

BMJ Open Acupuncture for postoperative pain following total knee arthroplasty: a systematic review protocol

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ABSTRACT

Introduction: Total knee arthroplasty (TKA) is a common surgical method in orthopaedics; however, pain management after TKA remains a significant challenge. This review provides a comprehensive evaluation of the effects of acupuncture for postoperative pain after TKA.

Methods and analysis: The following 10 databases will be searched until August 2015: MEDLINE, EMBASE, CENTRAL, AMED, CINAHL, three Chinese databases (the China National Knowledge Infrastructure Database, the Chongqing VIP Chinese Science and Technology Periodical Database, and Wanfang Database) and five Korean databases (the Korean Medical Database, the Korean Studies Information Service System, the National Discovery for Science Leaders, the Database Periodical Information Academic, and the Oriental Medicine Advanced Searching Integrated System). All eligible randomised controlled trials related to the use of acupuncture for postoperative pain after TKA will be included. Assessment of risk of bias will be performed with the Cochrane risk-of-bias method. Mean differences or standardised mean differences will be calculated with 95% CIs for continuous data; the risk ratio will be used with 95% CIs for dichotomous data.

Dissemination: This systematic review will be presented in a peer-reviewed journal. The result of this review will also be disseminated at a relevant conference presentation.

Trial registration number: PROSPERO 2015: CRD42015020924.

INTRODUCTION

Description of the condition

Total knee arthroplasty (TKA), the most common surgical technique to treat severe knee osteoarthritis and rheumatoid arthritis, is a highly successful procedure to improve knee function and pain.^{1 2} However, pain after TKA remains a major symptom, and rehabilitation, which is commonly performed following the procedure, is closely associated with pain management.^{3 4} Moreover, since opioid analgesics are in wide use for acute postoperative pain

Strengths and limitations of this study

- Selection of the studies, assessment of risk of bias, data extraction and data pooling will be carried out by two researchers independently to perform an objective and systematic evaluation of acupuncture on postoperative pain following total knee arthroplasty (TKA).
- The results of the systematic review should be useful to practitioners for making better-informed decisions about pain control and rehabilitation after TKA.
- There may be considerable heterogeneity as a result of the various forms of acupuncture therapies.

regulation, severe adverse effects relating to their use are frequently reported.^{5 6} Therefore, the gold standard for postoperative pain management remains unclear.⁷

Description of the intervention

Acupuncture is a complex and interactive intervention that can be used in the treatment, rehabilitation and/or management of various diseases and conditions (eg, acute and chronic pain disorders, cerebrovascular disease, chemotherapy for cancer, and post-traumatic stress disorder). Acupuncture is the most common treatment for various musculoskeletal pains.⁸ According to several recent systematic reviews (SRs), acupuncture exerts pain-relieving effects after various types of surgeries.^{9 10} Various studies have reported that the use of acupuncture can relieve postoperative pain and reduce the dosage of opioid analgesics and their related adverse effects in the postsurgical period.^{11 12}

How the intervention may work

Many studies have reported that acupuncture can be helpful for relieving pain.⁸ However, the precise mechanism by which acupuncture provides postoperative analgesia remains unclear. Some studies explain the pain-



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relieving effects of acupuncture in terms of a spinal mechanism (eg, gate control theory), hormonal effects and peripheral events (eg, local circulation, vasodilation and tissue healing).^{13 14} The pain-relieving effects after TKA are thought to occur via the same mechanisms. Recent studies have supported the belief that acupuncture can be a useful option for pain regulation for patients undergoing TKA;^{15 16} however, there have been few studies that demonstrate the mechanism(s).

Why it is important to perform this review

TKA is commonly used for the treatment of severe advanced osteoarthritis in aged patients, and its use is continuously increasing.^{1 2} When pain management and rehabilitation are performed in an appropriate manner after the operation, TKA can be considered a highly effective procedure. However, inadequate use of analgesics for postoperative pain impairs recovery from the operation and rehabilitation.⁷ Moreover, since most patients undergoing TKA are elderly, the use of analgesics, including opioids, requires careful consideration.¹⁷ As a result, multimodal approaches for postoperative pain control have been proposed, and the postoperative pain-relieving effects of acupuncture have been reported in a number of studies. In addition, acupuncture, which can be considered a type of therapeutic formula, has been systematised in comparison to other kinds of alternative therapies, such as herbal therapies, which are too heterogeneous to evaluate systematically.¹⁸ Furthermore, the safety of acupuncture has been reported by numerous studies, whereas the risks of other alternative therapies remain unclear.¹⁹ Thus, postoperative pain control using acupuncture therapies has more potential as a practical approach than other alternative therapies. However, the effects of acupuncture after TKA remain controversial.^{15 16 20} Moreover, no systematic review on the use of acupuncture for postoperative pain relief after TKA exists in the literature. Hence, a comprehensive review of the effects of acupuncture on postoperative pain following TKA may contribute to the rehabilitation of patients undergoing TKA surgery.

