	RCT	Thunder fire moxibustion with Duhuo Jisheng decoction combination	Celecoxib combined with glucosamine sulfate	60	60
Miao 2014[22]	China	RCT	Thunder fire moxibustion with point massage	Chinese medicine bath group	75	75
Wu 2021[25]	China	RCT	Thunder fire moxibustion with Juanbi decoction combination two times a day morning and evening for 4 weeks	Glucosamine sulfate capsules three times a day two tablets each time for four weeks	35	35
Zhang 2016[21]	China	RCT	Thunder fire moxibustion in combination with electroacupuncture 20 minutes once a day for 10 day treatment in one course for a total of two courses	Electroacupuncture 25 minutes once a day for 10 days over two courses	40	40
Zhu 2023[23]	China	RCT	Thunder fire moxibustion in combination with acupuncture	Beryllium needling	50	50

Abbreviations: RCT, Randomized controlled trial; NR, Not reported; NA, Not applicable.

Table 2 Risk of Bias Assessment (N=7)

Author Identifier	Randomization Process	Deviation from Intended Intervention	Missing Data	Measurement of Outcome	Selective Reporting of Results	Overall Risk
Deng 2020[8]	Low risk	Some concerns	Low risk	Low risk	Low risk	Some concerns
Hu 2019[9]	Low risk	Some concerns	Low risk	High risk	Low risk	High risk
Lin 2022[24]	Low risk	Some concerns	Low risk	Low risk	Low risk	Some concerns
Miao 2014[22]	Low risk	Low risk	Low risk	High risk	Low risk	High risk
Wu 2021[25]	Low risk	Some concerns	Low risk	Low risk	Low risk	Some concerns
Zhang 2016[21]	Low risk	Some concerns	Low risk	Low risk	Low risk	Some concerns
Zhu 2023[23]	Low risk	Some concerns	Low risk	High risk	Low risk	High risk

Total Effective Rate

The analysis included seven studies with a total of 655 participants using a random-effects inverse-variance model. The pooled RR was 1.119 (95% CI: 1.060 to 1.181), indicating a statistically significant overall effect ($z = 4.056$, $p < 0.0001$) of combination of thunder fire moxibustion with other forms of TCM when compared to standalone TCM/western medicine interventions (Figure 2). The analysis showed minimal heterogeneity among the included studies (Cochran's $Q = 3.46$, $df = 6$, $p = 0.750$; $I^2 = 0.0\%$), suggesting consistency in the results across studies.

Subgroup analysis differentiated between acupuncture and herbal TCM combinations with thunder fire moxibustion for treating knee osteoarthritis. For acupuncture combinations, the pooled RR was 1.130 (95% CI: 1.053 to 1.213) with minimal heterogeneity ($I^2 = 0.0\%$). Herbal TCM combinations showed a pooled RR of 1.103 (95% CI: 1.014 to 1.200), also demonstrating low heterogeneity ($I^2 = 0.0\%$). Overall, the combined effect size was significant (RR = 1.119, 95% CI: 1.060 to 1.181), indicating the effectiveness of both treatment approaches with no significant differences in heterogeneity across the subgroups (Figure 3). Publication bias assessment using Doi plot revealed a minor asymmetry (Figure 4) which was further confirmed by LFK index of 1.55. Leave one out sensitivity analysis did not reveal any substantial change in terms of pooled estimate magnitude and direction (Figure 5).

