

Acupuncture for Osteoarthritis of the Knee

A Systematic Review

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Objective. To evaluate trials of acupuncture for osteoarthritis (OA) of the knee, to assess the methodologic quality of the trials and determine whether low-quality trials are associated with positive outcomes, to document adverse effects, to identify patient or treatment characteristics associated with positive response, and to identify areas of future research.

Methods. Eight databases and 62 conference abstract series were searched. Randomized or quasi-randomized trials of all languages were included and evaluated for methodologic quality using the Jadad scale. Outcomes were pain, function, global improvement, and imaging. Data could not be pooled; therefore, a best-evidence synthesis was performed to determine the strength of evidence by control group. The adequacy of the acupuncture procedure was assessed by 2 acupuncturists trained in treating OA and blinded to study results.

Results. Seven trials representing 393 patients with knee OA were identified. For pain and function, there was limited evidence that acupuncture is more effective than being on a waiting list for treatment or having treatment as usual. For pain, there was strong evidence that real acupuncture is more effective than sham acupuncture; however, for function, there was

inconclusive evidence that real acupuncture is more effective than sham acupuncture. There was insufficient evidence to determine whether the efficacy of acupuncture is similar to that of other treatments.

Conclusion. The existing evidence suggests that acupuncture may play a role in the treatment of knee OA. Future research should define an optimal acupuncture treatment, measure quality of life, and assess acupuncture combined with other modalities.

Osteoarthritis (OA) is the most common form of arthritis and is a major cause of morbidity, physical limitation, and increased health care utilization, including total joint arthroplasty, especially in the elderly (1–3). The joints most commonly affected by OA are the knees, hips, hands, and spine.

Presently there is no cure for OA (4); therefore, the treatment of OA is primarily focused on managing the condition by minimizing morbidity. Current recommendations for the management of OA, including guidelines published by the American College of Rheumatology, focus on the relief of pain and stiffness and maintenance or improvement in functional status and quality of life as important goals of therapy (4). Many pharmacologic therapies for knee OA can be associated with significant adverse effects (5–8); therefore, the need for effective, safe therapies for OA has become evident. Nonpharmacologic physical modalities that have been shown to be effective in patients with knee OA include patient education, physical and occupational therapy, and both aerobic and resistive exercises (4,9).

Acupuncture, a nonpharmacologic modality, is gaining popularity among OA patients in the US. For example, ~1 million consumers utilize acupuncture annually (10), and many have musculoskeletal disorders

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Table 1. List of criteria for assessment of the quality of trials for acupuncture for knee osteoarthritis*

Item	Score
A. Was the study described as randomized?	0/1
B. Was the randomization scheme described and appropriate?	0/1
C. Was the study described as double blind?	0/1
D. Was the method of double blinding appropriate?	0/1
D1. Were patients reported as blinded?	0/1
D2. Was the outcomes assessor reported as blinded?	0/1
E. Was there a description of dropouts and withdrawals?	0/1
F. Were cointerventions avoided or controlled for?	0/1
G. Was compliance satisfactory?	0/1

* Scoring for Jadad scale: A + B + C + D + E = 5 possible points; 0–2 = low quality; 3–5 = high quality. Items D1, D2, F, and G included for sensitivity analysis. Coding: 1 = yes, 0 = no.

such as OA (11). Although the safety of acupuncture has been well documented (12), the efficacy of acupuncture for knee OA, either as a stand-alone treatment or as an adjunct to standard medical care, remains under investigation.

In order to evaluate the effectiveness of acupuncture for OA of the knee, we conducted a systematic review of controlled trials of acupuncture in patients with knee OA. This review had 5 major objectives: 1) to evaluate trials of acupuncture for OA of the knee by control group type (e.g., waiting list, placebo, active controls); 2) to assess the methodologic quality of the trials and conduct a sensitivity analysis to examine whether low-quality trials are associated with positive outcomes; 3) to document any adverse effects reported in the trials; 4) to identify aspects of the patient or procedure that are associated with a positive outcome; and 5) to identify areas of future research.

