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Review

Acupressure for Managing Osteoarthritis: A Systematic Review and Meta-Analysis

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Abstract: This review aims to evaluate the effectiveness of acupressure as a treatment method for osteoarthritis. Fourteen electronic databases were searched from the date of inception until 16 March 2021, for eligible studies. Studies comparing acupressure with sham acupuncture, no intervention or conventional intervention were eligible for inclusion. The risk of bias of the included studies was assessed using the Cochrane Collaboration's Risk of Bias Assessment tool Version 2.0. A total of eight trials were included in this review, focusing on the seven trials investigating knee osteoarthritis. The risk of bias is judged as low in only two trials and concerning in the remaining six trials. The meta-analysis showed that acupressure has equivalent effects in reducing pain ($p = 0.12$), relieving stiffness ($p = 0.38$), and improving physical function ($p = 0.12$), as compared to sham acupressure. Pooled results also showed similar results where acupressure has an equivalent effect in reducing pain ($p = 0.09$), and relieving stiffness ($p = 0.68$), but showed a favorable effect in improving physical function of joints (MD –6.30, CI 95%: −11.69 to −0.92, $p = 0.02$), as compared to no intervention. For acupressure complementing conventional intervention, pooled results showed superior effects for easing pain compared to conventional intervention alone (MD −3.72, 95% CI: −4.84 to −2.61, $p < 0.00001$). Overall, the studies included in this review have concerning quality and suffer from small sample sizes, and the findings of this review should be interpreted with caution. More clinical trials with proper methodology are needed to confirm the effectiveness of acupressure for osteoarthritis.

Keywords: acupoint massage; adjunctive therapy; complementary therapy; degenerative arthritis; musculoskeletal diseases

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1. Introduction

Osteoarthritis (OA) is a common joint disease, which is linked to joint degeneration, loss of cartilage, and alterations of the subchondral bone, and mainly affects the hands, knees, and hips [1,2]. OA is a highly predominant health condition, which has affected over 260 million people worldwide [3], and it is becoming even more common due to the combined effects of aging and obesity [4]. OA is even more problematic as it is associated with pain, disability, and personal and economic burden [5].

In terms of the treatment of OA, currently, there is no cure [4,5]. Still, there are many treatment approaches for the management of osteoarthritis, and they are generally non-pharmacologic, pharmacologic, surgical, or complementary and alternative approaches [6]. In particular, clinical practice guidelines for hip and knee OA suggest interventions such as patient education, exercise, and weight management as first-line treatments, pharmacological therapies and other therapies as second-line treatment, and surgical interventions for replacement as third-line treatment [7]. The complementary and alternative approaches,

including acupuncture, yoga, manual therapy, and electrotherapy, are recommended for the OA treatment by the National Clinical Guideline Centre in United Kingdom and the American Academy of Orthopedic Surgeons (AAOS) [8]. Among the complementary and alternative options for the treatment of OA, the clinical evidence of dry needling [3], moxibustion [2], and yoga [9] have been systematically evaluated, but the clinical evidence of acupressure for OA treatment has not been systematically examined yet.

Acupressure is a non-invasive and cost-efficient medical approach and involves applying pressure to the acupoints or meridian points as practiced in Chinese Medicine [10]. Acupressure has been used for various purposes. Previous systematic reviews have investigated the efficacy or the impact of acupressure as a sole intervention on pain [11], low back pain [10,12], labor or labor pain [13–15], neck pain syndrome [16], sleep quality, or sleep disorders [17–19], promoting the health of older adults [20], respiratory allergic diseases [21], postoperative gastrointestinal symptoms [22], chemotherapy-induced nausea and vomiting [23], primary dysmenorrhea [24–26], anxiety [27], neurological disorders [28], and symptom management [29–31]; and other reviews considered acupressure as a complementary intervention with acupuncture on cancer pain [32], cancer-related fatigue [33], weight reduction [34], uremic pruritus [35], premenstrual syndrome [36], and labor pain [37].

This review aims to add to the existing literature on acupressure as a treatment method for osteoarthritis by systematically reviewing clinical trials for its clinical efficacy.

2. Methods

2.1. Search Strategy

Two authors performed the systematic literature search from the date of inception until 16 March 2021, in the following 14 electronic databases: The Cochrane Library, PubMed, Embase, Allied and Complementary Medicine Database (AMED), 4 Chinese databases (The Chinese National Knowledge Infrastructure Database (CNKI), Chinese Biomedical Literature Database (CBM), Wanfang Database, and Chinese Science and Technique Journals Database (VIP)), and 6 Korean databases (Korean Association of Medical Journal database (KoreaMed), Oriental Medicine Advanced Searching Integrated System (OASIS), Research Information Service System (RISS), Korean Studies Information Service System (KISS), and DBpia). The search terms were "acupressure" and "osteoarthritis" in English, Chinese, and Korean. The detailed search strategy is provided in Supplement S1. We restricted our searches to studies published in English, Chinese and Korean. The use of indexing terms, such as medical subject headings (MeSH), was applied for wider search coverage. Clinical trial registries were also searched at The National Institutes of Health clinical trials registry and the WHO International Clinical Trials Registry Platform. All of the searches were re-conducted before the completion of this review to retrieve any further eligible studies.

2.2. Eligibility Criteria

2.2.1. Types of Studies

Studies were eligible if they were randomized controlled trials (RCTs) that included acupressure as a sole or complementary intervention for any type of osteoarthritis. Thesis and dissertations were also eligible. Clinical studies with quasi-experiment designs, observational studies, such as case-control studies, cohort studies, cross-sectional, case series, and case reports, conference proceedings, and abstracts were excluded.

2.2.2. Participants

Participants who were diagnosed with osteoarthritis (OA) in any joints or multiple joints were eligible, regardless of their age, sex and ethnicity. Studies including participants with other types of arthritis or several rheumatic disorders, where data of OA participants cannot be separated, were not eligible.

