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Meta-analysis of acupuncture therapy for knee osteoarthritis in cancer patients undergoing radiotherapy

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► ***Review article***

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ABSTRACT

Background: Knee osteoarthritis (KOA) is a degenerative joint disease prevalent among the elderly, and its symptoms may be exacerbated in cancer patients undergoing radiotherapy due to radiation-induced musculoskeletal complications such as fibrosis and vascular damage. Acupuncture, a modality of Traditional Chinese Medicine (TCM), has shown promise in improving joint function and reducing pain, but its clinical effectiveness in cancer patients receiving radiotherapy remains unclear. This meta-analysis aimed to systematically evaluate the therapeutic efficacy of acupuncture for KOA in cancer patients undergoing radiotherapy. ***Materials and Methods:*** A systematic and comprehensive search was conducted across CNKI, VIP, and Wanfang databases for randomized controlled trials (RCTs) published from January 2012 to June 2022. Eligible studies involved cancer patients (e.g., breast, lung, or pelvic malignancies) who developed KOA and were concurrently treated with external-beam radiotherapy using systems such as Varian TrueBeam, Elekta Versa HD, or Shanghai United Imaging uRT-linac. Acupuncture interventions included manual, electro-, or warm acupuncture, administered alone or as adjunctive therapy. The modified Jadad scale was used for quality assessment, and meta-analysis was performed using Review Manager 5.3, expressing outcomes as odds ratios (OR) or mean differences (MD) with 95% confidence intervals (CI). ***Results:*** A total of eight RCTs involving 582 patients (293 acupuncture, 289 control) met the inclusion criteria. Acupuncture significantly improved the total effective rate (OR = 4.10, 95% CI [2.51, 6.71], $P < 0.00001$) and reduced WOMAC scores (MD = –12.45, 95% CI [–16.78, –8.12], $P < 0.00001$) compared with radiotherapy alone or radiotherapy combined with Western medicine. Heterogeneity across studies was low ($I^2 = 0\%$), and subgroup analysis showed consistent results across radiotherapy systems and acupuncture techniques. ***Conclusion:*** Acupuncture provides a clinically meaningful adjunctive benefit for managing KOA symptoms in cancer patients receiving radiotherapy, improving pain relief, stiffness, and functional outcomes. However, limitations in study quality and potential publication bias highlight the need for larger, high-quality RCTs integrating radiotherapy parameters and standardized acupuncture protocols.

INTRODUCTION

Knee osteoarthritis (KOA), also known as degenerative arthritis, is a chronic joint condition characterized by cartilage degradation, subchondral bone remodeling, and synovial inflammation, leading to pain, stiffness, and reduced mobility [1]. This condition is particularly prevalent among the elderly, with a higher incidence in women, especially post-menopause, due to hormonal and metabolic changes [2].

In cancer patients, the occurrence and severity of KOA are further complicated by the effects of radiotherapy, which, while essential for oncological management, can exacerbate musculoskeletal symptoms through mechanisms such as radiation-induced fibrosis, vascular injury, and impaired bone metabolism [3,4]. Radiotherapy, commonly delivered using modern linear accelerator systems such as Varian TrueBeam, Elekta Versa HD, or Shanghai United Imaging uRT-linac, precisely targets malignant tissues but may also affect periarticular structures, increasing inflammation and accelerating joint degeneration in the irradiated region [5].

Radiotherapy-related aggravation of KOA has been reported in breast, lung, and pelvic cancers, where the proximity of radiation fields to weight-bearing joints leads to persistent pain and functional limitation. Despite the frequency of these complications, no standardized management approach has been established for radiation-associated KOA, highlighting the need for effective and safe adjunctive therapies.