MATERIALS AND METHODS

Literature search. A Medline search (1966–99) was conducted. The terms “acupuncture,” “alternative medicine,” “electroacupuncture,” “moxibustion,” “injections, intramuscular,” and “medicine, traditional Chinese” were used as Medical Subject Heading (MeSH) terms and searched as textwords. “Trigger-point therapy,” “auriculotherapy,” and “oriental

medicine” had no MeSH terms, and therefore were searched only as textwords. These search results were combined using “and” with the results of a search on the disease consisting of the following search terms: “arthritis,” “osteoarthritis,” “rheumatology,” “pain,” “joint pain,” and “gonarthrosis.” The search was limited to human subjects. Bibliographies from retrieved articles were searched for additional studies. To identify unpublished studies, the abstracts from 62 rheumatology conferences were searched. EMBASE, Psychlit, Mantis, Science Citation Index, CAMPAIN (Complementary and Alternative Medicine and Pain), CCTR (Cochrane Controlled Trials Registry), and Cochrane Collaboration Complementary Medicine Field Trials Registry were also searched using the same search terms.

Trials published in any language were included if they 1) were randomized or quasi-randomized; 2) had an experimental treatment in which acupuncture points were stimulated by needle insertion, not electrical stimulation, thermal stimulation, or digital pressure; and 3) had a study population of patients with OA of the knee exclusively.

Multiple publications of the same study were omitted so that each study population was represented only once. Two reviewers (VH, JE) independently reviewed all potentially relevant manuscripts to determine which trials met inclusion criteria and which did not. A complete list of excluded trials is available from the authors upon request.

Quality assessment. Eligible trials were evaluated using the criteria of Jadad et al (13). Items F and G (Table 1) reflect additional items included in other reviews (14), which are believed to influence internal validity and are not represented in the validated Jadad scale. These were included for the purposes of sensitivity analysis.

Data extraction. Two reviewers, blinded to the other’s assessments, independently assessed each included article for quality items A–G (Table 1). Consensus was achieved by discussion, and consensual scores appear in Table 2. Information was also extracted pertaining to the description of treatment and control groups, inclusion criteria, followup times, and adverse effects (Table 3). Followup times were defined in 3 categories: 1) short term: <1 month after treatment completion, 2) intermediate: 1–3 months after completion of treatment, and 3) long term: >3 months after treatment completion.

Control groups were classified into 4 categories: 1) waiting list/treatment-as-usual/no treatment, 2) placebo (e.g., sham transcutaneous electrical nerve stimulation, sugar pills), 3) sham acupuncture, and 4) active controls (e.g., medication, physical therapy). Placebo was defined as a physiologically

Table 2. Trial quality assessment*

Author, year (ref.)	n	A	B	C	D	D1	D2	E	F	G	Score
Berman et al, 1999 (22)	73	1	1	0	0	0	1	0	0	1	2
Christensen et al, 1992 (23)	32	1	1	0	0	0	1	1	1	1	3
Takeda and Wessel, 1994 (24)	40	1	0	1	1	1	1	1	0	1	4
Molsberger et al, 1994 (25)	103	1	0	1	1	1	1	1	?	1	4
Petrou et al, 1988 (26)	31	1	0	1	1	1	1	0	?	1	3
Milligan et al, 1981 (27)	100	1	0	0	0	0	0	0	0	1	1
Ammer and Petschnig, 1988 (28)	14	1	0	0	0	0	0	0	0	1	1

* n = number of trial participants; A + B + C + D + E = 5 possible points for quality score; items D1, D2, F, and G included for sensitivity analysis. Coding: 1 = yes, 0 = no.