2.2.3. Intervention Groups

Studies were included if acupressure is used as a sole therapy. Studies where the intervention group received acupressure in adjunction to the therapy received by the control group were also eligible. There were no limitations on the application method, acupoint selection, and treatment course. Combined interventions of other alternative therapies such as acupuncture, moxibustion, acupoint injection, and auricular acupressure were excluded as they share similar therapeutic effects and the evaluation of the effectiveness of acupressure will be affected. Other forms of massage such as Tuina, reflexology, and trigger point massage were also not eligible.

2.2.4. Comparison Groups

Comparison groups that received sham acupuncture, no intervention or conventional intervention of first-line (e.g., patient education, rehabilitation), second-line (e.g., pharmacological therapies, viscosupplementation), and third-line treatment (e.g., surgical interventions) were eligible. Comparator groups that use similar interventions or complex interventions affecting the evaluation of acupressure effects were excluded.

2.2.5. Outcome Measures

The primary outcomes were pain, stiffness, and physical function of the joint as measured by validated instruments. Those instruments include Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), Lequesne index, Multidimensional Health Assessment Questionnaire (MDHAQ), and Arthritis Impact Measurement Scales (AIMS) for multidimensional measures, and visual analogue score (VAS) and numeric rating scale (NRS) for pain measures. Outcomes measured with other kinds of disease-specific validated instruments were also eligible. The secondary outcomes were quality of life (QoL) and adverse events (AEs).

2.3. Study Selection and Data Extraction

Two review authors (LA and ES) searched the databases independently, removed duplicates, and assessed the eligibility of the studies. Based on the predefined inclusion criteria, the potentially eligible studies were screened with the full texts. Any discrepancies in the selection of a study for inclusion in this review were discussed with a third review author (MSL) until a consensus was reached.

For data extraction, the two review authors (LA and ES) independently extracted the data using a standard data extraction form. The following information was extracted: first author's last name, publication year, country, study design, sample size (total number and male/female numbers), patient age, type of OA, disease course (years and severity), details of the interventions and controls (regimens), outcome measures, study results, and adverse events. All disagreements between the two authors' judgments were resolved with the third review author (MSL) through discussion. The authors of the included studies were contacted for unreported data or missing data.

2.4. Assessment of Risk of Bias

Two review authors (LA and ES) individually assessed the risk of bias of the included studies using the Cochrane Collaboration's Risk of Bias Assessment tool Version 2.0 (RoB 2.0). The five domains of bias including (1) randomization process, (2) deviations from intended interventions, (3) missing outcome data, (4) measurement of outcome, and (5) selection of the reported results were assessed for each included study. The judgment of each domain was categorized into 'low', 'high', or 'some concerns' risk of bias. Any disagreements over a specific domain or study were resolved through discussion or with the involvement of all authors when necessary.

2.5. Data Analysis

All data analyses were performed using Review Manager (RevMan) version 5.4.1 software program for Windows (The Nordic Cochrane Centre, The Cochrane Collaboration, Copenhagen, Denmark). The mean differences (MDs) with 95% confidence intervals (CIs) were presented for the treatment effect of continuous outcomes, while risk ratios (RRs) or odds ratios (ORs) with 95% CIs were presented for the treatment effect of dichotomous outcomes. The standardized mean difference (SMD) with 95% Cis were used for outcomes measured with different scales.

The heterogeneity levels of the included studies were assessed using the chi-square test and I^2 statistics. As there were only a few studies included in this review, subgroup analysis was not performed. As the variability between the included studies was taken into consideration, the random-effects model was used for the meta-analysis of outcome measures. Subgroup analyses were not performed due to insufficient studies included. We attempted to evaluate the publication bias using a funnel plot but the included studies were relatively few to allow this.

3. Results

3.1. Literature Search

The searches identified 2214 records and 2091 records were screened for eligibility using title and abstracts. The full text of 55 records was retrieved after the exclusion of 2036 records due to the type of study. Forty-seven randomized controlled trials (RCTs) were then excluded based on the predefined inclusion and exclusion criteria, of which 36 trials used combined therapy of acupressure and other alternative therapies as intervention, nine trials used acupuncture, massage, and other alternative therapies as comparator, one trial employed quasi-experimental design, and one trial assessed the feasibility and fidelity of participants, which is inappropriate for the outcome assessment of this review. Finally, a total of eight RCTs [38–45] met the inclusion criteria and were included in this review for further analysis. The study selection flow diagram is presented in Figure 1.

3.2. Study Characteristics

Of the eight RCTs, two [40,41] originated from United States, two [44,45] originated from China, two [38,39] were from Iran, and one [43] from India. Four RCTs [38–40,44] adopted a three-arm parallel design, three RCTs [41–43] adopted a two-arm parallel design and one RCT [45] adopted a four-arm parallel design. The number of participants in the trials varied from 35 to 212, with a total of 873 participants. Participants were diagnosed with knee OA according to American College Rheumatology (ACR) criteria in three RCTs [39,40,42] and TCM criteria of diagnosis and therapeutic effect of diseases and syndromes (TCM-DTDS) in one RCT [44], whereas the other three RCTs [38,41,43] did not provide relevant information. Participants in the remaining RCT [45] were diagnosed with cervical OA, also known as cervical spondylosis, based on TCM-DTDS.

As there is only one RCT [45] investigated on the effectiveness of acupressure for cervical OA, we are unable to further analyze the data or compute relevant pooled effects. Therefore, the results of this RCT are presented in Appendix A and the results of the remaining seven RCTs will be presented in the Results section as below. Key data from the seven RCTs investigating knee OA are summarized in Table 1.

