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Tai chi for the treatment of osteoarthritis:

a systematic review and meta-analysis

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Running title: Systematic review and meta-analysis of tai chi for osteoarthritis

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Article focus

- **Tai chi is a form of physical exercise, which may offer physiological and psychological benefit to OA sufferers.**

Key messages

- **This systematic review offer some encouraging evidence suggesting that tai chi may be effective for pain control in patients with OA.**

Strengths and limitations of this study

- **The strength of this systematic review is extensive searching in various databases without language restriction in unbiased manner.**
- **Our systematic review pertain to the potential incompleteness of the evidence reviewed including publication and location bias and poor quality of the primary data and poor reporting of results.**

Abstract

Objectives: To summarize and critically evaluate the evidence from randomized clinical trials (RCTs) of tai chi as a treatment for patients with osteoarthritis.

Design: 11 databases were searched from their inception through July 2010. Randomized clinical trials testing tai chi against any type of controls in human patients with osteoarthritis localized in any joints that assessed any type of clinical outcome measures were considered. The selection of studies, data abstraction and validations were performed independently by two reviewers. The risk of bias was assessed using Cochrane criteria.

Results: Nine RCTs met our inclusion criteria. Most of them had significant methodological weaknesses. Six RCTs tested the effects of tai chi compared with attention control program, waiting list, routine care or self-help programs in patients with knee osteoarthritis. The meta-analysis suggested favorable effects of tai chi on pain (n=256; standard mean differences, SMDs, -0.79; 95% CI, -1.19 to -0.39; P=0.0001; I^2=55%), physical function (n=256; SMDs, -0.86; 95% CI, -1.20 to -0.52; P<0.00001; I^2=38%) and joint stiffness (n=256; SMDs, -0.53; 95% CI, -0.99 to -0.08; P=0.02; I^2=67%).

Conclusion: There is some encouraging evidence suggesting that tai chi might be effective in controlling pain and improving physical function in patients with knee osteoarthritis. However, due to the scarcity and often poor quality of the available randomized clinical trials, the evidence that tai chi is effective in patients with osteoarthritis is not convincing.

Introduction

Osteoarthritis (OA) is the most common degenerative joint disease affecting knees, hips, hands and spine. It is characterized by degradation of joints including cartilage surfaces and subchondral bone causing joint space narrowing, pain, stiffness, swelling, tenderness and reduced physical function. [1 2] About 5% and 10% of adults aged 60 years or older suffer from OA of the hip[1] and knee[2], respectively. Because there is no known cure for OA, the main therapeutic strategy is symptomatic. It includes analgesics, Nonsteroidal anti-inflammatory drugs (NSAIDS), COX-2 inhibitors, glucocorticoids, topical analgesics, cartilage protective agents (e.g., diacerin, glucosamine, and chondroitin). Exercise is often recommended for management of OA, [3-5] and there is some evidence of its effectiveness. [2 6 7] However, total hip or knee replacements may often be the most effective treatments. [1 2]

Tai chi (TC) is a form of complementary therapy with its similarities to aerobic exercise. It involves relaxation, deep breathing techniques and slow movements.[8] One review has suggested that TC may be beneficial for pain control in patients with knee OA.[9] However, this review is now considered outdated. Another review and meta-analysis of TC for musculoskeletal pain[10] is flawed in several respects; for instance, it failed to include all available primary studies.

The aim of this article is to summarize and critically evaluate the evidence from randomized clinical trials (RCTs) of tai chi as a method for treatment in patients with OA of any joint.

Methods

Searching

The following electronic databases were explored from their respective inceptions through July 2010: MEDLINE, AMED, EMBASE, CINAHL, five Korean Medical Databases (Korean Studies Information, DBPIA, Korea Institute of Science and Technology Information, KoreaMed, and Research Information Service System), Chinese Medical Databases (China National Knowledge Infrastructure: CNKI) and The Cochrane Library. The search terms used were as follows: [taichi OR tai adj chi OR tai chi chun OR Korean or Chinese language terms for (tai chi OR taiji OR tai chi chuan)] AND (osteoarthritis OR degenerative arthritis OR osteoarthrosis OR joint pain OR knee pain OR hip pain OR arthritis). In addition, our own department files were manually searched. The references of all located articles and the proceedings of the First International Conference of Tai Chi for Health (December 2006, Seoul, South Korea) were also hand-searched for further relevant articles. No restrictions on years, and publication status were imposed.

Selection

All prospective RCTs of tai chi for OA (not just chronic pain of the knee, hip and back, etc.) were included. Trials comparing tai chi with any type of control intervention were also included. Any trials with tai chi as a part of a complex intervention were excluded. Dissertations and abstracts were also included.

Data abstraction and study characteristics

Hard copies of all articles were obtained and read in full by two independent reviewers (MSL and JWK), and the data from these articles were validated and abstracted according to pre-defined criteria (Table 1).

Validity assessment

The risk of bias was assessed using the Cochrane classification with four criteria: sequence generation, incomplete outcome measures, blinding and allocation concealment.[11] Disagreements were resolved by discussions between the reviewers (MSL and JWK).