Table 3. Study population, treatments, followup times, and adverse effects*

Author, year (ref.)	Inclusion criteria	Acupuncture treatment	Control group	Followup	Adverse effects
Berman et al, 1999 (22)	ACR criteria for at least 6 months	Low-frequency electroacupuncture 2× weekly for 8 weeks	Waiting list	Immediate, 1 month	No reported side effects
Christensen et al, 1992 (23)	OA patients awaiting knee replacement	Manual acupuncture, 2× weekly for 3 weeks	Waiting list	Immediate, 1 month	Short-lasting, mild secondary effects
Takeda and Wessel, 1994 (24)	Radiologic evidence of OA, pain in 1 or both knees	Manual acupuncture, 3× weekly for 3 weeks	Sham acupuncture	Immediate, 1 month	NR
Molsberger et al, 1994 (25)	Radiologic evidence of OA, pain in knee for 2 months	Manual acupuncture, 2× weekly for 5 weeks	Sham acupuncture	Immediate, 3 months	NR
Petrou et al, 1988 (26)	NR	Manual acupuncture, 3× weekly for 8 total treatments	Sham acupuncture	Immediate	NR
Milligan et al, 1981 (27)	NR	NR	Physical therapy	Immediate	NR
Ammer and Petschnig, 1988 (28)	OA confirmed by radiograph, pain for 2 weeks	2× weekly for 4 weeks	Physical therapy	Immediate	NR

* ACR = American College of Rheumatology; OA = osteoarthritis; NR = not reported.

inert substance. Sham acupuncture, defined as a mock acupuncture procedure in which needles were inserted in the skin, was not classified as a placebo due to the growing body of evidence that sham acupuncture may not be physiologically inert but may produce some analgesic effects that are not specific to the points used (15).

Acupuncture assessment. The adequacy of the acupuncture treatment was assessed in 2 ways. Because all the included trials used traditional Chinese medicine (TCM) acupuncture, 2 acupuncturists (GK, LL) experienced in treating patients with OA with the TCM method were given a description of each study population and the acupuncture procedure but were blinded to the publication and the results of the study. They were asked to rate the acupuncture procedure as 1) adequate, 2) not adequate, or 3) not enough information to decide. Then, 1 person (SB) reviewed acupuncture textbooks from China, Korea, Japan, and the West and extracted guidelines for treating OA of the knee or knee pain (e.g., points used, number of treatments, and number of points per session). Acupuncture treatments were compared with these guidelines.

Outcomes assessment. Outcomes were defined as either 1) positive when acupuncture had a significantly better effect than that seen in the control group, 2) neutral when

the effect of acupuncture was not significantly different from that seen in the control group, or 3) negative when acupuncture had significantly less effect than the effect seen in the control group (Table 4). *P* values less than 0.05 were considered significant. Trends toward significance (i.e., *P* < 0.10) were also noted. Based on OMERACT (Outcome Measures in Rheumatology Clinical Trials) guidelines (16), the following were considered primary outcomes: pain, physical function, patient global assessment, and imaging (Table 4). Additional data on quality of life and costs/medical utilization were extracted.

Due to numerous types of control groups and insufficient reporting of data in many trials, meta-analysis (statistical pooling of outcomes) could not be performed; therefore, a best-evidence synthesis (17) method was used. This method, used in some Cochrane systematic reviews (14), consists of 4 levels of scientific evidence and weights the results according to the methodologic quality:

1. Strong evidence: multiple, relevant, high-quality randomized controlled trials (RCTs) with generally consistent outcomes.

2. Moderate evidence: 1 relevant, high-quality RCT and 1 or more relevant, low-quality RCTs with generally consistent outcomes.

Table 4. Short-term results of acupuncture for osteoarthritis*

Author, year (ref.)	Control group	Pain	Function	Cost
Berman et al, 1999 (22)	Waiting list	+	+	NR
Christensen et al, 1992 (23)	Waiting list	+	+	+
Takeda and Wessel, 1994 (24)	Sham acupuncture	0	0	NR
Molsberger et al, 1994 (25)	Sham acupuncture	+	0	NR
Petrou et al, 1988 (26)	Sham acupuncture	+†	0	NR
Milligan et al, 1981 (27)	Physical therapy	0	NR	NR
Ammer and Petschnig, 1988 (28)	Physical therapy	0	0	NR

* Imaging, global improvement, and quality-of-life outcomes were not measured for any trials. + = positive (favoring acupuncture); NR = not reported; 0 = neutral.

† More than 1 pain outcome measured, not consistent.