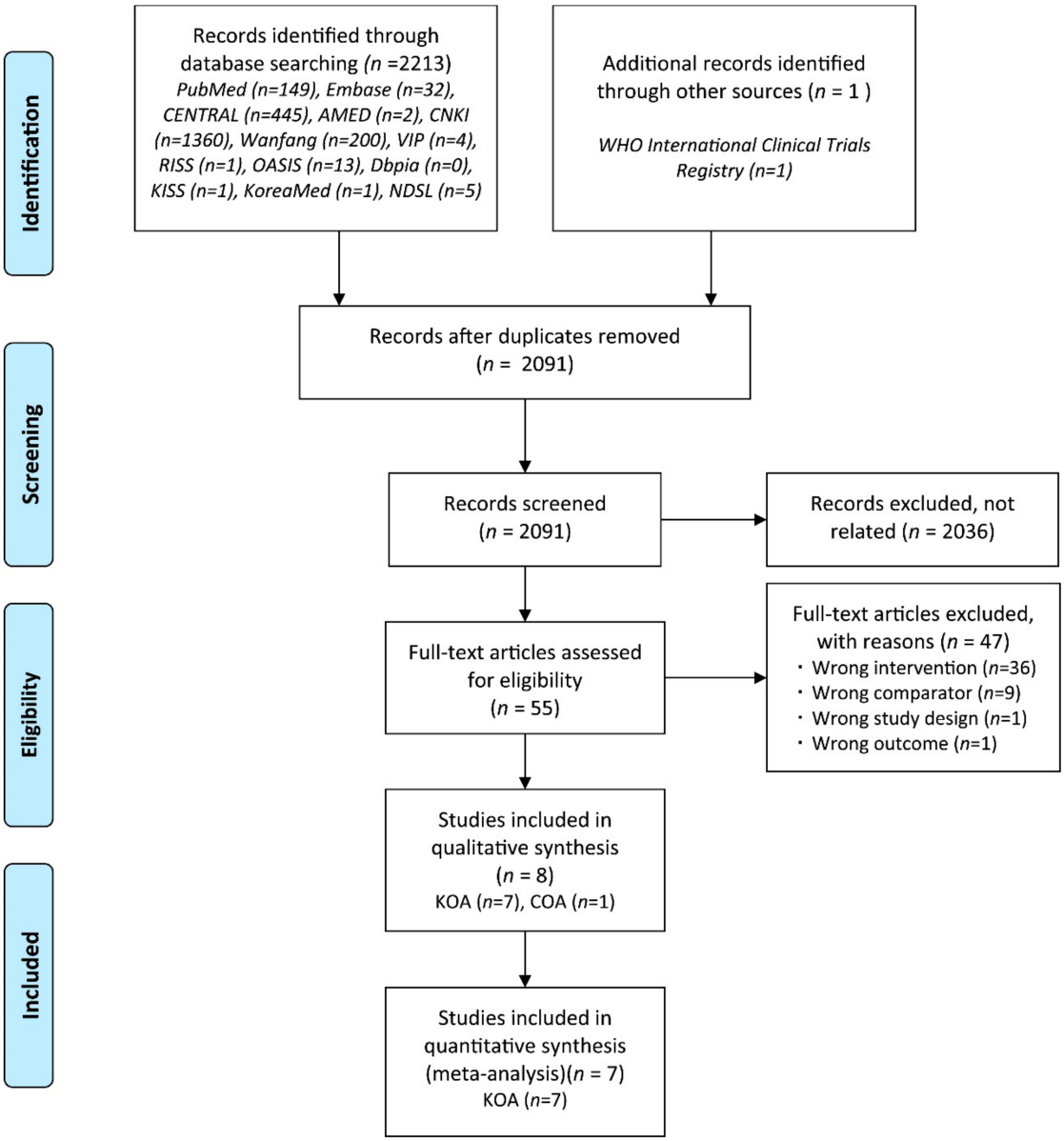


Figure 1. Study selection process. COA: cervical osteoarthritis, KOA: knee osteoarthritis.

For the intervention group, five RCTs [38–42] used acupressure as the sole intervention and two RCTs [43,44] used acupressure as the complementary intervention. As the choice of comparator, four RCTs used no intervention [38–41] while the other three RCTs each used knee health education (conventional first-line treatment) [42], pharmacological treatment (conventional second-line treatment) [43], and viscosupplementation (conventional second-line treatment) [44]. Six RCTs [38–42] reported that participants continued their usual care, whereas two RCTs did not provide relevant information. For outcome measures, five RCTs used WOMAC [38–42] and two RCTs used VAS [43,44]. Other tools used to measure the outcome include NRS, 36-Item Short-Form Health Survey (SF-36), and Short-Form Six-Dimension (SF-6D). The most frequently used acupoints in the RCTs were ST34, ST36, SP9, SP10, and GB34 [38,39,41–44], followed by ST35 and EX-LE4, and then other points.

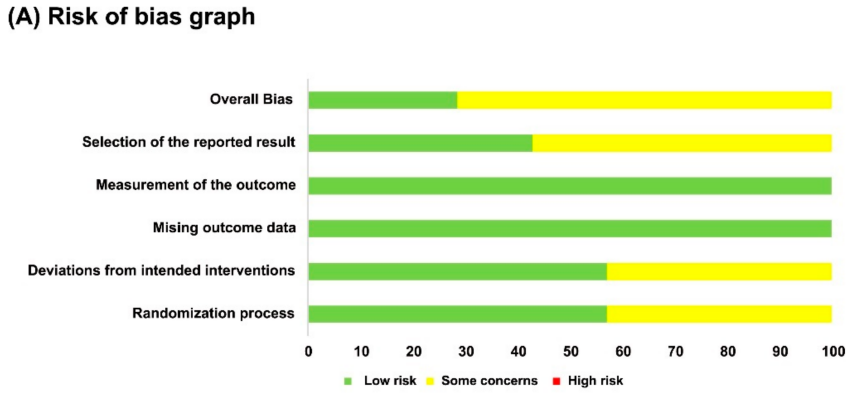
Table 1. Summary of included studies.