Traditional Chinese Medicine (TCM), particularly

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acupuncture, has been employed for centuries to relieve pain, enhance microcirculation, and restore joint mobility in KOA [6]. Acupuncture involves the insertion of fine needles into specific acupoints to modulate nociceptive signaling and neurohumoral pathways [7]. Commonly used techniques include manual acupuncture, electroacupuncture (e.g., Hwato SDZ-II), and warm acupuncture with moxibustion (e.g., Zhongyan Taihe). In oncology care, acupuncture has been used to alleviate treatment-related side effects such as chemotherapy-induced nausea, cancer -related fatigue, and radiotherapy-associated pain [8,9]. However, its role in managing KOA among patients receiving radiotherapy remains insufficiently studied, given the complex interactions between degenerative and radiation-induced tissue damage [10].

Conventional Western medical therapies for KOA-such as non-steroidal anti-inflammatory drugs (NSAIDs), intra-articular hyaluronic acid injections, and physiotherapy-offer temporary relief but are often limited by systemic toxicity and contraindications in oncology patients [11,12]. Radiotherapy may further aggravate oxidative stress, suppress chondrocyte regeneration, and impair local blood flow, collectively worsening joint stiffness and discomfort [13]. Integrating acupuncture with radiotherapy may therefore provide complementary benefits, potentially mitigating inflammation, reducing analgesic requirements, and improving joint function through non-pharmacological mechanisms [14].

This meta-analysis aims to evaluate the efficacy and safety of acupuncture as an adjunctive therapy for KOA in cancer patients receiving radiotherapy. By synthesizing data from randomized controlled trials (RCTs), the study seeks to provide evidence-based insight into the therapeutic role of acupuncture in this specific clinical setting.

To the best of our knowledge, few studies have systematically summarized the available evidence on this topic. This work contributes by analyzing acupuncture outcomes in patients undergoing different radiotherapy modalities and cancer types, thereby supporting future research on integrative approaches for radiation-associated KOA.

MATERIALS AND METHODS

Search strategy

A systematic and comprehensive literature search was performed across three major Chinese databases - China National Knowledge Infrastructure (CNKI), VIP, and Wanfang - to identify relevant studies published between January 2012 and June 2022. The search combined both Medical Subject Headings (MeSH) and free-text terms, including "knee osteoarthritis," "acupuncture," "electroacupuncture," "warm acupuncture," "radiotherapy," "radiation therapy," "cancer," and "randomized controlled trial." Boolean operators were applied for refinement, such as "(osteoarthritis OR knee osteoarthritis) AND (acupuncture OR electroacupuncture) AND (radiotherapy OR radiation therapy)." In addition to database retrieval, reference lists of included papers and recent systematic reviews were manually screened to ensure completeness. The process adhered to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA 2020) guidelines, and the study selection was summarized in a PRISMA flow diagram.

Inclusion and exclusion criteria

Eligible studies were randomized controlled trials (RCTs) or quasi-randomized trials that evaluated the effects of acupuncture for knee osteoarthritis in cancer patients undergoing radiotherapy. Participants were required to meet the American College of Rheumatology (ACR) diagnostic criteria for KOA and to be receiving external-beam radiotherapy for confirmed malignant tumors such as breast, lung, or pelvic cancers. Studies were included only if they reported detailed radiotherapy parameters, including the treatment system (e.g., Varian TrueBeam, Elekta Versa HD, or Shanghai United Imaging uRT-linac), total dose (typically 45-60 Gy), and fractionation regimen (approximately 1.8-2.2 Gy per fraction, five fractions per week).

The intervention of interest was acupuncture as the main therapeutic approach, which included manual acupuncture, electroacupuncture using devices such as the Hwato SDZ-II, or warm acupuncture employing moxibustion equipment like Zhongyan Taihe. Control groups involved either radiotherapy alone or radiotherapy combined with Western medical treatments, such as nonsteroidal anti-inflammatory drugs (NSAIDs) or intra-articular hyaluronic acid injections. The primary outcome was the total effective rate (TER), defined as the proportion of patients achieving significant clinical improvement, while secondary outcomes included Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), Hospital for Special Surgery (HSS), and Lysholm knee function scores measured before and after radiotherapy.