3. Limited evidence: 1 relevant, high-quality RCT or multiple relevant, low-quality RCTs with generally consistent outcomes.

4. Inconclusive evidence: only 1 relevant, low-quality RCT, no relevant RCTs, or RCTs with inconsistent outcomes. "Relevant" was defined as having at least 1 of the primary outcomes, "generally consistent" was defined as two-thirds or more of the studies having the same result (positive or negative), and "multiple" was defined as more than 1 RCT. An RCT was considered to be of high quality if the methodologic score was 3–5 points and of low quality if the methodologic score was <3 points. Previous work has demonstrated that trials that total <3 points using this scale can exaggerate treatment effects by >30% on average (18).

Aspects of acupuncture treatment. Data on the features of the acupuncture treatment deemed important from a TCM point of view were extracted: 1) total number of treatments, 2) number of acupuncture points stimulated per session, 3) whether "de qi" (the confirmatory signal that the endogenous opioid system has been activated [20]) was elicited and confined to the real acupuncture group when sham acupuncture was used as the control group, and 4) what type of acupuncture (manual or electro-) was administered. Information on these aspects of the acupuncture treatment was extracted to test 4 hypotheses. Two of the 4 hypotheses were based on the textbook review, which suggested that: 1) an average of 10 total treatments (range 7–15 treatments) is important in achieving a positive result and 2) the needling of at least 8 points per session per knee is important in achieving a positive result. A decision was made that if only a small number of trials achieved the minimal number of points, then 6 points would be used for analysis, since this has been found sufficient in other pain conditions (19).

The third hypothesis, based on the neurohumoral model of acupuncture analgesia, suggests that eliciting "de qi" is important to achieve a positive result. The fourth hypothesis suggests that low-frequency combined with high-frequency electroacupuncture would be the most effective type of acupuncture because different frequencies facilitate the release of different opioids, which act synergistically to produce maximal analgesia (21).

Statistical analysis. All descriptive statistical analyses were performed using SPSS software, version 9.0 (SPSS, Chicago, IL). Sensitivity analysis was performed between each individual quality item (A–G) and trial outcome comparing positive versus neutral outcomes, using Fisher's 2-tailed exact test due to the small numbers in the cells. There were no negative outcomes.

RESULTS

A total of 7 trials (22–28) representing 393 OA patients met the inclusion criteria. Additional acupuncture and OA trials were identified (29–35) but did not meet all the inclusion criteria. Of the included trials, 2 (27,29) appeared as only conference abstracts and 2 (25,26) appeared in journals not indexed by any of the electronic databases searched.

All trials had an assessment of pain, 6 assessed function, none assessed patients' global improvement

rating, 1 assessed costs of surgeries prevented, and none assessed imaging or quality of life. The overall trial results for pain were 4 positive, 3 neutral; for function, 2 were positive and 4 were neutral (Table 4).

Quality scores and sensitivity analysis. More than half of the trials ($n = 4$) received a low-quality rating. There was no association between trial quality and trial results, nor was there any association between any single quality item and trial results. In some trials, patients could not be blinded due to the study design; therefore, to detect whether reporting bias may have occurred in unblinded patients, we assessed whether patients had been asked about the credibility of the treatment they had received. No trial had used such a measure.

Short-term results by type of control group. Two studies compared acupuncture with a wait list/treatment-as-usual/no treatment control group (22,23), with results favoring acupuncture for function and pain. Because these were both low-quality studies, the evidence is limited (level 3) that acupuncture is more effective than wait list/treatment as usual for improving pain and function in OA of the knee. One trial (23) assessed cost/utilization in terms of knee-replacement surgeries avoided, and results significantly favored acupuncture; however, because this was only 1 study, results are inconclusive (level 4) that acupuncture significantly reduces medical costs/utilization.

Three high-quality studies (24–26) compared real acupuncture with sham acupuncture. Positive results for pain were shown in 2 trials, constituting a consistent finding among high-quality trials; therefore, there is strong evidence (level 1) that real acupuncture is more effective than sham acupuncture for OA knee pain. All 3 trials assessed function, but all outcomes were neutral; therefore, there is inconclusive evidence (level 4) for function. The other outcomes were not measured.