	Sample Size (N, M/F) Age (Mean) Type of OA (Diagnostic Criteria) Disease Course (yrs, Severity)	Intervention (Regimen, *n* = Randomized/Analyzed)	Control (Regimen, *n* = Randomized/Analyzed)	Outcome Measures	Main Results	Adverse Events (AEs) Study Design (Trial Registration Number) Country Notes
Akbarnezhad 2019 [38]	49 (19/30) 60–95 KOA (n.r.) 1->15 (Grade II to III)	(A) Acupressure (Trained personnel, 3 times weekly for 3 weeks, *n* = 15/14)] Acupoints: ST34, ST35, EX-LE4, EX-LE2, GB34, SP10, SP9, ST36	(B) Sham acupressure (manipulation of points selected away from the real acupoint with gentle pressure, *n* = 15/14) (C) No intervention (*n* = 21/21)	(1) Pain (WOMAC †) (2) Stiffmess (WOMAC †) (3) Function (WOMAC †) (4) WOMAC (Total)	(1) A vs. B: MD −4.93 [−6.89, −2.97], $p < 0.001$; A vs. C: MD −6.34 [−7.69, −4.99], $p < 0.001$ (2) A vs. B: MD −0.50 [−1.57, 0.57], NS; A vs. C: MD −0.69 [−1.57, 0.19], NS (3) A vs. B: −10.14 [−16.90, −3.38], $p < 0.05$; A vs. C: MD −15.69 [−22.15, −9.23], $p < 0.001$ (4) A vs. B: MD −15.57 [−24.21, −6.93], $p < 0.001$; A vs. C: MD −22.71 [−30.47, −14.95], $p < 0.001$	n.r. 3-arm parallel study (IRCT20150415217 58N2) Iran
Jaberi 2019 [39]	96 (31/65) 70.28 KOA (ACR) n.r.	(A) Acupressure (Trained personnel, 3 times weekly for 3 weeks, *n* = 32/32) Acupoints: LI4, SP10, SP9, GB34, ST36, ST34	(B) Sham acupressure (manipulation of points selected near the real acupoints of similar patterns without pressure, *n* = 32/32) (C) No intervention (*n* = 32/32)	(1) Pain (WOMAC †) (2) Stiffness (WOMAC †) (3) Function (WOMAC †) (4) WOMAC (Total)	(1) A vs. B: MD−0.47 [−1.97, 1.03], NS; A vs. C: MD −1.41 [−2.76, −0.06], $p < 0.05$ (2) A vs. B: MD −0.16 [−0.87, 0.55], NS; A vs. C: MD 0.68 [−0.00, 1.36], NS (3) A vs. B: MD 0.00 [−3.73, 3.73], NS; A vs. C: MD −2.56 [−6.03, 0.91], NS (4) A vs. B: MD −0.63 [−6.15, 4.89], NS; A vs. C: MD −3.29 [−8.26, 1.68], NS	n.r. 3-arm parallel study (IRCT20180114038366N1) Iran
Li 2018 [40]	150 (98/62) 72.7 KOA (ACR) n.r.	(A) Acupressure (Self-administered, 5 days weekly for 8 weeks, *n* = 50/41) Acupoints: EX-HN3, EX-HN16, HT7, SP6, LV3	(B) Sham acupressure (manipulation of points that were not on meridians with pressure, *n* = 50/41) (C) No intervention (*n* = 50/42)	(1) Pain (WOMAC †) (2) Pain (NRS †,*) (3) Function ((WOMAC †)	(1) A vs. B: MD −0.70 [−1.93, 0.53], NS; A vs. C: MD −1.50 [−2.84, −0.16], $p < 0.05$; (2) A vs. B: *, NS; A vs. C: *, $p < 0.05$ (3) A vs. B: MD −3.90 [−7.90, 0.10], NS; A vs. C: MD −5.50 [−9.57, −1.43], $p < 0.05$	Broken skin and soreness at simulation site (no details given) 3-arm parallel study (NCT02003443) United States
Zhang 2012 [41]	36 (0/36) 61.67 KOA (n.r.). >6 months (n.r.)	(A) Acupressure (Self-administered, once daily, 5 days weekly for 12 weeks, *n* = 15/15) Acupoints: ST34, ST35, ST36, SP9, SP10, GB34, EX-LE2, EX-LE4	(B) No intervention (*n* = 21/21)	(1) Pain (WOMAC †) (2) Stiffmess (WOMAC †) (3) Function (WOMAC †) (4) WOMAC (Total) (5) QoL (SF−36 ††,*)	(1) MD 0.08 [−2.36, 2.52], NS (2) MD −0.94 [−2.29, 0.41], NS (3) MD −1.88 [−10.58, 6.82], NS (4) MD −3.74 [−15.65, 8.17], NS (5) *, NS	none 2-arm parallel study (n.r.) United States
Cheung 2020 [42]	35 (8/27) 62.14 KOA (ACR) 4.29 (n.r.)	(A) Acupressure (Self-administered, twice daily for 6 weeks, *n* = 17/17) Acupoints: ST34, ST35, ST36, SP9, SP10, GB34, EX-LE2, EX-LE4	(B) Knee health education (self-care strategies, *n* = 18/18)	(1) Pain (WOMAC †) (2) Pain (NRS †) (3) Stiffness (WOMAC †) (4) Function (WOMAC †) (5) QoL (SF-6D ††)	(1) MD 0.54 [0.07, 1.01], $p < 0.05$ (2) Current pain, MD −0.60 [−0.84, −0.36], $p < 0.001$; worst pain, MD −0.39 [−0.67, −0.11], $p < 0.01$; least pain, MD 0.13 [−0.15, 0.41], NS (3) MD −0.04 [−0.32, 0.24], NS (4) MD −0.85 [−2.60, 0.90], NS (5) MD −0.07 [−0.09, −0.05], $p < 0.001$	Pain at simulation sites (A:3), worsening of knee pain (A:2), pricking pain sensation on the legs (A:1), bruising at simulation sites (A:1) 2-arm parallel study (NCT03155737) Hong Kong, China
Rani 2020 [43]	212 (105/107) 58.07 KOA (n.r.) 4.99 (Grade II to III OA)	(A) Acupressure (Self-administered, twice daily, 5 days weekly for 8 months, *n* = 106/98), plus B Acupoints: ST34, ST35, ST36, SP9, SP10, GB34	(B) Pharmacological treatment (nonsteroidal anti-inflammatory drugs, *n* = 106/103)	Pain (VAS †)	MD −3.13 [−3.76, −2.50], $p < 0.001$	n.r. 2-arm parallel study (n.r.) India
Tian 2016 [44]	135 (56/79) 54.35 KOA (TCM-DTDS) 4.9 (n.r.)	(A) Acupressure (Trained personnel, once daily for 4 weeks, *n* = 45/45), plus C (B) Acupressure only (*n* = 45/45) Acupoints: EX-LE4, EX-LE5, GB34, SP9, BI40, BI58, BI57, ST36, SP6, SP10, ST34, Ashi point	(C) Viscosupplementation (20 mg sodium hyaluronate injections, once per week, *n* = 45/45)	Pain (VAS)	B vs. C: MD 5.44 [5.06, 5.82]. $p < 0.001$ A vs. C: MD −4.27 [−4.70, −3.84], $p < 0.001$	Itchiness at simulation site (A:1, B:1) 3-arm parallel study (n.r.) China