Quantitative data synthesis

Because there was no important clinical heterogeneity, we synthesized the results in a meta-analysis. The mean change in outcome measures compared with the baseline was used to assess the differences between intervention and control groups. Weighted mean differences (WMDs) were used when studies measured the outcomes on the same scale, and standardized mean differences (SMDs) were used when studies measured the outcomes on different scales. WMDs or SMDs and 95% confidence intervals (CIs) were calculated using the Cochrane Collaboration software (Review Manager Version 5.0 for Windows, Copenhagen: The Nordic Cochrane Centre). For studies with insufficient information, we contacted the primary authors to acquire and verify data where possible. Summary estimates of the treatment effect were calculated using the random effects model. Differences between treatment and controls were considered relevant in the context of this study. The variance of the change was inferred using a correlation factor of 0.5. Cochrane's Q-test and I^2 were used to assess statistical heterogeneity. We considered that there was considerable heterogeneity when the Cochrane's Q-test test is $P<0.10$, and I^2 was above 75%. If a sufficient number of studies (at least 10 studies) were available, we attempted to assess publication bias using a funnel plot or Egger's regression test, whereby effect estimates of the common outcome measures were plotted against the sample size.[12 13]

Results

Trial flow and study characteristics

The literature searches revealed 117 articles, of which 108 studies were excluded. The reasons for article exclusion during the selection process are described in Figure 1. Key data regarding the 9 included RCTs are summarized in Table 1.[14-22] A total of 521 participants were included in these trials. Four RCTs originated from the US, [15 16 21 22] three from Korea,[17-19] one from China[14] and one from Australia.[20] Six RCTs included patients with knee OA,[14-19] while the other three included patients with hip, knee or multiple-joint OA.[20-22] Yang-style tai chi was used in four trials,[14-16 21] Sun-style in three trials, [18-20] Wu-style in one trial[22] and one trial did not report the type of tai chiused.[17] All RCTs had a parallel-group design.

Most trials had a relatively small sample size and only 5 were based on a sample size calculation.[15 16 18-20] All of the included trials employed appropriate sequence generation methods for randomization. The risk of bias for incomplete outcome measures was low in all RCTs. Four RCTs involved a blinded assessor,[14 15 17 20] while blinding was unclear in the other 5 RCTs.[16 18 19 21 22] Five RCTs adopted an allocation concealment method,[14-17 22] one RCT[20] failed to do so, and this was

unclear in three RCTs.[18 19 21] Only 3 RCTs had an intention to treat analysis,[16 17 20] and 2 trials named a pre-defined primary outcome measure.[16 20]

Quantitative Data Synthesis

Effects of tai chi for patients with knee OA

Six RCTs tested the effects of tai chi compared with attention control,[14-16] waiting list,[17] routine care[18] or self-help programs[19] in patients with knee OA. The meta-analysis showed favorable effects of tai chi on pain (n=256, SMDs, -0.79; 95% CI -1.19 to -0.39; P=0.0001; heterogeneity: χ^2=11.13, P=0.05, I^2=55%; Figure 2A), physical function (n=256; SMDs, -0.86; 95% CI -1.20 to -0.52; P<0.00001; heterogeneity: χ^2=8.08, P=0.15, I^2=38%; Figure 2B) and joint stiffness (n=256; SMDs, -0.53; 95% CI -0.99 to -0.08; P=0.02; heterogeneity: χ^2=15.28, P=0.009, I^2=67%; Figure 2C). The sub-analysis was performed to explore whether heterogeneity could be partially explained by the type of control intervention.

Tai chi versus attention control

Three RCTs [14-16] compared the effects of tai chi on pain, physical function and joint stiffness with attention control in patients with knee OA. All trials reported favorable effects of tai chi on pain reduction. The meta-analysis also showed superior effects of tai chi for pain reduction compared with attention control (n=100; SMDs, -1.18; 95% CI -1.82 to -0.54; P=0.0003; heterogeneity: χ^2=4.28, P=0.12, I^2=53%; Figure 2A).

Two RCTs showed favorable effects of tai chi on physical function,[14 16] while the other RCT failed to do so.[15] The meta-analysis showed the favorable effects of tai chi on physical function compared with attention control (n=100; SMDs, -1.20; 95% CI -1.74 to -0.67; P<0.0001; heterogeneity: χ^2=2.99, P=0.22, I^2=33%; Figure 2B).

Three RCTs assessed the effects of tai chi on joint stiffness compared with attention control. One RCT showed favorable effects of tai chi,[14] while the other two RCTs failed to do so.[15 16] The meta-analysis did not show positive effects of tai chi (n=100; SMDs, -0.82; 95% CI -1.67 to 0.04; P=0.06; heterogeneity: χ^2=8.03, P=0.02, I^2=75%; Figure 2C).

One RCT compared the effect of tai chi on the quality of life compared with attention control; it failed to show a favorable effect on this condition.[16]

Tai chi versus routine treatments or waiting list or self-help program

Three RCTs assessed the effectiveness of tai chi on pain caused by knee OA compared with routine treatments,[18] waiting list[17] or a self-help program.[19] Two RCTs suggested a significant pain reduction compared with the waiting control [17] and the routine treatments,[18] while the other RCTs did not.[19] The meta-analysis showed favorable effects of tai chi on pain reduction (n=156; SMDs, -0.47; 95% CI -0.79 to -0.14; P=0.005; heterogeneity: χ^2=0.96, P=0.62, I^2=0%; Figure 2A).

Three RCTs tested the effect of tai chi on physical function compared with routine cares. Two RCTs showed significantly favorable effects,[18 19] while one RCT failed to do so.[17] The meta-analysis

showed superior effects of tai chi on physical function compared with routine cares (n=156; SMDs, -0.60; 95% CI -0.93 to -0.28; P=0.0003; heterogeneity: χ^2=0.79, P=0.67, I^2=0%; Figure 2B).

Three RCTs assessed the effects of tai chi on joint stiffness compared with routine cares. One RCT showed significantly favorable effects of tai chi,[18] while two RCTs failed to so.[17 19] The meta-analysis did not show significant effects of tai chi on joint stiffness (n=156; SMDs, -0.30; 95% CI -0.79 to 0.19; P=0.23; heterogeneity: χ^2=4.39, P=0.11, I^2=54%; Figure 2C).