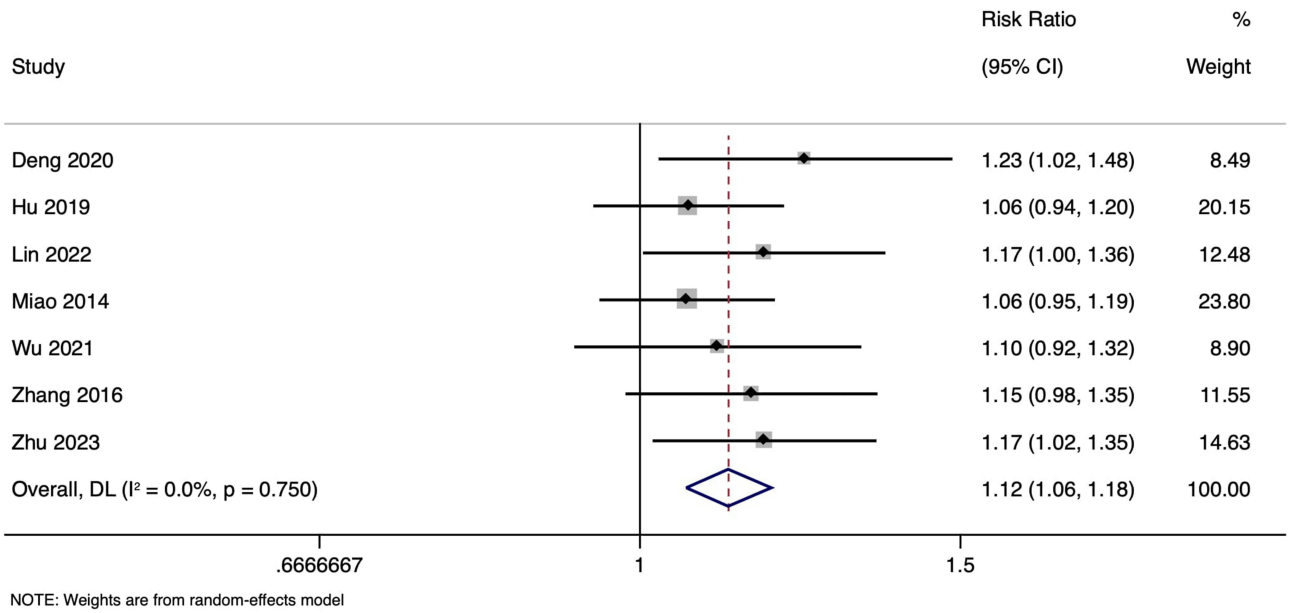

Figure 2 Forest plot showing the effectiveness of thunder fire moxibustion with other TCM approaches on therapeutic effective rate for osteoarthritis knee.