ACR, diagnostic and therapeutic criteria committee of the American rheumatism association; KOA, knee osteoarthritis; NRS, numeric rating scale; SF-36, 36-Item Short Form Health Survey; SF-6D, Short-form six-dimension; TCM-DTDS, TCM criteria of diagnosis and therapeutic effect of diseases and syndromes; VAS, visual analog scale; WOMAC, Western Ontario and McMaster universities osteoarthritis index. *, full data not reported; † a lower score indicates a better condition; †† a higher score indicates a better condition.

3.3. Risk of Bias Assessment

Figure 2 outlines the risk of bias graph and summary of each RCT.



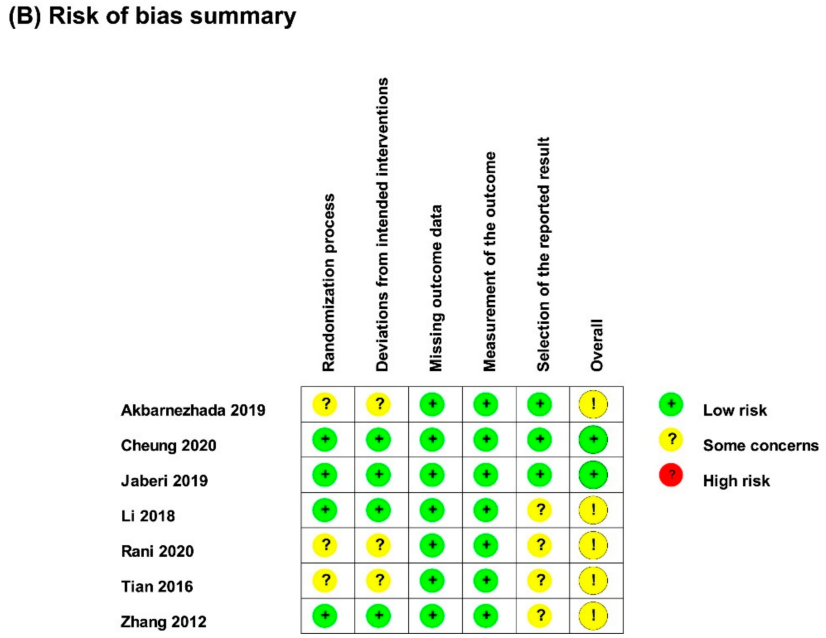


Figure 2. Risk of bias. (**A**) Risks of bias of the included studies. The authors reviewed each item's risk of bias for each included study. (**B**) Risks of bias of individual studies. +: low risk of bias; −: high risk of bias; ?: unclear risk of bias.

For the randomization process, four RCTs [39–42] were judged as low risk of bias as the allocation sequence of participants was adequately randomized and concealed. Another four RCTs [38,43–45] were judged as concerning, where one RCT [38] had improper randomization methods and two RCTs [43,44] did not provide information on allocation concealment. The bias due to deviations from the intended interventions was judged to be low for four RCTs [19,25] and concerning for the remaining RCTs. Except for one trial [44] that did not provide any information on blinding, three trials [38–40] were reported to be double-blinded, one trial [42] were single-blinded, and two trials [41,43] were open-labeled. Three RCTs [39,42,44] performed intention-to-treat analysis, two RCTs [38,43] performed per-protocol analysis, and two RCTs [40,41] performed both analyses to estimate the effect of assignment to intervention.

All trials were judged as low risk for missing outcome data. Data for all participants were available in three RCTs [39,41,44] whereas the percentage of missing data in other RCTs was low with drop-outs reasons provided and assessed to be insubstantial. Besides, the bias due to measure of outcomes was also judged as low for all trials. Although only

four RCTs [38–40,42] reported on the blinding of outcome assessors, the remaining studies measured their outcomes with appropriate methods where the assessors' knowledge of intervention were to be not likely influence the outcomes.

The bias in selection of the reported results was judged as low for three RCTs [38,39,42] and concerning for the remaining RCTs. Both outcome measures and analyses in three RCTs [38,39,42] were consistent with their trial protocols and one RCT [40] was inconsistent with their trial protocols in terms of missing outcome. Trials protocols were not available for the remaining trials even though all reported outcomes correspond to the outcome measurements. Overall, the risk of bias is judged as low only in two RCTs [39,42] and concerning in the remaining five RCTs.

3.4. Outcome Assessment

3.4.1. Primary Outcomes

Pain

Acupressure vs. sham acupressure

Three RCTs [38–40] compared acupressure with sham acupressure, where one trial [38] reported that acupressure has positive effect in reducing pain and two trials [39,40] reported otherwise. The meta-analysis showed that acupressure has equivalent effect on reducing pain (n = 174, MD −1.93, CI 95%: −4.38 to 0.51, p = 0.12, I^2 = 87%, Figure 3A), as compared to sham acupressure.