OBJECTIVES

This review protocol provides a comprehensive evaluation of the effects of acupuncture on postoperative pain following TKA. The primary objective is to determine the efficacy of acupuncture in the treatment of postoperative pain after TKA. The secondary objectives are to assess the effects of acupuncture on knee movement and quality of life (QOL), and to investigate the safety of acupuncture therapies.

METHODS

Criteria for including studies in this review

Types of studies

Prospective randomised controlled trials (RCTs) of acupuncture therapy for postoperative pain after TKA will

be included. Nonrandomised studies (NRS), including case-control trials and case studies, will be excluded. No language restriction will be applied.

Types of participants

Patients undergoing TKA will be included. We will not exclude eligible patients based on the reason for TKA.

Types of interventions

Acupuncture therapy will be defined as various needling procedures that stimulate acupoints, such as manual acupuncture, auricular acupuncture or electroacupuncture. Non-penetrating stimulation on acupoints, such as acupressure or laser acupuncture, will be excluded. We will include traditional acupuncture, auricular acupuncture and electroacupuncture; therefore, we will be able to comprehensively evaluate the effects of acupuncture on postoperative pain after TKA. We will also include trials that compared acupuncture plus another typical treatment with other typical treatments alone. Control interventions will include sham/placebo acupuncture, no treatment, waiting list membership and conventional therapies (eg, usual care, analgesics, manual therapy).

Types of outcome measures

Primary outcomes

1. Pain: a pain-associated scale will be included (eg, visual analogue scale or numerical rating scale).
2. Functional evaluation of knee joint: the Western Ontario and McMaster Universities Arthritis Index (WOMAC).

Secondary outcomes

1. The range of motion of the knee joint.
2. QOL: a QOL-associated scale will be included (eg, Euro-QoL (EQ5D) and the 36-Item Short-Form Health Survey (SF-36)).
3. Adverse events related to acupuncture treatment.

Search methods for identification of studies

Electronic searches

According to the core standard ideal (COSI) model,²¹ the following databases will be searched for the period from the time of their inception to August 2015 to identify relevant articles: MEDLINE/PubMed, EMBASE, the Cochrane Central Register of Controlled Trials (CENTRAL), the Allied and Complementary Medicine Database (AMED), and the Cumulative Index to Nursing and Allied Health Literature (CINAHL). We will also search the following three Chinese medical databases: the China National Knowledge Infrastructure Database (CNKI), the Chongqing VIP Chinese Science and Technology Periodical Database (VIP), and Wanfang Database. In addition, we will search the following five Korean medical databases: the Korean Medical Database (KMBASE), the Korean Studies Information Service System (KISS), the National Discovery for Science Leaders (NDSL), the Database Periodical Information

Academic (DBPIA), and the Oriental Medicine Advanced Searching Integrated System (OASIS).

Searching other resources

We will manually investigate ambiguous literature to avoid missing eligible trials. We will search reference lists of all eligible studies. In addition, the clinical trial registers (eg, Clinical trials.gov, Current Controlled Trials, Chinese Clinical Trial Register and Australian and New Zealand Clinical Registry) also will be searched for ongoing or unpublished trials.

Search strategy

The search strategies for MEDLINE/PubMed are described in online supplementary appendix 1, and we will modify these search strategies for other databases.

Data collection and analysis

Selection of studies

Two independent review authors will screen the titles and abstracts of all searched studies, and studies will be selected through a full-text review if they meet the pre-defined eligibility criteria. When a consensus on the selection process cannot be obtained through consultations, the third author will ultimately decide. The selection process of this review will be presented in the PRISMA flow chart (figure 1).²²

Data extraction and management

Data will be extracted from all eligible studies by two independent reviewers. When a consensus on the data extraction cannot be obtained through consultations, the third author will decide. When the collected data are incomplete or unclear, the arbiter will contact the corresponding authors of the original articles to request additional data or an explanation of the relevant issue. We will extract the characteristics of the participants (eg, average age, gender, hospitalisation day, analgesics consumption, and inclusion and exclusion criteria), type of intervention, type of control intervention, sample size of each intervention group, randomisation, allocation concealment and blinding method, outcome measures, duration of follow-up, type and source of financial support, and publication status from trial reports.