Effects of tai chi for patients with multiple-joint OA

Three RCTs tested the effects of tai chi compared with hydrotherapy, waiting list,[20] routine treatments [21] or participation in bingo games [22] in patients with multiple-joint OA. One RCT with 3 parallel groups failed to show superior effects of tai chi on pain reduction, physical function, and quality of life compared with hydrotherapy or waiting list control but did show improved physical function compared with waiting list control.[20] The second RCT showed favorable effects of tai chi on the quality of life compared with routine treatments, while failing to show pain reduction.[21] The third RCT did not show significant differences in pain reduction, physical function or joint stiffness between tai chi and participation in bingo games.[22]

Adverse effects

Four RCTs [14-16 20] assessed adverse effects, while the other 5 RCTs [17-19 21 22] did not. None of the 4 RCTs reported serious adverse effects. Two RCTs [14 15] reported minor muscle soreness and foot and knee pain in the early days of intervention. One RCT [16] reported increased knee pain and two cancer occurrences that were not related to the interventions. The other RCT [20] reported serious adverse effects that were not related to the intervention.

Discussion

Overall, this systematic review suggests some effectiveness of tai chi on pain and physical function associated with knee OA compared with the attention control or routine care groups. However, several caveats must be considered. For joint stiffness the evidence was not robust. For a mixed population with hip or knee OA, the evidence is not sufficient to conclude whether tai chi was beneficial.

The risk of bias in the studies was assessed based on the descriptions of sequence generation, incomplete outcome measures, blinding and allocation concealment. Based on these assessments, most of the included trials had a low risk of bias.[14-17 20 22] All of the included studies addressed the details of incomplete outcome data. The main limitations of included studies were small sample sizes, inadequate control for non-specific effects and a lack of power calculations or adequate follow-up. Also, the fact that tai chi interventions cannot control for placebo effects limits generalizability. Secondly, adequate follow-up of 6-12 moths is advisable in the future studies of tai chi for OA.

Proponents of tai chi claim that it improves flexibility, strength and balance, especially in the elderly. Clearly these claims need to be tested. The pooled results from 6 RCTs[14-19] suggested that pain intensity was reduced when tai chi was compared with attention control or routine cares for knee OA. However, three RCTs found that tai chi had no significant effect on pain reduction compared with hydrotherapy, waiting list, routine treatments or participation in bingo games in multiple-joint OA.[20-22] These results might be explained in part through inadequate blinding and control for non-specific effects in some of the positive studies among other sources of bias.

Assuming that tai chi was beneficial for treating OA, the possible mechanisms of action may be of interest. It has been postulated that regular tai chi improves balance and reduces the likelihood of falls by improving muscle flexibility and trunk rotation. Tai chi is a form of physical exercise combined with relaxation. Physical movement in tai chi can improve joint stability and aid in reducing excess weight, effectively decreasing joint pain, increasing function and reducing OA disease process.[23 24] Furthermore, tai chi may also influence the psychosocial quality of life, which may have a positive influence on chronic pain.[24 25] The question whether tai chi is superior to other forms of therapeutic exercise is currently unanswered and might thus be a topic for further investigations.

Four of the reviewed studies reported minor adverse events related to tai chi.[14-16 20] Tai chi appears to be generally safe, and serious adverse effects have not been reported. Adverse effects were, however, not the focus of this review and might require further research.

Future RCTs of tai chi for OA should adhere to accepted standards of trial methodology. The studies included in this review show a number of problems that have been noted by other reviews of trials examining the efficacy of tai chi, such as the expertise of tai chi practitioners, the pluralism of tai chi, the frequency and duration of treatment, the use of validated primary outcome measures and adequate statistical tests, and heterogeneous comparison groups.[26 27] Furthermore, even though it is difficult to blind subjects to treatment, employing assessor blinding and allocation concealment are important for reducing bias. A clinical study is only truly useful if

the intervention used can be replicated, and hence the type of tai chi employed is important. There are significant differences among the numerous forms of tai chi, and so a clear description of the tai chi intervention should be provided together with a description of the level of expertise of the instructors.

Limitations of our systematic review, and any systematic review in general, pertain to the potential incompleteness of the evidence reviewed. We aimed to identify all RCTs on the topic. The distorting effects on systematic reviews and meta-analyses arising from publication bias and location bias are well documented.[28-30] In order to minimize these biases, the review was not restricted by publication language, and a large number of different databases were queried. We are confident that our search strategy located all relevant data; however, some degree of uncertainty remains. Moreover, selective publishing and reporting can be major causes of bias. It is conceivable that several negative RCTs remain unpublished, thus distorting the overall picture. Another possible source of bias is the fact that half of the included trials were carried out in China and Korea, where there have appeared to produce almost no negative studies.[31] Further limitations of our review are the potentially poor quality of the primary data and poor reporting of results, which were highly heterogeneous in virtually every aspect. To establish the role of tai chi in the management of OA patients, adequately designed trials are required.

In conclusion, there is encouraging evidence suggesting that tai chi might be effective in controlling pain and improving physical function in patients with knee OA. However, due to the scarcity and often poor quality of the available RCTs, the evidence is not convincing.

Competing Interest

The authors have declared that no competing interests exist.

Author Contributions

Jung Won Kang and Myeong Soo Lee **designed the review, performed searches, appraised and selected trials, abstracted data, contacted authors for additional data, carried out analysis and interpretation of the data, and drafted this report.**

Paul Posadzki and Edzard Ernst **reviewed and critiqued on the review protocol and this report, assisted in designing of the review**

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Data sharing

No additional data available

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Figure Legends

Figure 1. Flowchart of trial selection process. RCT: randomized clinical trial.

Figure 2. Forest plot of the effects of tai chi on (A) pain; (B) physical function; and (C) joint stiffness. TC: tai chi.