Acupressure vs. no intervention

Of the four RCTs [38–41] comparing acupressure with no intervention, three trials [38–40] reported that acupressure has positive effect in reducing pain and one trial [41] reported otherwise. The meta-analysis showed that acupressure has equivalent effect on reducing pain (n = 218, MD −2.37, CI 95%: −5.13 to 0.40, p = 0.09, I^2 = 92%, Figure 3B), as compared to no intervention.

Acupressure plus conventional intervention vs. conventional intervention

Two RCTs [43,44], comparing acupressure complementing conventional intervention with conventional intervention, reported that acupressure has superior effect in reducing pain. The pooled results also showed similar results (n = 291, MD −3.72, 95% CI: −4.84 to −2.61, $p < 0.00001$, I^2 = 88%, Figure 3C), where acupressure as complementary intervention has superior effect in reducing pain compared to conventional intervention alone.

Acupressure only vs. conventional intervention

One RCT [44] evaluated the effectiveness of acupressure alone in comparison with conventional intervention and showed superior effect in reducing pain (n = 90, MD 5.44, 95% CI: 5.06 to 5.82, $p < 0.00001$).

Acupressure only vs. health education

One RCT [42] evaluated the effectiveness of acupressure alone in comparison with health education and showed favorable effect in reducing pain (n = 35, MD 0.54, 95% CI: 0.07 to 1.01, p = 0.03).

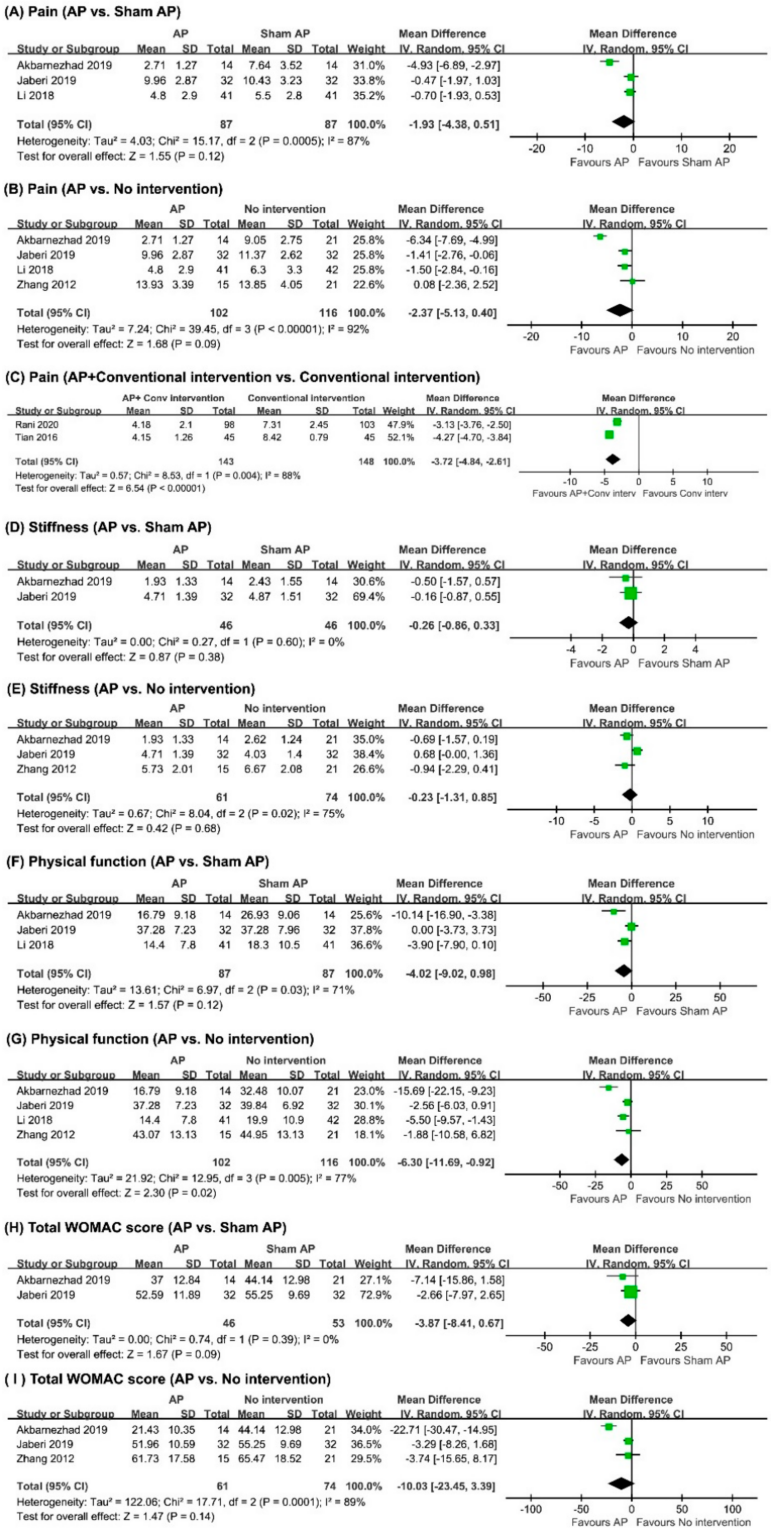


Figure 3. Forest plot of (**A**) pain (acupressure vs. sham acupressure); (**B**) pain (acupressure vs. no intervention); (**C**) pain (acupressure plus conventional intervention vs. conventional intervention) (**D**) stiffness (acupressure vs. sham acupressure) (**E**) stiffness (acupressure vs. no intervention); (**F**) physical function (acupressure vs. sham acupressure); (**G**) physical function (acupressure vs. no intervention); (**H**) total WOMAC score (acupressure vs. sham acupressure); (**I**) total WOMAC score (acupressure vs. no intervention). AP: acupressure; CI: conventional intervention.

Stiffness

Acupressure vs. sham acupressure

Two RCTs [38,39] compared acupressure with sham acupressure and reported equivalent effect in relieving stiffness for both groups. The meta-analysis showed that acupressure has failed to show superior effects in relieving stiffness (n = 92, MD −0.26, CI 95%: −0.86 to 0.33, p = 0.38, I^2 = 0%, Figure 3D), as compared to sham acupressure.