Assessment of risk of bias and reporting quality in included studies

Two independent review authors will evaluate the risk of bias of included studies using the Cochrane Collaboration's risk-of-bias (ROB) assessment method.²³ Assessment of the ROB will be performed according to the following seven domains: (1) random sequence generation, (2) allocation concealment, (3) blinding of participants and personnel, (4) blinding of outcome assessors, (5) incomplete outcome data, (6) selective reporting and (7) other sources of bias. The ROB of trials will be categorised as low, unclear or high risk of bias. When a consensus on assessment of the ROB

cannot be achieved through consultations, the third author will decide.

Measures of treatment effect

Mean differences (MDs) with 95% CIs will be used for the analysis of continuous data; standardised mean differences (SMDs) with 95% CIs will be used if different scales were used to measure a certain outcome variable. Dichotomous data will be analysed using the relative risk (RR) with 95% CIs.

Unit-of-analysis issues

We will only focus on patient randomised studies. If crossover designed trials are included, we will only use data from the first session. Unit of analysis issues may arise from different follow-up times; we will group the data into three follow-up periods: (1) short term (less than 24 h), (2) medium term (1–7 days) and (3) long term (more than 1 week).

Dealing with missing data

If possible, we will contact the corresponding authors of the original trials to request missing data. If it is not possible to contact the original authors or obtain missing data, the analysis will rely on the available data.

Assessment of heterogeneity

According to the guidelines of the Cochrane Handbook for Systematic Reviews of Interventions, heterogeneity will be assessed in the following three ways: (1) a visual check of the forest plot, (2) a heterogeneity χ^2 test and (3) Higgins I^2 statistic. In terms of the interpretation of the heterogeneity χ^2 test, a significance level of $p < 0.10$ will be considered meaningful heterogeneity. In terms of the interpretation of the Higgins I^2 statistic, more than 50% will be considered meaningful heterogeneity.²⁴ If meaningful heterogeneity among the included studies is identified, we will perform a subgroup analysis or a meta-regression analysis to determine the reason; if the heterogeneity cannot be resolved through additional analysis, we will not pool the data.