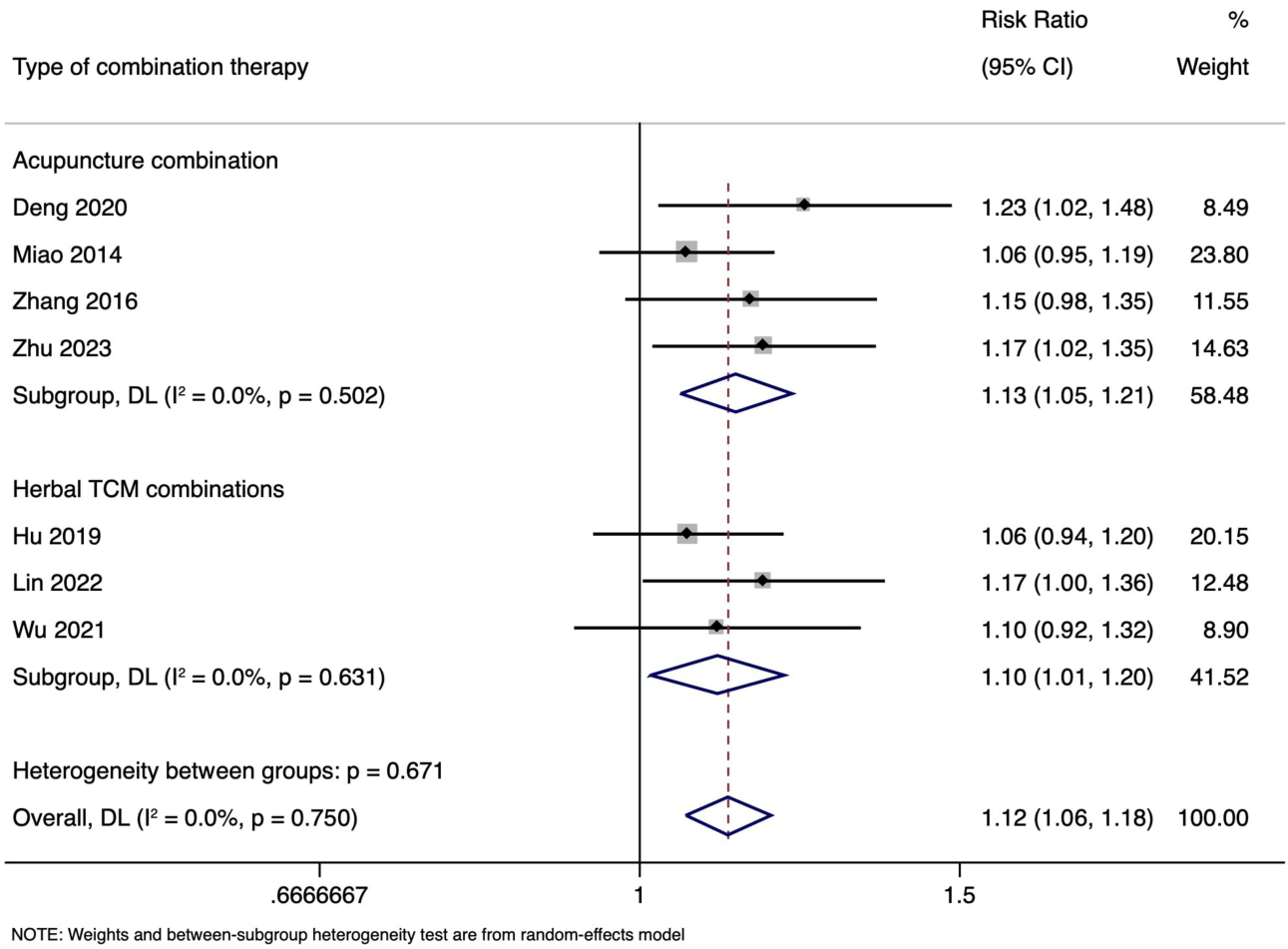

Figure 3 Forest plot showing the subgroup analysis based on the type of combination TCM with thunder fire moxibustion for osteoarthritis knee.

Incidence of Adverse Reactions

The analysis included two studies with 190 participants and the pooled RR was 0.572 (95% CI: 0.173 to 1.890), indicating a non-significant overall effect (z = −0.915, p=0.360) (Figure 6). The analysis showed minimal heterogeneity among the included studies (Cochran's Q = 0.02, df = 1, p = 0.896; I^2 = 0.0%), suggesting consistency in the results across studies.

GRADE Assessment Results

Our GRADE assessment (Table 3) for the main outcome therapeutic effective rate started with an initial classification of the evidence as high quality, This starting point was chosen due to the inclusion of only RCTs.

Risk of Bias Assessment

A significant concern in our analysis was the risk of bias. For some of the studies, this risk was deemed high, leading to a single downgrade in the quality of evidence to "moderate". The high risk of bias in these studies stemmed from methodological issues that could potentially affect the validity of their findings.

Indirectness of Evidence

Another critical factor was the indirectness of the evidence, particularly concerning the type of TCM combination with thunder fire moxibustion. However, appropriate subgroup analysis was performed and separate estimates are provided and hence, there is no need to downgrade based on indirectness of the evidence.