Table 1. Summary of randomized clinical trials of tai chi for osteoarthritis

First author (year) Country	Sample size OA site Age (yrs) Duration of OA (yrs)	Experimental intervention (regimen)	Control intervention (regimen)	Main outcomes	Intergroup differences	Risk bias* ITT analy
Ni (2010) [14] China	35 Knee 62.9; 63.5 ≥ 1 yrs	TC (30 min, 2 – 4 times weekly for 24 weeks, n=18) Yang-style (simplified 24 forms)	Attention control program (45 min, wellness and stretching, n=17)	1) Pain (WOMAC) 2) Physical function (WOMAC) 3) Joint stiffness (WOMAC) 4) Total WOMAC score	1) P=0.001 2) P=0.000 3) P=0.043 4) P=0.000	Y,Y,Y No
Brisme e (2007) [15] USA	41 Knee 70.8; 68.8 n.r.	TC (40 min, 3 times weekly for 6 weeks plus home-based tai chi for 6 weeks, n=22) Yang-style (simplified 24 forms)	Attention control program (40 min, lecture, once weekly for 6 weeks, n=19)	1) Pain (VAS) 2) Physical function (WOMAC) 3) Joint stiffness (WOMAC)	1) P<0.05 2) NS 3) NS	Y,Y,Y No

Wang (2009) [16] USA	40 Knee 63; 68 n.r.	TC (60 min, twice weekly for 12 weeks, n=20) Yang-style (10 forms)	Attention control program (60 min, wellness and stretching, once weekly for 12 weeks, n=20)	1) Pain (WOMAC) 2) Physical function (WOMAC) 3) Joint stiffness (WOMAC) 4) Quality of Life (SF-36)	1) P=0.005 2) P=0.001 3) NS 4) NS	Y,Y,U Yes
Lee (2009) [17] Korea	44 Knee 70.2; 66.9 n.r.	TC (60 min, twice weekly for 8 weeks, n=29) n.r. (18 movements)	Waiting list (n=15)	1) Pain (WOMAC) 2) Physical function (WOMAC) 3) Joint stiffness (WOMAC) 4) Total WOMAC score 5) Quality of Life (SF-36)	1) P=0.03 2) NS 3) NS 4) NS 5) P=0.024	Y,Y,Y Yes
Song (2003) [18] Korea	72 Knee 64.8; 62.5 10.4; 9.2	TC (60 min, 3 times weekly for 12 weeks, n=22) Sun-style (12 forms)	Routine care (n=21)	1) Pain (WOMAC) 2) Physical function (ADL) 3) Joint stiffness (WOMAC)	1) P<0.05 2) P<0.01 3) P=0.08	Y,Y,U No

Song (2009)[19] Korea	82 Knee 62.4; 59.9 0.5 - 10	TC [(60 min, twice weekly for the first 3 weeks and once weekly for the next 6 months) plus 6 instances of self-help program, n=41] Sun-style (31 forms)	Self- help program (2 hr, once monthly for 6 months, n=39)	1) Pain (WOMAC) 2) Physical function (WOMAC) 3) Joint stiffness (WOMAC)	1) NS 2) P=0.03 3) NS	Y,Y,U No
Franse n (2007)[20] Austra lia	152 Hip or knee 70.8; 70.0; 69.6 n.r. (mean)	(A) TC (60 min, twice weekly for 12 weeks, n=56) Sun-style (modified 24 forms)	(B) Hydrotherapy (60 min, twice weekly for12 weeks, n=55) (C) Waiting list (n=41)	1) Pain (WOMAC) 2) Physical function (WOMAC) 3) Quality of Life (SF-12)	1) A vs. B, NS; A vs. C, NS 2) A vs. B, NS; A vs. C, P<0.05 3) Physical: A vs. B, NS; A vs. C, NS Mental: A vs. B, NS; A vs. C, NS	Y,Y,Y Yes
Hartm an (2000)[21] USA	35 Multiple joint (hip, knee, ankles, foot) 68.6; 67.5 n.r. (mean)	TC (60 min, twice weekly for 12 weeks, n=19) Yang-style (9 forms)	Routine care (usual physical activity plus total of 3 group meetings and telephone discussion every 2 weeks, n=16)	1) Pain (AIMS) 2) Quality of life (AIMS)	1) NS 2) tension, P<0.005; satisfaction, P<0.001	Y,Y,U No

Adler (2007)[22] USA	22 Hip or knee 70.8; 72.8 n.r.	TC (60 min, once weekly for 10 weeks, n=11) Wu-style (16 forms)	Bingo games (non-physical activity, n=11)	1) Pain (WOMAC) 2) Physical function (ADL) 3) Psychological symptoms	1-3) NS	Y,Y,U No

ADL: Activities of Daily Living; AE: adverse effects; AIMS: Arthritis Impact Measurement Scale; ITT: intention-to-treat; n.r.: not reported; NS: not significant; OA: osteoarthritis; TC: tai chi; VAS: visual analogue scale; WOMAC: Western Ontario and McMaster Universities Osteoarthritis Index; *Risk of bias (sequence generation, incomplete outcome measures, assessor blind, allocation concealment), Y: a low risk of bias; U: unclear; N: a high risk of bias

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Tai chi for the treatment of osteoarthritis:

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License statement

Article focus

- Tai chi is a form of physical exercise and may offer physiological and psychological benefit to osteoarthritis (OA) sufferers.

Key messages

- This systematic review offers encouraging evidence suggesting that tai chi may be effective for pain control in patients with OA.

Strengths and limitations of this study

- The strength of this systematic review is its extensive, unbiased search of various databases without language restriction.
- Our systematic review pertains to the potential incompleteness of the evidence reviewed, including publication and location bias, poor quality of the primary data and poor reporting of results.

Abstract

Objectives: To summarise and critically evaluate the evidence from randomised clinical trials (RCTs) of tai chi as a treatment for patients with osteoarthritis.

Design: Eleven databases were searched from their inception through July 2010. RCTs testing tai chi against any type of controls in human patients with osteoarthritis localised in any joints that assessed any type of clinical outcome measures were considered. The selection of studies, data abstraction and validations were performed independently by two reviewers. The risk of bias was assessed using Cochrane criteria.

Results: Nine RCTs met our inclusion criteria. Most of them had significant methodological weaknesses. Six RCTs tested the effects of tai chi compared with attention control program, a wait list, routine care or self-help programs in patients with osteoarthritis in the knee. The meta-analysis suggested favourable effects of tai chi on pain (n=256; standard mean

difference (SMD), -0.79; 95% CI, -1.19 to -0.39; P=0.0001; I^2=55%), physical function (n=256; SMD, -0.86; 95% CI, -1.20 to -0.52; P<0.00001; I^2=38%) and joint stiffness (n=256; SMD, -0.53; 95% CI, -0.99 to -0.08; P=0.02; I^2=67%).