Acupressure vs. no intervention

Three RCTs [38–41], comparing acupressure with no intervention, also reported equivalent effect in relieving stiffness for both groups. The meta-analysis presented similar result where acupressure failed to show superior effects in relieving stiffness (n = 135, MD −0.23, CI 95%: −1.31 to 0.85, p = 0.68, I^2 = 75%, Figure 3E), as compared to no intervention.

Acupressure only vs. health education

The only RCT [42] that compared acupressure with health education also failed to show beneficial effects of acupressure in relieving stiffness (n = 35, MD: −0.04, 95% CI: −0.32 to 0.24, p = 0.78).

Physical Function

Acupressure vs. sham acupressure

Three RCTs [38–40] compared acupressure with sham acupressure, where one trial [38] reported that acupressure has positive effect in improving physical function and two trials [39,40] reported otherwise. The meta-analysis showed that acupressure has equivalent effects on improving physical function (n = 174, MD −4.02, CI 95%: −9.02 to 0.98, p = 0.12, I^2 = 71%, Figure 3F), as compared to sham acupressure.

Acupressure vs. no intervention

Of the four RCTs [38–41] comparing acupressure with no intervention, two trials [38,40] reported that acupressure has positive effect in improving physical function and two trials [39,41] reported otherwise. The meta-analysis showed that acupressure has superior effects (n = 218, MD −6.30, CI 95%: −11.69 to −0.92, p = 0.02, I^2 = 77%, Figure 3G), as compared to no intervention.

Acupressure vs. health education

The only RCT [42] comparing acupressure with health education did not show beneficial effects of acupressure in improving physical function (n = 35, MD: −0.85, 95% CI: −2.60 to 0.90, p = 0.34).

WOMAC Total Score

Acupressure vs. sham acupressure

Two RCTs [38,39] compared acupressure with sham acupressure for KOA, where one trial [38] reported that acupressure has positive effect in improving WOMAC total score and the other trial [39] reported otherwise. The meta-analysis showed that acupressure has equivalent effects on improving WOMAC total score (n = 135, MD −3.87, CI 95%: −8.41 to 0.67, p= 0.09, I^2 = 0%, Figure 3H), as compared to sham acupressure.

Acupressure vs. no intervention

Of the three RCTs [38,39,41] comparing acupressure with no intervention for KOA, one trial [38] reported that acupressure has positive effect in improving WOMAC total score and two trials [39,41] reported otherwise. The meta-analysis showed that acupressure has no superior effects (n = 218, MD −10.03, CI 95%: −23.45 to 3.39, p = 0.14, I^2 = 89%, Figure 3I), as compared to no intervention.

3.4.2. Secondary Outcomes

QoL

One RCT [41], comparing acupressure with no intervention, investigated the QoL in OA patients using SF-36 and showed equivalent results between both groups. In contrast, another RCT [42] that compared acupressure with health education assessed QoL in OA patients using SF-6d, which is derived from SF-36, and showed that acupressure has a superior effect on increasing the quality of life in OA patients (n = 35, MD: −0.07, 95% CI: −0.09 to −0.05, $p < 0.00001$).

Adverse Events (AEs)

Four RCTs [40–42,44] assessed adverse events in their trials. In terms of the acupressure group, one trial [40] reported broken skin and soreness at simulation site, one trial [42] reported pain and bruising at simulation sites, worsening of knee pain, and pricking pain sensation on the legs, one trial [44] reported itchiness at simulation site, and one RCT [41] reported that no adverse events were found. For the comparator group, no adverse events were found. The remaining 4 RCTs [38,39,43,45] did not report on adverse events.

4. Discussion

4.1. Summary of Main Results

This systematic review included eight RCTs assessing the effectiveness of acupressure for OA treatment, focusing on the seven RCTs that studied knee OA. According to our meta-analysis, acupressure did not show favorable effects in reducing pain, relieving stiffness, and improving physical function, as compared to sham acupressure. In comparison to no intervention, the meta-analysis also showed similar results where acupressure has equivalent effect in reducing pain and relieving stiffness but showed a favorable effect in improving physical function of joints. For acupressure complementing conventional intervention, pooled results showed superior effects for easing pain compared to conventional intervention alone. In terms of WOMAC, acupressure showed superior effect in reducing the total score compared to no intervention but otherwise as compared to sham acupressure. Only minor AEs, mostly regarding the simulation site of acupressure, were reported. The risk of bias of the seven RCTs was generally concerning except for two RCTs, limiting the drawing of a firm conclusion on the effectiveness of acupressure in treating knee OA.

4.2. Overall Completeness and Applicability of Evidence

A comprehensive and systematic search of numerous databases and multiple languages was attempted and performed in this review. However, there might still be a possibility of having a few relevant studies that we missed if they are published in other languages or indexed in other databases. We also excluded studies where acupressure was used as complementary intervention with other non-conventional interventions, which might reduce the significance of our findings.

Our findings are mostly based on knee OA even though we attempt to include OA of any joint. As the trials included in this review were performed in several countries, our findings could be fairly generalizable. Nevertheless, conclusions cannot be drawn about the effectiveness of acupressure in treating knee OA due to the small sample size and few studies included. Although the intervention duration, frequency, and acupoint selection varied among the studies, most studies in this review used acupoint ST34, ST36, SP9, SP10, and GB34 for knee OA at least three times a week. There were too few studies evaluating the severity of disease and acupressure intensity to assess how these could affect the overall effectiveness of the acupressure for OA. Moreover, pain perception and threshold vary from individual to individual. Even though the pain outcomes in this review were measured using psychometric instruments, there were still limitations and uncontrollable variables in those instruments that can skew the results, including possibilities of misleading responses and false negatives. This factor should also be taken into consideration and the significance

of acupressure in reducing pain for OA requires further validation. In general, this review presents robust evidence regarding the effect of acupressure in treating knee OA even though the findings of this review should be interpreted with caution.