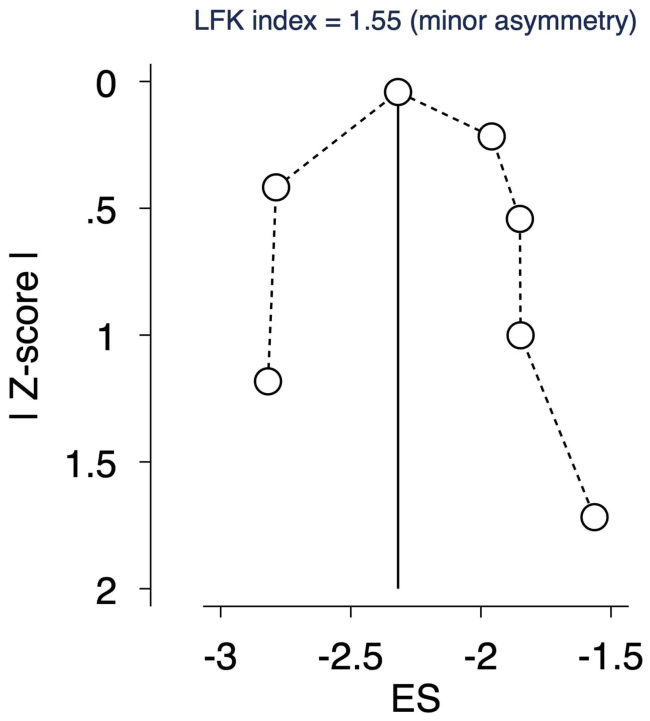

Figure 4 Doi plot.

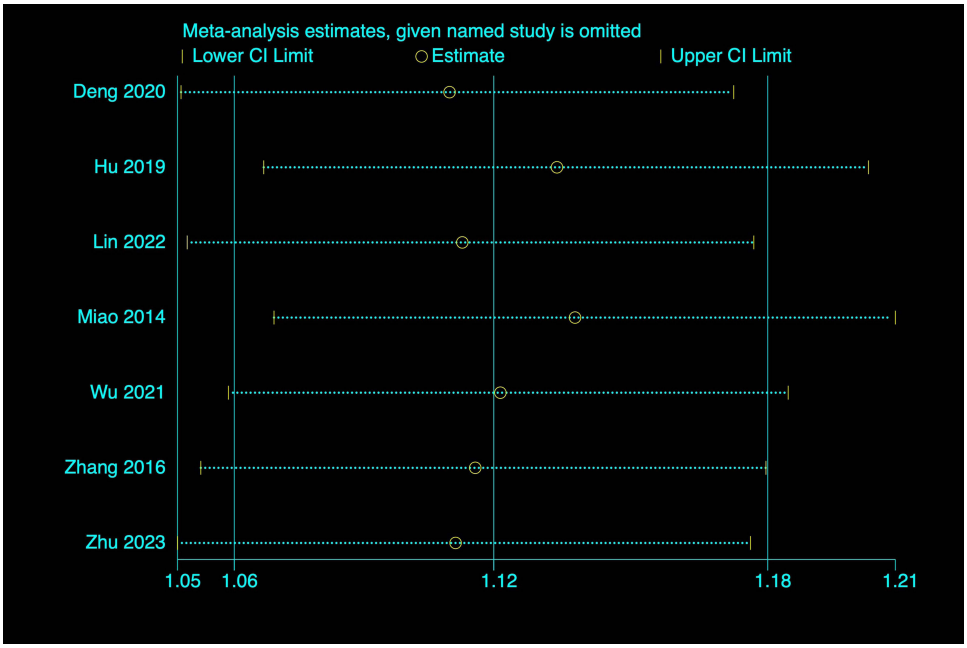

Figure 5 Sensitivity analysis plot.

Imprecision

There was no imprecision observed, as the CI was robust, and there was no crossing of the null value, which meant that there was no need for a downgrade in this domain.