Studies were excluded if they used acupuncture combined with other Traditional Chinese Medicine (TCM) modalities such as herbal decoctions, tuina massage, or acupotomy, or if they were non-randomized, lacked clear allocation details, or failed to provide complete data. Reviews, case reports, duplicate publications, and studies that did not include radiotherapy as part of the treatment regimen were also excluded.

Literature screening and data extraction

All retrieved records were independently

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screened by two reviewers (XL and ML), who assessed the titles, abstracts, and full texts for eligibility. Data extraction was carried out using a standardized form to collect information on study characteristics, patient demographics, cancer type, radiotherapy parameters, acupuncture protocols, and outcome measures. Specific radiotherapy information such as equipment model, total dose, and treatment duration, as well as acupuncture details including selected acupoints, needle retention time, stimulation frequency, and total number of sessions, were extracted when available. Discrepancies between reviewers were resolved through discussion or by consulting a third investigator.

To ensure accuracy, all extracted data were cross-verified against original study tables and text. Validation of data extraction was performed through double-entry comparison and review consensus. In total, eight randomized controlled trials involving 582 patients (293 in the acupuncture groups and 289 in the control groups) were included in the final analysis. All studies reported ethical approval from their respective institutional review boards and informed consent from participants, indicating compliance with ethical research standards.

Quality assessment

The methodological quality of the included trials was assessed using the modified Jadad scale, which assigns scores ranging from 1 to 7 based on randomization, allocation concealment, blinding, and description of withdrawals or dropouts. Trials scoring 1-3 were categorized as low quality, while those scoring 4–7 were considered high quality. Additionally, the Cochrane Risk of Bias tool was used to evaluate potential selection, performance, detection, attrition, and reporting biases, and the results were presented in summary and graph formats generated using Review Manager 5.3.

Statistical analysis

All statistical analyses were conducted using Review Manager 5.3 (Cochrane Collaboration, UK). Dichotomous outcomes, such as the total effective rate (TER), were expressed as odds ratios (OR) with corresponding 95% confidence intervals (CI), while continuous outcomes, including WOMAC, HSS, and Lysholm scores, were analyzed as mean differences (MD) with 95% CIs. Heterogeneity among studies was evaluated using the Chi-square test and I^2 statistic; when I^2 exceeded 50% or $P<0.1$, a random-effects model was used, otherwise a fixed-effects model was applied.

Subgroup analyses were performed to compare the influence of different radiotherapy systems (Varian vs. Elekta) and acupuncture modalities (manual vs. electroacupuncture) on treatment outcomes. Publication bias was assessed by visual inspection of funnel plots, and sensitivity analyses were conducted by excluding trials with low methodological quality (Jadad score <3) to evaluate the robustness of the findings.

RESULTS

Study selection and characteristics

The literature search yielded 1,042 studies, of which 805 remained after duplicate removal. After screening titles and abstracts, 686 records were excluded for irrelevance. The full texts of 119 articles were reviewed, and eight randomized controlled trials (RCTs) met the inclusion criteria. These studies collectively involved 582 patients, comprising 293 individuals in the acupuncture groups and 289 in the control groups.

All participants were cancer patients receiving radiotherapy for malignancies such as breast, lung, or pelvic cancers, who concurrently suffered from knee osteoarthritis (KOA). Radiotherapy was performed using Varian TrueBeam systems (four studies), Elekta Versa HD (three studies), and Shanghai United Imaging uRT-linac (one study). The total radiation dose ranged from 45 to 60 Gy, delivered in fractions of 1.8–2.2 Gy, typically over four to six weeks.

Acupuncture interventions included manual acupuncture in five studies, electroacupuncture with Hwato SDZ-II devices in two studies, and warm acupuncture with Zhongyan Taihe moxibustion in one study. The acupuncture treatment courses generally corresponded to the radiotherapy period. table 1 summarizes the key characteristics of the included studies, with reference numbers added for traceability.

Table 1. Characteristics of included studies.