4.3. Quality of Evidence

Even though we aimed for RCTs that provide sufficient statistical power for the evaluation of acupressure, the studies included in this review are generally small sample-sized and lack of high-quality. The pooled estimate of our findings may be lower in magnitude as we included all relevant studies in the evaluation regardless of their quality. As the studies included in this review are presumed to be relatively low statistical power due to small sample size or small effect size, the magnitude of our effect estimates might attain a certain risk of exaggeration, resulting in the low chance of identifying true effects. The assessment of bias within and across the studies is also challenging as the methodology and outcomes of the RCTs included were mostly poorly reported, resulting in the possibility of studies being higher biased than the grading received. Poor presentation and reporting of outcome measures in a few RCTs also limit us to extract data for meta-analysis. Nonetheless, the findings of this review reveal the potential role of acupressure in treating knee OA.

4.4. Potential Biases in the Review Process

The main limitation of this review is the small number of studies with small sample size, limiting the number of studies included in the meta-analysis. We included the statistical analysis of acupressure as compared to sham acupressure. However, the designs of sham acupressure are yet to be clearly defined in clinical trials. The designs of sham acupressure in the studies are described as the manipulation of points selected away from the real acupoint with gentle pressure in one trial [38], manipulation of points selected near the real acupoints of similar patterns without pressure in one trial [39], and manipulation of points that were not on meridians with pressure in another trial [40]. Different designs of sham acupressure may more or less produce placebo effects, affecting the evaluation of the true acupressure effect. Therefore, the significance of our results on the comparison of acupressure with sham acupressure should be interpreted carefully.

Moreover, three RCTs [41,43,44] did not register their trials where pre-specified analysis intentions for the trial cannot be acquired. Of the four RCTs [38–40,42] that registered their trial, the reported results for the outcome domain in one trial [40] mostly correspond to intended outcome measurements, except for one additional scale were reported for pain assessment and one intended outcome is missing from the reported results, resulting in selective reporting bias. Due to the characteristics of acupressure, two RCTs [41,43] also used an open-labeled design where the trial is non-blinded; therefore, increasing their performance bias. As we included all studies relevant to our review question, it is probable that our findings may be overstated and the evidence may be distorted.

4.5. Agreements and Disagreements with Other Studies or Reviews

Currently, there is no systematic review on acupressure for OA. In comparison to prior systematic reviews on acupressure for musculoskeletal conditions including low back pain [10,12], neck pain syndrome [16], and musculoskeletal pain [46], our results are found to be only partially consistent with their findings on acupressure showing positive effect in pain reduction. Our pooled results showed that acupressure has superior effects in reducing pain as a complementary intervention to conventional intervention, but not as sole intervention. In the meantime, the effectiveness of acupressure is equivalent to sham acupressure. Our review also overcome several limitations of these systematic reviews by including the latest information, conducting a more comprehensive literature search, excluding mixed intervention of similar effects for the evaluation of true effect of acupressure and critically appraising the included trials. Hence, our findings reflecting the effect of acupressure for OA is more reliable.

4.6. Implications for Practice and Research

The clinical effectiveness of acupressure as sole intervention in reducing pain, relieving stiffness, improving physical function, and improving QoL remained uncertain in the treatment of OA. As complementary intervention, its effectiveness for reducing pain was suggestive but required further validation. Hence, it is conceivable that acupressure should be recommended to OA patients with caution as its effectiveness is not convincing. Due to the small effect sizes and lack of high quality among the included studies, the effectiveness of acupressure in reducing pain or other specific symptoms should be further confirmed with more high-quality studies.

Future studies should prospectively register in the clinical trial registry and report their study according to recommended reporting guidelines CONSORT to reduce potential bias on the selection of reported results. Furthermore, future clinical trials should also include increasing sample sizes, a proper methodology of randomization and blinding, and selecting outcomes of relevance.

5. Conclusions

This systematic review indicates that acupressure as a sole or complementary intervention is lacking apparent advantages in the management of OA. More trials of rigorous designs are needed to further validate and overcome the limitation of current evidence.

Supplementary Materials: The following are available online at https://www.mdpi.com/article/10.3390/app11104457/s1, Table S1: Search strategies.

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Appendix A

Only one RCT [45] investigated on the effectiveness of acupressure for cervical OA and reported that acupressure has beneficial effects in pain reduction for COA, as compared to no intervention (n = 80, MD −2.03, CI 95%: −2.37 to −1.69, $p < 0.00001$). However, the risk of bias of this study was concerning as substantial information on the allocation seqeunce, blinding, and trial registration were unavailable. More RCTs concerning acupressure for the management of cervical OA are highly warranted in near future. The key data of the study was summarized in Table A1.

Table A1. Summary of study.

	Sample Size (N, M/F) Age (Mean) Type of OA (Diagnostic Criteria) Disease Course (yrs, Severity)	Intervention (Regimen, *n* = Randomized/Analyzed)	Control (Regimen, *n* = Randomized/Analyzed)	Outcome Measures	Main Results	AEs Study Design (Trial Registration Number) Country Notes
Ma 2016 [45]	160 (66/94) 43.88 COA (TCM-DTDS) 1 week–1 month (n.r.)	(A) Acupressure (Trained personnel, once daily for 2 weeks, *n* = 40/40) Acupoints: DU14, DU16, Cervical EX-B2, GB20, GB21, SI11, LI11, LI10, LI4	(B) No intervention (*n* = 40/40) (C) Chinese medicine fumigation (*n* = 40/40) * (D) Acupressure and Chinese medicine fumigation (*n* = 40/40) *	(1) Pain (VAS †) (2) Function (NDI †)	(1) A vs. B: MD −2.03 [−2.37, −1.69], $p < 0.001$ (2) A vs. B: MD −4.25 [−5.40, −3.10], $p < 0.001$	n.r. 4-arm parallel study (n.r.) China

NDI, Neck disability index; TCM-DTDS, TCM criteria of diagnosis and therapeutic effect of diseases and syndromes; VAS, Visual analog scale; † A lower score indicates a better condition. * We did not analysis these controls because they were in the exclusion criteria.

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