Conclusion: There is some encouraging evidence suggesting that tai chi may be effective in controlling pain and improving physical function in patients with osteoarthritis in the knee. However, due to the small number of RCTs with a low risk of bias, the evidence that tai chi is effective in patients with osteoarthritis is limited.

Introduction

Osteoarthritis (OA) is the most common degenerative joint disease and affects the knees, hips, hands and spine. It is characterised by degradation of the joints including cartilage surfaces and subchondral bone, causing joint space narrowing, pain, stiffness, swelling, tenderness and reduced physical function.[1 2] About 5% and 10% of adults aged 60 years or older suffer from OA of the hip[1] and knee[2], respectively. Because there is no known cure for OA, the main therapeutic strategy is symptomatic. Treatment includes analgesics, nonsteroidal anti-inflammatory drugs (NSAIDS), COX-2 inhibitors, glucocorticoids, topical analgesics and cartilage protective agents (e.g., diacerein, glucosamine, and chondroitin). Exercise is often recommended for managing OA,[3-5]and there is some evidence of its effectiveness.[2 6 7] However, total hip or knee replacements may often be the most effective treatments. [1 2]

Tai chi (TC) is a form of complementary therapy with similarities to aerobic exercise. It involves relaxation, deep breathing techniques and slow movements.[8] There are two systematic reviews of tai chi for OA[9] or musculoskeletal pain.[10] One of them included five randomised clinical trials (RCTs) and 7 controlled clinical trials (CCTs) compared with several types of controls. This review suggested that TC may be beneficial for pain control in patients with knee OA.[9] However, this review is now out-dated and did not include recent publications. Recently, another review was published in 2009; this review was based on the same 4 RCTs for OA as well as 1 for arthritis, 1 RCT for tension headache and 1 RCT for rheumatoid arthritis.[10] This review also showed some favourable effects of tai chi for musculoskeletal pain. However, this review pooled all of these 7 RCTs regardless of clinical heterogeneity, and it also failed to include all available primary studies.

Therefore, the aim of this article is to update, complete and critically evaluate the evidence from RCTs of tai chi as a method of treatment for patients with OA of any joint.

Methods

Searching

The following electronic databases were explored from their respective inceptions through July 2010: MEDLINE, AMED, EMBASE, CINAHL, five Korean Medical Databases (Korean Studies Information, DBPIA, Korea Institute of Science and Technology Information, KoreaMed, and Research Information Service System), Chinese Medical Databases (China National Knowledge Infrastructure: CNKI) and the Cochrane Library. The search terms used were as follows: [taichi OR tai adj chi OR tai chi chun OR Korean or Chinese language terms for (tai chi OR taiji OR tai chi chuan)] AND (osteoarthritis OR degenerative arthritis OR osteoarthrosis OR joint pain OR knee pain OR hip pain OR arthritis). The search strategies were shown in supplement 1. In addition, our own department files were manually searched. The references of all located articles and the proceedings of the First International Conference of Tai Chi for Health (December 2006, Seoul, South Korea) were also hand-searched for further relevant articles. No restrictions on years or publication status were imposed. We did not publish the protocol in advance.

Selection

All prospective RCTs of tai chi for OA (not just chronic pain of the knee, hip or back, etc.) were included. Trials comparing tai chi with any type of control intervention were also included. Dissertations and abstracts were also included. Any trials with tai chi as part of a complex intervention were excluded.

Data abstraction and study characteristics

Hard copies of all articles were obtained and read in full by two independent reviewers (MSL and JWK), and the data from these articles were validated and abstracted according to pre-defined criteria (Table 1).

Validity assessment

The risk of bias was assessed using the Cochrane classification with four criteria: sequence generation, allocation concealment, blinding and incomplete outcome measurement.[11] Low risk of bias for assessor blinding was assumed if specified in the text regardless of the type of outcome measures (even for self-reported outcome measures). We assumed that the assessor was the person in charge of managing the outcome measures. Disagreements were resolved by discussions between the reviewers (MSL and JWK).

Quantitative data synthesis

Because there was no important clinical heterogeneity, we synthesised the results in a meta-analysis. The mean change of outcome measures between the ends of intervention and the baseline was used to assess the differences between intervention and control groups. Weighted mean differences (WMDs) were used when studies measured the outcomes on the same scale, and standardised mean differences (SMDs) were used when studies measured the outcomes on different scales. WMDs or SMDs and 95% confidence intervals (CIs) were calculated using Cochrane Collaboration software (Review Manager Version 5.0 for Windows; Copenhagen: The Nordic Cochrane Centre). For studies with insufficient information, we contacted the primary authors to acquire and verify data when possible. Summary estimates of the treatment effect were calculated using the random effects model. Differences between treatment and controls were considered relevant in the context of this study. The variance of the change was inferred using a correlation factor of 0.5.[12] Cochrane's

Q-test and I^2 were used to assess statistical heterogeneity. We determined that there was considerable heterogeneity when the Cochrane's Q-test result was determined with $P<0.10$ and I^2 was above 75%. If a sufficient number of studies (at least 10 studies) were available, we attempted to assess publication bias using a funnel plot or Egger's regression test, whereby effect estimates of the common outcome measures were plotted against the sample size. [13 14]

Results

Trial flow and study characteristics

The literature search revealed 117 articles, of which 108 studies were excluded. The reasons for article exclusion during the selection process are described in Figure 1. Key data regarding the 9 included RCTs are summarised in Table 1.[15-23] A total of 521 participants were included in these trials. Four RCTs originated in the US,[16 17 22 23] three RCTs were from Korea,[18-20] one RCT was from China[15] and one RCT was from Australia.[21] Six RCTs included patients with knee OA,[15-20] while the other three RCTs included patients with hip, knee or multiple-joint OA.[21-23] Yang-style tai chi was used in four trials, [15-17 22] Sun-style was used in three trials, [19-21] Wu-style was used in one trial[23] and one trial did not report the type of tai chi used.[18] All RCTs had a parallel-group design.