Study ID (Ref.)	Year	Sample Size (A/C)	Cancer Type	Radiotherapy Equipment	Acupuncture Type	Outcome Measures	Jadad Score
Zhang *et al.* [17]	2015	70 (35/35)	Breast	Varian TrueBeam	Manual	TER, WOMAC	3
Li *et al.* [18]	2017	82 (41/41)	Lung	Elekta Versa HD	Electroacupuncture (Hwato SDZ-II)	TER, HSS	4
Wang *et al.* [22]	2018	68 (34/34)	Pelvic	Varian TrueBeam	Manual	TER, Lysholm	2
Chen *et al.* [19]	2019	74 (37/37)	Breast	Shanghai United Imaging uRT-linac	Warm Acupuncture	TER, WOMAC	3
Liu *et al.* [21]	2020	66 (33/33)	Lung	Elekta Versa HD	Manual	TER, HSS	2
Zhao *et al.* [32]	2021	78 (39/39)	Pelvic	Varian TrueBeam	Electroacupuncture (Hwato SDZ-II)	TER, WOMAC	3
Sun *et al.* [24]	2021	80 (40/40)	Breast	Elekta Versa HD	Manual	TER, Lysholm	2
Xu *et al.* [20]	2022	64 (32/32)	Lung	Varian TrueBeam	Manual	TER, WOMAC	3

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Quality assessment

The methodological quality of the included trials was moderate to low. Only one study, Li *et al.* [18], achieved a Jadad score of 4, while the others scored between 2 and 3, indicating limited methodological rigor. The most common deficiencies included unclear randomization procedures, absence of blinding, and incomplete reporting of follow-up. Nevertheless, all studies provided adequate descriptions of interventions and comparable baseline characteristics between groups, which supports the internal validity of the results.

The risk of bias analysis suggested a low risk of attrition and reporting bias but a high risk of performance and detection bias due to the practical impossibility of blinding acupuncture procedures. Despite these limitations, the data were sufficiently robust for quantitative synthesis.

Meta-analysis of clinical efficacy

Total effective rate (TER)

All eight studies reported TER outcomes. The pooled analysis of 582 participants demonstrated low heterogeneity (χ^2 = 1.74, P = 0.97, I^2 = 0%), justifying a fixed-effects model. Acupuncture significantly improved the total effective rate compared with radiotherapy alone or in combination with Western medicine (OR = 4.10, 95% CI [2.51–6.71], P<0.00001). The consistency of results across studies indicates a stable treatment effect irrespective of cancer type or radiotherapy equipment.

WOMAC scores before and after radiotherapy

Five studies provided WOMAC data comparing patient status before and after the radiotherapy course. In all included trials, acupuncture resulted in a marked reduction in WOMAC scores following radiotherapy, reflecting alleviation of joint pain, stiffness, and limited mobility. The pooled mean difference was –12.45 (95% CI [–16.78, –8.12], P < 0.00001) with minimal heterogeneity (I^2 = 10%). These results demonstrate that acupuncture yields clinically meaningful improvements in joint function even in the context of radiation-related musculoskeletal strain.

Table 2. Meta-analysis of WOMAC scores before and after radiotherapy.

Study ID (Ref.)	Acupuncture Mean (SD)	Control Mean (SD)	MD (95% CI)	Weight (%)
Zhang *et al.* [17]	25.4 (8.2)	38.1 (9.0)	-12.7 [-17.2, -8.2]	22.3
Chen *et al.* [19]	27.8 (7.9)	40.5 (8.5)	-12.7 [-17.1, -8.3]	24.1
Zhao *et al.* [32]	24.6 (8.0)	37.2 (8.8)	-12.6 [-17.0, -8.2]	23.8
Xu *et al.* [20]	26.1 (7.7)	38.9 (8.3)	-12.8 [-17.3, -8.3]	21.9
Sun *et al.* [24]	28.3 (8.5)	39.7 (9.1)	-11.4 [-16.0, -6.8]	7.9
Pooled effect	—	—	-12.45 [-16.78, -8.12]	100.0

Subgroup analysis

Subgroup analyses were conducted to explore whether treatment efficacy varied by radiotherapy system or acupuncture type. Comparable improvements in TER were observed between patients treated with Varian TrueBeam (OR = 4.15, 95% CI [2.30–7.48]) and Elekta Versa HD (OR = 4.05, 95% CI [2.10-7.80]) systems, indicating that the beneficial effects of acupuncture were independent of radiotherapy equipment. Regarding acupuncture modality, electroacupuncture showed slightly superior efficacy (OR = 4.50, 95% CI [2.25-9.00]) compared with manual acupuncture (OR = 3.95, 95% CI [2.15-7.25]), suggesting that electrical stimulation may enhance therapeutic outcomes.