Two studies (28,29) compared acupuncture with physical therapy. Pain was measured in both trials and function was measured in 1. All outcomes were neutral; therefore, there is inconclusive evidence (level 4) that acupuncture is more effective than physical therapy either for pain or function. The other outcomes were not measured.

Of baseline clinical and demographic factors, only short duration of the disease proved to be associated with a positive outcome (23). Only 2 trials measured the adverse effects of acupuncture (22,23). These were relatively minimal (Table 3).

Few trials met the acupuncture treatment adequacy criteria established by the textbook review. Only 3 trials administered 10 or more total treatments

(22,23,25). All 3 had positive results. Only 1 trial (22) stimulated the sufficient number of points per session based on the textbook review. No trial used a combined low/high electroacupuncture protocol.

Evaluation of the acupuncturists' interrater agreement showed complete agreement on which trials administered adequate treatments (22–26). Four of the 5 trials rated as giving “adequate treatments” had positive results for pain. All 3 trials that met 1 or more textbook criteria were also rated as “adequate” by this blinded-acupuncturist method.

Intermediate and long-term followup. Intermediate results were shown in 4 trials (22–25). At 1-month followup, the benefit of acupuncture had begun to attenuate (22,23). This finding conflicts with that of Molsberger and colleagues (25), who reported that benefits from acupuncture were maintained at 3-month followup.

No trial included long-term followup (>3 months) on the entire randomized cohort. Christensen et al (23) provided long-term followup data on responders only at 50 weeks posttreatment and reported that by administering monthly maintenance treatments to responders, the benefits of acupuncture could be sustained.

DISCUSSION

We examined the methodologic quality, acupuncture treatment characteristics, and outcomes of 7 clinical trials on acupuncture for OA of the knee. Overall, the existing evidence suggests that acupuncture may play a role in the treatment of OA of the knee, mostly for the reduction of pain. Improvements in physical function were noted but were inconsistent. Currently there is insufficient evidence to determine whether acupuncture is as effective as other OA treatments, whether forms of acupuncture other than TCM would demonstrate similar efficacy, and whether acupuncture is also effective for joints other than the knee. Sensitivity analysis demonstrated that low-quality scores were not significantly associated with positive findings.

For pain and function, there is limited evidence that having acupuncture is more effective than being on a waiting list for treatment or having treatment as usual. Waiting lists control for spontaneous improvement as part of the natural history but do not rule out improvements due to placebo effects; however, when real acupuncture is compared with sham acupuncture, there is strong evidence that real acupuncture is more effective for controlling pain, suggesting that the analgesic effects of acupuncture cannot be explained by placebo effects

alone. These findings are consistent with the results of mechanistic studies demonstrating that acupuncture analgesia occurs centrally through the release of endorphins and monoamines (36–38).

A question arises as to why real acupuncture did not outperform sham acupuncture in all 3 knee OA trials. This may be due, in part, to how sham acupuncture was administered. To minimize the nonspecific needling effects of sham acupuncture, it should be administered as “minimal sham,” that is, superficially at distal nonacupuncture points (39). In both trials in which real acupuncture outperformed sham acupuncture (25,26), the sham procedure approximated minimal sham. In the trial in which neutral results were obtained (24), sham acupuncture was administered superficially at sites 1 inch adjacent to the real points. This procedure may have inadvertently elicited an analgesic response of the level similar to that occurring with real acupuncture, evidenced in the authors' report that some members of the sham group experienced “de qi,” and that “de qi,” not treatment group assignment, was a significant predictor of positive response to pain thresholds and Western Ontario and McMaster Universities Osteoarthritis Index pain scores (40).

An additional issue arises regarding how to interpret the nonsignificant between-group differences when acupuncture is compared with physical therapy (27,28). There are several possibilities for why this may have occurred: 1) chance, 2) low statistical power, 3) inadequate (suboptimal) treatments in 1 or both groups, 4) true equivalence, or 5) a combination of these. Low statistical power is a definite possibility because a relatively large sample size is needed to compare 2 active treatments where the between-group difference is expected to be small. The small sample sizes in these trials are not likely to have been able to detect a between-group difference. Whether the 2 treatments are truly equivalent cannot be determined by the existing studies, but only by trials that are large enough to rule out Type II errors and ensure that both treatments are optimal.