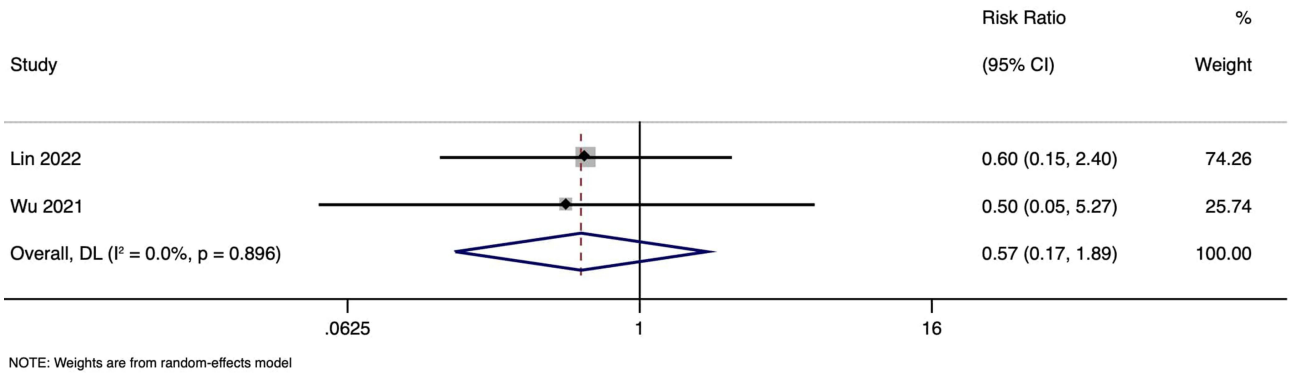

Figure 6 Forest plot showing the effectiveness of thunder fire moxibustion with other TCM approaches on incidence of adverse reactions for osteoarthritis knee.

Heterogeneity

There was no heterogeneity present in the outcome, which meant that there was no necessity to downgrade based on this domain.

Publication Bias

Finally, our assessment revealed the presence of minor asymmetry, indicating the possibility of publication bias. The presence of publication bias introduces a systematic error that could skew the overall findings, leading to a further downgrade in the quality of evidence from moderate to low quality.

Overall Quality of Evidence

Considering these factors, the overall quality of the evidence for the therapeutic effective rate was deemed to be "low". The cumulative impact of the high risk of bias in some studies, and the presence of publication bias all contributed to this final assessment. The "low" quality rating indicates that there is some amount of uncertainty about the accuracy of the effect estimates for the outcome.

Discussion

This study's meta-analysis revealed a pooled RR of 1.119 (95% CI: 1.060 to 1.181), indicating a statistically significant overall effect of combining Thunder Fire Moxibustion with other TCM modalities compared to standalone TCM or Western medicine interventions. This finding suggests that the integrated approach in TCM, specifically the inclusion of Thunder Fire Moxibustion, may enhance therapeutic efficacy in the treatment of knee osteoarthritis. No heterogeneity observed ($I^2 = 0.0\%$) across the included studies underscores the consistency and reliability of these results.

Furthermore, our analysis considered the incidence of adverse reactions in the studies reviewed. The non-significant overall result, coupled with the minimal heterogeneity observed ($I^2 = 0.0\%$), suggests that the adverse reactions associated with the combined TCM treatments, including Thunder Fire Moxibustion, are not significantly higher than those observed in standard treatments. This finding is crucial as it indicates that the integration of these TCM modalities into osteoarthritis management does not markedly increase the risk of adverse effects, thus supporting the safety profile of these treatments. However, the limited number of studies and participants underlines the need for more extensive research to comprehensively understand the safety aspects of these therapies.

The findings of this study are in line with the growing body of evidence supporting the effectiveness of TCM in managing osteoarthritis. Previous studies have shown similar trends, where integrated TCM approaches, particularly those involving acupuncture and herbal medicine, demonstrate improved outcomes in osteoarthritis management.[12–14,26,27] However, our study extends this knowledge by specifically focusing on Thunder Fire Moxibustion in combination with other TCM methods, a relatively less explored area in existing literature. The significant effect size observed in our analysis contrasts with some earlier studies that reported more modest benefits, possibly due to differences in study designs,

Table 3 GRADE Summary of Findings Table

Outcome	Studies (n, Participants)	Effect Estimate (95% CI)	Risk of Bias	Indirectness	Imprecision	Inconsistency	Publication Bias	Overall	Comments
Total effective rate	7 studies (n=655)	RR 1.119 (1.060 to 1.181)	Some concerns	Not serious	Not serious	Not serious	Minor concerns	Low	Although results were consistent across studies, the overall confidence is limited due to some risk of bias and minor publication bias.
Incidence of adverse reactions	2 studies (n = 190)	RR 0.572 (0.173 to 1.890)	Some concerns	Not serious	Serious	Not serious	Some concerns	Low	Due to the very small number of studies and wide confidence intervals, the evidence quality is low despite acceptable risk of bias and consistency.