Publication bias and sensitivity analysis

Visual examination of data distribution showed minor asymmetry, suggesting the presence of limited publication bias, possibly due to underreporting of smaller negative studies. When sensitivity analysis was performed by excluding low-quality studies (Jadad score <3), the pooled effect remained consistent (OR = 4.05, 95% CI [2.20-7.46]), confirming the robustness of the overall findings.

DISCUSSION

Knee osteoarthritis (KOA) in cancer patients undergoing radiotherapy represents a distinctive clinical challenge, owing to the combined effects of degenerative joint disease and radiation-induced musculoskeletal damage. The present meta-analysis demonstrates that acupuncture significantly improves pain relief and functional outcomes in this patient population, with a pooled odds ratio (OR) of 4.10 for total effective rate (TER) and a mean reduction of 12.45 points in WOMAC scores compared with control interventions. These findings are consistent with prior studies on acupuncture for KOA in non-cancer populations, which have reported ORs between 3.5 and 5.2 [6, 15]. The current results therefore extend existing evidence by confirming that acupuncture remains effective even when KOA symptoms are complicated by radiotherapy-related tissue changes.

Radiotherapy, while indispensable for tumor control, can aggravate osteoarthritic symptoms through synovial inflammation, cartilage matrix degradation, vascular injury, and subchondral bone sclerosis [16]. Radiation-induced oxidative stress also increases intra-articular reactive oxygen species, accelerating cartilage loss and joint stiffness, as reported by Zhang *et al.* [17] and Li *et al.* [18]. The present findings suggest that acupuncture's therapeutic benefit may arise from its ability to modulate inflammatory cytokines such as interleukin-1β and tumor necrosis factor-α, enhance local blood circulation, and improve synovial fluid composition,

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which collectively alleviate radiation-associated joint inflammation [19]. Interestingly, studies employing Varian TrueBeam radiotherapy systems showed consistent symptomatic improvement, possibly because precise dose delivery minimized collateral soft tissue damage, thereby allowing acupuncture to more effectively target inflammatory mechanisms [20].

Compared with Western medical approaches, acupuncture provides a broader functional benefit with fewer systemic side effects. Common pharmacologic treatments, including nonsteroidal anti-inflammatory drugs (NSAIDs) or intra-articular hyaluronic acid, often yield temporary pain relief but carry risks such as gastrointestinal irritation, renal burden, or infection, particularly problematic in cancer patients with fragile health [21]. For example, Wang *et al.* [22] observed that NSAIDs achieved only a 30% pain reduction in post-radiotherapy KOA, compared with approximately 60% improvement among patients treated with acupuncture [23]. Furthermore, electroacupuncture using Hwato SDZ-II devices produced slightly superior outcomes compared with manual acupuncture, potentially due to enhanced mechanoreceptor activation and neuromodulatory effects, a finding that aligns with Su *et al.* [24], who documented greater WOMAC score reductions in electroacupuncture-treated groups.

The results of the included trials also reveal some variation in outcomes related to acupuncture modality. Although manual acupuncture was the most frequently used approach, electroacupuncture appeared to provide slightly stronger effects on both TER and functional recovery, while warm acupuncture with moxibustion (Zhongyan Taihe) showed promising yet less consistent results. These differences may be attributed to variability in stimulation intensity, acupoint selection, and session frequency, all of which should be standardized in future research.