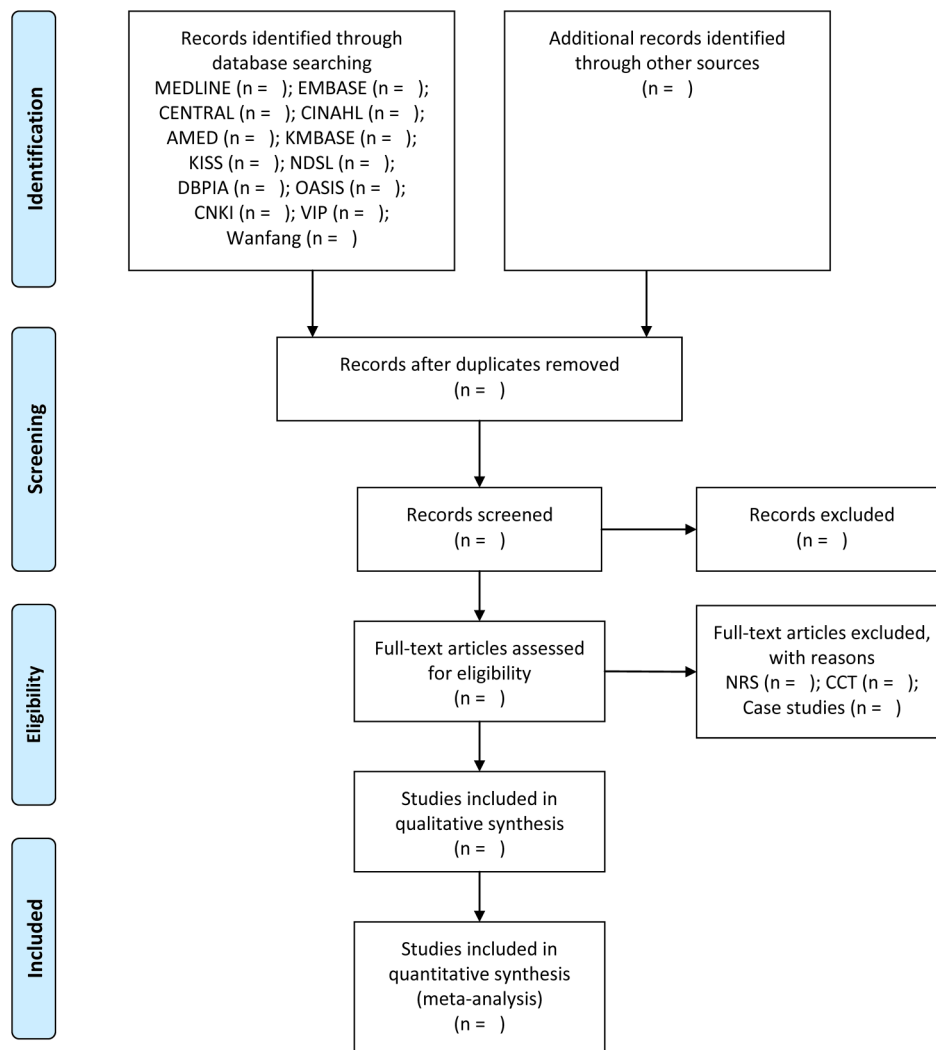
Assessment of reporting biases

If more than 10 studies are included, we will assess the reporting biases through funnel plots. When funnel plot asymmetry is detected, we will attempt to identify possible reasons (eg, publication bias, small study effect and true heterogeneity) through visual evaluation of the funnel plot and statistical analysis, such as Egger's test.²⁵

Data synthesis

We will conduct a meta-analysis to estimate differences in primary and secondary outcomes. A meta-analysis will be performed using Review Manager Software (RevMan, V.5.3.5 for Windows; the Nordic Cochrane Centre, Copenhagen, Denmark).²⁶ Depending on the level of heterogeneity among included studies, we will apply a fixed-effects model or a random-effects model.

Figure 1 PRISMA flow chart of the trial selection process (NRS, nonrandomised studies).



When considerable heterogeneity is observed, a random-effects model with 95% CIs will be used in the analysis of pooled effect estimates. If meaningful heterogeneity, which cannot be explained by any additional assessment such as subgroup analysis, is identified among the included studies, we will not attempt to perform a meta-analysis. If necessary, subgroup analysis will be performed with careful consideration of each subgroup.

Subgroup analysis and investigation of heterogeneity

When it is necessary to interpret the heterogeneity of included studies and the data are sufficient, we will use subgroup analysis, according to the following:

1. Type of control intervention (eg, no treatment, usual care or sham acupuncture);
2. Type of acupuncture (eg, manual acupuncture, electroacupuncture or auricular acupuncture);
3. Period of follow-up (<24 h, 1–7 days and more than 1 week).

Sensitivity analysis

We will implement a sensitivity analysis according to the following:

1. Sample size: studies will be categorised into those with small or large samples according to whether they included fewer or more than 40 participants in each group.
2. Analysis issues (eg, procedure for management of missing data).
3. Methodological qualities.

Summary of evidence

The results of the primary outcomes will be presented in summary of findings tables (SOF Tables). The evidence level of the primary outcomes will be analysed through the Grading of Recommendations Assessment Development and Evaluation (GRADE) method.

DISCUSSION

Numerous recent SRs and clinical trials have supported the effects of acupuncture for various types of postoperative pain;^{9 10} however, no reviews have assessed the evidence for the effects of acupuncture for postoperative pain following TKA. Furthermore, the types of acupuncture examined by most of the RCTs that evaluated the effects of this treatment for pain after knee surgery have

been too diverse to assess the overall effects.^{15 16 20} Thus, we will comprehensively analyse the effects of acupuncture for postoperative pain after TKA; for this purpose, subgroup analysis will be conducted according to the type of acupuncture treatment, the type of control intervention and follow-up period. With respect to duration of follow-up, the condition of patients can be significantly influenced by various factors, such as psychological characteristics and presurgical conditions in the subacute or chronic postoperative period;²⁷ therefore, we will divide our assessment into three different sessions (eg, short term, medium term and long term), and evaluate the results of each session separately. This review will provide current evidence for the effectiveness of acupuncture therapy for postoperative pain after TKA and will clarify the benefits experienced by patients undergoing TKA to increase the knowledge base of practitioners of both traditional and complementary medicine.

Contributors S-hC contributed to the conception of this review. The review protocol was drafted by J-YJ, and was revised by S-hC. The search strategy was established by all authors. J-YJ and J-HC will independently screen the searched studies, extract the data from the eligible studies, assess the risk of bias and conduct the meta-analysis. All authors approved the publication of this review protocol.

Competing interests None declared.

Provenance and peer review Not commissioned; externally peer reviewed.

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