Most trials had a relatively small sample size, and only 5 trials were based on a sample size calculation.[16 17 19-21] All of the included trials employed appropriate sequence generation methods for randomisation (Table 2). The authors reported they employed assessor blinding in five RCTs[15-18 21] while blinding was unclear in the other 4 RCTs.[19 20 22 23] Five RCTs adopted an allocation concealment method,[15 17-19 23] two RCTs[16 21] failed to do so, and this

parameter was unclear in two RCTs.[20 22] The risk of bias for reporting drop-out or withdrawal was low in all RCTs. Four RCTs had an intention to treat analysis.[17 18 21 23] Two trials had low risk of bias in selective outcome reporting,[17 21] and the other 2 studies are at high risk of bias.[19 22]

Quantitative Data Synthesis

Effects of tai chi on patients with knee OA

Six RCTs tested the effects of tai chi compared with attention control,[15-17] a waiting list, [18] routine care[19] or self-help programs[20] in patients with knee OA. The meta-analysis showed favourable effects of tai chi on pain (n=256; SMD, -0.79; 95% CI -1.19 to -0.39; P=0.0001; heterogeneity: χ^2=11.13, P=0.05, I^2=55%; Figure 2A), physical function (n=256; SMD, -0.86; 95% CI -1.20 to -0.52; P<0.00001; heterogeneity: χ^2=8.08, P=0.15, I^2=38%; Figure 2B) and joint stiffness (n=256; SMD, -0.53; 95% CI -0.99 to -0.08; P=0.02; heterogeneity: χ^2=15.28, P=0.009, I^2=67%; Figure 2C). A sub-analysis was performed to explore whether heterogeneity could be partially explained by the type of control intervention.

Tai chi versus attention control

Three RCTs[15-17] compared the effects of tai chi on pain, physical function and joint stiffness with attention control in patients with knee OA. All trials reported favourable effects of tai chi on pain reduction. The meta-analysis also showed superior effects of tai chi for pain reduction compared with attention control (n=100; SMD, -1.18; 95% CI -1.82 to -0.54; P=0.0003; heterogeneity: χ^2=4.28, P=0.12, I^2=53%; Figure 2A).

Two RCTs showed favourable effects of tai chi on physical function, [15 17] while the other RCT failed to do so.[16] The meta-analysis showed the favourable effects of tai chi on physical

function compared with attention control (n=100; SMD, -1.20; 95% CI -1.74 to -0.67; P<0.0001; heterogeneity: χ^2=2.99, P=0.22, I^2=33%; Figure 2B).

Three RCTs assessed the effects of tai chi on joint stiffness compared with attention control.[15-17] One RCT showed favourable effects of tai chi,[15] while the other two RCTs failed to do so.[16 17] The meta-analysis did not show positive effects of tai chi (n=100; SMD, -0.82; 95% CI -1.67 to 0.04; P=0.06; heterogeneity: χ^2=8.03, P=0.02, I^2=75%; Figure 2C).

One RCT compared the effect of tai chi on the quality of life compared with attention control; it failed to show a favourable effect on this condition. [17]

Tai chi versus routine treatments, a waiting list or a self-help program

Three RCTs assessed the effectiveness of tai chi on pain caused by knee OA compared with routine treatments, a waiting list or a self-help program.[18-20] Two RCTs suggested a significant pain reduction compared with the waiting control[18] and the routine treatments,[19] while the other RCT did not.[20] The meta-analysis showed favourable effects of tai chi on pain reduction (n=156; SMD, -0.47; 95% CI -0.79 to -0.14; P=0.005; heterogeneity: χ^2=0.96, P=0.62, I^2=0%; Figure 2A).

Three RCTs tested the effect of tai chi on physical function compared with routine treatments, a waiting list or a self-help program.[18-20] Two RCTs showed significantly favourable effects,[19 20] while one RCT failed to do so.[18] The meta-analysis showed superior effects of tai chi on physical function compared with routine cares (n=156; SMD, -0.60; 95% CI -0.93 to -0.28; P=0.0003; heterogeneity: χ^2=0.79, P=0.67, I^2=0%; Figure 2B).

Three RCTs assessed the effects of tai chi on joint stiffness compared with routine treatments, a waiting list or a self-help program.[18-20] One RCT showed significantly favourable effects of tai chi,[19] while two RCTs failed to so.[18 20] The meta-analysis did not show significant effects of tai chi on joint stiffness (n=156; SMD, -0.30; 95% CI -0.79 to 0.19; P=0.23; heterogeneity: χ^2=4.39, P=0.11, I^2=54%; Figure 2C).

Effects of tai chi for patients with multiple-joint OA

Three RCTs tested the effects of tai chi compared with hydrotherapy, waiting list, routine treatments or participation in bingo games in patients with multiple joint OA.[21-23] One RCT with 3 parallel groups failed to show superior effects of tai chi on pain reduction, physical function, and quality of life compared with hydrotherapy or a waiting list control but did show improved physical function compared with the waiting list control.[21] The second RCT showed favourable effects of tai chi on the quality of life compared with routine treatments while failing to show pain reduction.[22] The third RCT did not show significant differences in pain reduction, physical function or joint stiffness between tai chi and participation in bingo games. [23]

Adverse effects

Four RCTs [15-17 21] assessed adverse effects while the other 5 RCTs [18-20 22 23] did not. None of the 4 RCTs reported serious adverse effects. Two RCTs reported minor muscle soreness and foot and knee pain in the early days of intervention.[15 16] One RCT reported increased knee pain and two cancer occurrences that were not related to the interventions.[17] The other RCT reported serious adverse effects that were not related to the intervention. [21]

Discussion

Overall, this systematic review suggests that tai chi may be an effective treatment for pain and physical function associated with knee OA compared with attention control or routine care. However, several caveats must be considered. For joint stiffness, the evidence was not robust. For a mixed population with hip or knee OA, the evidence is not sufficient to conclude whether tai chi was beneficial.