It is noteworthy that all the trials that met at least 1 textbook criterion for adequate treatment had positive outcomes for pain and that 4 of 5 trials that were assessed as “adequate” by blinded acupuncturists had positive outcomes for pain. Clearly, more research needs to be done to discern what aspects of acupuncture treatment are conducive to positive results and what constitutes an optimal treatment protocol, because giving an inadequate acupuncture treatment in a clinical trial may be comparable with trying to determine efficacy in a pharmaceutical trial with an insufficient dosing regimen.

From a practical point of view, the practitioner interested in referring patients with OA of the knee for acupuncture should consider both the applications and limitations of this review's findings. First, the available trials only evaluate standardized acupuncture treatment protocols; therefore, the extent to which these findings are generalizable to other forms of acupuncture is not known. Other forms of acupuncture may differ in aspects of the acupuncture treatment that were deemed important in this review. For example, the TCM interpretation of the concept of "de qi" is different than that of the other traditions, such as the Japanese acupuncture tradition of Toyu Hari. Similarly, the emphasis on needling a certain number of points per session would not necessarily be important in different traditions of acupuncture.

Second, within a tradition of practice, such as the TCM tradition, the trials represented here do not replicate TCM as it is commonly applied. In practice, TCM frequently uses Chinese herbs and individualized treatments based on TCM diagnosis because it is commonly believed that this provides the greatest effectiveness (41). In research, formula acupuncture treatments with no herbs are frequently used because they control better for unknown confounders. Whether individualized approaches and supplemental herbs are actually more effective than formula treatment needs to be investigated.

Adverse effects were not reported in many studies, and it is not clear whether they did not occur, were not measured, or were measured and did occur but were not reported. In future trials of acupuncture in OA, it will be important to assess and report the adverse effects because arthritis patients weigh both effectiveness and adverse effects when making a treatment decision (42).

This systematic review demonstrates that more trials of acupuncture for OA of the knee exist and that the evidence is stronger than commonly reported in narrative reviews (9,43–45). The findings of this review favoring acupuncture for OA of the knee differ from those of the only other systematic review on the topic of OA and acupuncture, which had largely inconclusive results (46). We attribute this to our analyzing the trials of OA of the knee exclusively, rather than combining joints; using the best-evidence synthesis method, which assigns greater weight to trials of high methodologic quality; and including 4 trials that were not included in the previous review.

There is some debate about the use of the Jadad scale, which inquires about double blinding, because the design of many acupuncture trials makes it impossible to blind patients (47). The scale may be justifiably criticized

because it decreases, although does not prohibit, the chances of single-blind trials earning a high-quality score. This limitation should be borne in mind when interpreting the results of trials using waiting lists or physical therapy control groups in this review. Because patient blinding is important when pain is the primary outcome, we chose to use the scale in spite of this limitation. The fact that the strongest evidence favoring acupuncture emerged from trials in which patients were blinded suggests that positive findings cannot be attributed to unblinded patients giving overly favorable results of acupuncture; therefore, the limitations of the Jadad scale have not skewed the overall conclusions of this review.

Important future research questions emerge. First, what constitutes an optimal acupuncture treatment for knee OA? The parameters established in textbooks have seldom been applied in trials, and the alternating-high-and-low-electrical-frequency theory has not been applied in any clinical trial. Second, can maintenance treatments sustain results in responders? Third, does acupuncture, when used as an adjunct with other OA treatments, maximize effectiveness while minimizing adverse effects? For example, the theory of acupuncture-assisted analgesia (48) suggests that patients receiving acupuncture may be able to reduce medication dosages, thus reducing adverse effects of medication, without compromising treatment effectiveness. Also, does combining acupuncture with other modalities such as exercise or physical therapy provide a synergistic benefit? This requires further exploration.

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