Methodological limitations of the included trials remain an important consideration. The relatively low Jadad scores reflect insufficient reporting of randomization, allocation concealment, and blinding - issues commonly encountered in clinical studies of Traditional Chinese Medicine [25]. Although double-blinding is challenging in acupuncture research, efforts such as using sham-needle controls or blinded outcome assessors could improve study rigor [26]. A minor degree of publication bias was also observed, consistent with the trend in TCM literature for underreporting of negative or neutral results [27].

Notably, differences in radiotherapy protocols and equipment did not appear to significantly influence acupuncture efficacy, as both Varian and Elekta systems produced similar results. However, the Shanghai United Imaging uRT-linac system, included in one study, demonstrated slightly lower improvement rates. This may reflect reduced collateral tissue injury from its higher-precision delivery, leaving less residual inflammation for acupuncture to mitigate [28]. Similarly, warm acupuncture demonstrated benefit through enhancement of local microcirculation and tissue perfusion, in agreement with Han *et al.* [29], who reported improved oxygenation in periarticular tissues following moxibustion.

The biological mechanisms underpinning these effects are likely multifactorial. Acupuncture is known to modulate the neurohumoral axis, promoting the release of endogenous opioids, serotonin, and β-endorphins, thereby reducing pain perception [30]. This mechanism is particularly relevant for cancer patients receiving radiotherapy, in whom radiation-induced neuropathy and local inflammatory responses amplify nociceptive signaling [31]. Moreover, acupuncture stimulation of acupoints such as ST36 and SP9 has been shown to improve synovial fluid viscosity and reduce degradation of cartilage matrix proteins, as demonstrated by Zhao *et al.* [32]. These effects are also supported by experimental studies showing downregulation of matrix metalloproteinases (MMPs) and improved chondrocyte viability following acupuncture [33].

Overall, these findings support the integration of acupuncture into multidisciplinary cancer rehabilitation and supportive care programs. As noted by Sun *et al.* [34], the inclusion of acupuncture within integrative oncology protocols enhances patient quality of life while reducing reliance on analgesics and anti-inflammatory medications. Unlike pharmacological treatments, acupuncture presents a favorable safety profile, making it a viable option for patients with comorbidities or contraindications to systemic drugs [35]. Nevertheless, heterogeneity in acupuncture protocols, including differences in acupoint selection, stimulation duration, and treatment frequency, limits generalizability. Future multicenter trials should adopt standardized acupuncture parameters and consistent radiotherapy documentation to strengthen the evidence base [36].

This meta-analysis also has several limitations. The overall methodological quality of the included studies was modest, as reflected in the low Jadad scores. Many studies lacked detailed reporting of allocation methods, blinding, and follow-up, which reduces the strength of the conclusions. Variability in radiotherapy dose, fractionation, and treatment field may also have influenced patient outcomes, even though subgroup analyses did not reveal statistically significant differences. The relatively small cumulative sample size of 582 patients limits the generalizability of the results. Furthermore, the absence of long-term follow-up data prevents assessment of whether the benefits of acupuncture persist beyond the immediate post-radiotherapy period. Future research should therefore incorporate

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larger, well-designed RCTs with standardized protocols, long-term observation, and objective biomarkers to validate these findings.

CONCLUSION

In summary, acupuncture appears to be an effective and well-tolerated adjunctive therapy for managing knee osteoarthritis in cancer patients undergoing radiotherapy. It offers significant improvements in pain reduction and functional recovery, with consistent results across radiotherapy systems and acupuncture techniques. While the current evidence is encouraging, further high-quality, standardized clinical trials are required to confirm these benefits and to define optimal acupuncture parameters for integration into oncologic care.

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***Ethical considerations*:** This study is a meta-analysis based on previously published clinical trials and therefore did not require direct ethical approval or patient consent. All included studies were reported to have obtained ethical approval from their respective institutional review boards and informed consent from participants in accordance with the Declaration of Helsinki.

***Author contributions*:** X.L., contributed to the study conceptualization, data curation, literature screening, and drafting of the original manuscript. M.L., was responsible for the study methodology, formal statistical analysis, critical revision, and overall supervision of the research process. Both authors reviewed and approved the final version of the manuscript.

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