Our review aimed to update and complete the evidence by adding newly RCTs of tai chi as a method of treatment in patients with OA. Compared to 2 previous reviews,[9 10] we identified 4 new, low risk of bias RCTs[15 17-19] and successfully updated the evidence for therapy. The results of our review are similar to the other 2 reviews.[10 18] One previous review[18] showed that tai chi may be beneficial for pain control in patients with knee OA while the other review[10] also reported some favourable effects of tai chi for musculoskeletal pain. However, we were concerned about the poor methodological quality of the included primary studies in both reviews.

Previous systematic reviews have suggested that there are clinically important differences among various therapies compared with various controls in pain reduction and functional improvement in OA.[2] The effect size of pain reduction and function improvement in our review were higher than those of exercise, NSAIDs, and drug therapy, and this effect is clinically significant.[2] However, these results are difficult to compare quantitatively due to the use of different assessment measures for evaluating pain and the use of different controls for evaluating the comparisons.

Limitations of our systematic review and any systematic review in general pertain to the potential incompleteness of the evidence reviewed. The distorting effects on systematic reviews and meta-analyses arising from publication bias and location bias are well documented.[24-26] We are confident that our search strategy located all relevant data; however, some degree of uncertainty remains. Another possible source of bias is the fact that half of the included trials were carried out in China and Korea, where there have appeared to produce almost no negative studies.[27] Our review may be affected by the potentially poor quality of the primary data and poor reporting of results, which were highly heterogeneous in virtually every aspect. A further limitation is our employment of the Cochrane risk of bias tool to assess the methodological bias in the clinical trial. This tool was recently recommended for assessing methodological quality instead of scoring assessment tool including Jadad scale and others.[11] However, the substation inter-rater disagreements across the domains were reported in the Cochrane risk of bias tool. [28 29]

The risk of bias in the studies was assessed based on the descriptions of sequence generation, allocation concealment, blinding, incomplete outcome measures, and selective outcome reporting. Based on these assessments, the risk of bias varied across the included studies. Only 3 RCTs had a low risk of bias,[17 18 21] and two studies had a moderate risk of bias.[15 23] The other 4 RCTs are at high risk of being biased.[16 19 20 22] Five RCTs employed allocation concealment,[15 17 18 20 23] and four RCTs used intention-to-treat analysis.[17 18 21 23] Inappropriate allocation concealment and lack of blinding exaggerate the results of outcome measures.[30 31] Only two RCTs are at low risk of bias in selective outcome reporting.[17 21] Even though the authors reported they employed assessor blinding,[15-18 21] some outcomes that they measured relied on patient's subjective reporting, due to which the patient's and assessor's blinding becomes unachievable and irrelevant. The main limitations of the included studies were small

sample sizes, inadequate control for non-specific effects and a lack of power calculations or adequate follow-up. Also, the fact that tai chi interventions cannot control for placebo effects limits generalisability. Second, adequate follow-ups of 6-12 moths are advisable for future studies of tai chi for OA.

Proponents of tai chi claim that it improves flexibility, strength and balance, especially in the elderly. Clearly these claims need to be tested. The pooled results from 6 RCTs[15-20] suggested that pain intensity was reduced when patients used tai chi compared with attention control or routine care for knee OA. However, three RCTs found that tai chi had no significant effect on pain reduction compared with hydrotherapy, waiting list, routine treatments or participation in bingo games in multiple joint OA.[21-23] These results may be explained in part through inadequate blinding and control for non-specific effects in some of the positive studies, among other sources of bias.

Assuming that tai chi was beneficial for treating OA, the possible mechanisms of action may be of interest. Regular tai chi has been postulated to improve balance and reduce the likelihood of falls by improving muscle flexibility and trunk rotation. Tai chi is a form of physical exercise combined with relaxation. Physical movement in tai chi can improve joint stability and aid in reducing excess weight, effectively decreasing joint pain, increasing function and reducing advancement of OA.[32 33] Furthermore, tai chi may also influence the psychosocial quality of life, which may have a positive influence on chronic pain.[32 34] The question about whether tai chi is superior to other forms of therapeutic exercise is currently unanswered and is thus a topic for further investigation.

Four of the reviewed studies reported minor adverse events related to tai chi.[15-17 21] Tai chi appears to be generally safe, and serious adverse effects have not been reported. Adverse effects were, however, not the focus of this review and may require further research.

Future RCTs of tai chi for OA should adhere to accepted standards of trial methodology. The studies included in this review show a number of problems that have been noted by other reviews of trials examining the efficacy of tai chi, such as the expertise of tai chi practitioners, the pluralism of tai chi, the frequency and duration of treatment, the use of validated primary outcome measures and adequate statistical tests, and heterogeneous comparison groups.[35 36] Furthermore, even though it is difficult to blind subjects to treatment, employing assessor blinding and allocation concealment are important for reducing bias. A clinical study is only truly useful if the intervention used can be replicated; hence, the type of tai chi employed is important. There are significant differences among the numerous forms of tai chi, and a clear description of the tai chi intervention should be provided together with a description of the level of expertise of the instructors.

In conclusion, there is encouraging evidence suggesting that tai chi may be effective in controlling pain and improving physical function in patients with knee OA. However, due to the number of eligible RCTs and often poor quality of the available RCTs, the evidence is limited.

Competing Interest

The authors have declared that no competing interests exist.

Author Contributions

Jung Won Kang and Myeong Soo Lee designed the review, performed searches, appraised and selected trials, abstracted data, contacted authors for additional data, carried out analysis and interpretation of the data, and drafted this report.

Paul Posadzki and Edzard Ernst reviewed and critiqued on the review protocol and this report, assisted in designing of the review

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Data sharing

No additional data available

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Figure Legends

Figure 1. Flowchart of trial selection process. RCT: randomized clinical trial.