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interventions used, and patient populations. This highlights the unique contribution of our study to the existing body of knowledge on TCM applications in osteoarthritis.

Additionally, the findings of this study underscore the importance of patient-centered approaches in managing chronic conditions like osteoarthritis. The positive response to Thunder Fire Moxibustion and other TCM modalities reflects a growing patient preference for treatments that align with a holistic health perspective. This trend encourages healthcare providers to consider integrating traditional and complementary medicine practices into mainstream healthcare, fostering a more inclusive and diverse therapeutic landscape.

Moreover, the economic implications of these findings warrant consideration. The integration of effective TCM treatments like Thunder Fire Moxibustion could potentially offer cost-effective alternatives to more expensive conventional treatments, particularly in settings where healthcare resources are limited. This aspect is particularly relevant for countries where access to affordable healthcare is a priority. Future economic analyses, focusing on the cost-effectiveness of such integrative treatments, could provide valuable insights for healthcare policy and decision-making.

The role of patient education and awareness in the adoption of TCM practices also cannot be overstated. Enhancing understanding and acceptance of TCM among patients and healthcare professionals is crucial for its successful integration. Educational initiatives and awareness programs could help in dispelling misconceptions about TCM and promote its evidence-based use in clinical practice.

Our findings suggest that the efficacy of Thunder Fire Moxibustion, when used in combination with other TCM practices, may be attributed to the holistic approach of TCM. Thunder Fire Moxibustion's heat therapy potentially enhances local circulation and reduces inflammation, which, when combined with the systemic balancing effects of acupuncture and herbal remedies, could offer a more comprehensive treatment for knee osteoarthritis. This aligns with TCM's principle of treating the whole body rather than isolated symptoms, potentially explaining the enhanced effectiveness observed in our study.[8,9]

One of the key strengths of this study is its rigorous methodology, including the use of a random-effects inverse-variance model, which adds robustness to our findings. Additionally, the inclusion of a significant number of participants across multiple studies providing precise estimates, consistency of findings during sensitivity analysis, additional subgroup analysis provides a solid basis for the conclusions drawn. However, the study is not without limitations. The presence of publication bias and the high risk of bias in some included studies could potentially affect the validity of the findings. These methodological issues highlight the need for cautious interpretation of the results and suggest an area for improvement in future research.

The implications for clinical practice from this review are significant. The demonstrated effectiveness of Thunder Fire Moxibustion in combination with acupuncture and herbal TCM suggests that such integrative approaches could be more widely adopted in the treatment of knee osteoarthritis. This could lead to more personalized, holistic treatment plans that align with patients' preferences for non-pharmacological interventions. For TCM practice, these findings reinforce the value of combining different modalities, potentially guiding practitioners in optimizing treatment strategies for osteoarthritis patients.

Future research should focus on long-term outcomes of these combined TCM treatments and explore their comparative effectiveness against conventional osteoarthritis treatments. Studies with larger sample sizes and diverse populations are needed to validate these findings further. Additionally, research into the mechanisms of action of these TCM modalities and their interactions could provide deeper insights into their therapeutic effects. It is also crucial to address the identified risks of bias and publication bias in future studies to enhance the quality and reliability of the evidence.

Data Sharing Statement

Data will be made available upon reasonable request from researchers.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work;.

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Disclosure

Wei Wei and Yeyu Qin are co-first authors for this study. The authors report no conflicts of interest in this work.

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