Figure 2. Forest plot of the effects of tai chi on (A) pain; (B) physical function; and (C) joint stiffness. TC: tai chi.

Table 1. Summary of randomized clinical trials of tai chi for osteoarthritis

First author (year) Country	Sample size OA site Age (yrs) Duration of OA (yrs)	Experimental intervention (regimen)	Control intervention (regimen)	Main outcomes	Adverse effects	Author's conclusion
Ni (2010)[15] China	35 Knee 62.9; 63.5 ≥ 1 yrs	TC (30 min, 2 – 4 times weekly for 24 weeks, n=18) Yang-style (simplified 24 forms)	Attention control program (45 min, wellness and stretching, n=17)	1) Pain (WOMAC) 2) Physical function (WOMAC) 3) Joint stiffness (WOMAC) 4) Total WOMAC score	Not serious AE Minor muscle soreness, pain in foot and knee (n=5)	"[...] TC provide safe, feasible and useful exercise option for Chinese female patients with knee OA"
Brisme e (2007)[16] USA	41 Knee 70.8; 68.8 n.r.	TC (40 min, 3 times weekly for 6 weeks plus home-based tai chi for 6 weeks, n=22) Yang-style (simplified 24 forms)	Attention control program (40 min, lecture, once weekly for 6 weeks, n=19)	1) Pain (VAS) 2) Physical function (WOMAC) 3) Joint stiffness (WOMAC)	Minor muscle soreness, pain in foot and knee (n.r.)	"[...] TC [...] provided significant knee pain reduction and physical function improvement in elderly subjects with knee OA"
Wang (2009)[17] USA	40 Knee 63; 68 n.r.	TC (60 min, twice weekly for 12 weeks, n=20) Yang-style (10 forms)	Attention control program (60 min, wellness and stretching, once weekly for 12 weeks, n=20)	1) Pain (WOMAC) 2) Physical function (WOMAC) 3) Joint stiffness (WOMAC) 4) Quality of Life (SF-36)	Increased knee pain (TC: 1); cancer (TC: 1; control: 1)	"TC reduces pain and improves physical function [...]"
Lee (2009)[18] Korea	44 Knee 70.2; 66.9 n.r.	TC (60 min, twice weekly for 8 weeks, n=29) n.r. (18 movements)	Waiting list (n=15)	1) Pain (WOMAC) 2) Physical function (WOMAC) 3) Joint stiffness (WOMAC) 4) Total WOMAC score 5) Quality of Life (SF-36)	n.r.	"TC appears to have beneficial effects [...]"
Song (2003)[19] Korea	72 Knee 64.8; 62.5 10.4; 9.2	TC (60 min, 3 times weekly for 12 weeks, n=22) Sun-style (12 forms)	Routine care (n=21)	1) Pain (WOMAC) 2) Physical function (ADL) 3) Joint stiffness (WOMAC)	n.r.	"[...] TC [...] was effective in improving [...]"

Song (2009)[20] Korea	82 Knee 62.4; 59.9 0.5 - 10	TC [(60 min, twice weekly for the first 3 weeks and once weekly for the next 6 months) plus 6 instances of self-help program, n=41] Sun-style (31 forms)	Self- help program (2 hr, once monthly for 6 months, n=39)	1) Pain (WOMAC) 2) Physical function (WOMAC) 3) Joint stiffness (WOMAC)	n.r.	"TC combined with self-help program was more effective than the self-help only program [...]"
Franse n (2007)[21] Australia	152 Hip or knee 70.8; 70.0; 69.6 n.r. (mean)	(A) TC (60 min, twice weekly for 12 weeks, n=56) Sun-style (modified 24 forms)	(B) Hydrotherapy (60 min, twice weekly for12 weeks, n=55) (C) Waiting list (n=41)	1) Pain (WOMAC) 2) Physical function (WOMAC) 3) Quality of Life (SF-12)	11 serious AE that are not related to intervention. Low back pain (hydrotherapy: 1; TC: 1)	"[...] TC [...] can provide large and sustained improvement in physical function [...]'
Hartman (2000)[22] USA	35 Multiple joint (hip, knee, ankles, foot) 68.6; 67.5 n.r. (mean)	TC (60 min, twice weekly for 12 weeks, n=19) Yang-style (9 forms)	Routine care (usual physical activity plus total of 3 group meetings and telephone discussion every 2 weeks, n=16)	1) Pain (AIMS) 2) Quality of life (AIMS)	n.r.	"TC is a safe and effective [...]"
Adler (2007)[23] USA	22 Hip or knee 70.8; 72.8 n.r.	TC (60 min, once weekly for 10 weeks, n=11) Wu-style (16 forms)	Bingo games (non-physical activity, n=11)	1) Pain (WOMAC) 2) Physical function (ADL) 3) Psychological symptoms	n.r.	"The current study will serve as a feasibility study for future TC research"

ADL: Activities of Daily Living; AE: adverse effects; AIMS: Arthritis Impact Measurement Scale; ITT: intention-to-treat; n.r.: not reported; NS: not significant; OA: osteoarthritis; TC: tai chi; VAS: visual analogue scale; WOMAC: Western Ontario and McMaster Universities Osteoarthritis Index

Table 2. Risk of bias of included RCTs.*

Study	Random sequence generation	Allocation concealment	Patient blinding	Assessor blinding	Reporting drop-out or withdrawal†	Intention-to-treat analysis†	Selective outcome reporting
Ni (2010) [15]	L	L	H	L	L	H	U
Brismee (2007) [16]	L	H	H	L	L	H	U
Wang (2009) [17]	L	L	H	L	L	L	L
Lee (2009) [18]	L	L	H	L	L	L	U
Song (2003) [19]	L	L	H	U	L	H	H
Song (2009) [20]	L	U	H	U	L	H	U
Fransen (2007) [21]	L	H	H	L	L	L	L
Hartman (2000) [22]	L	U	H	U	L	H	H
Adler (2007) [23]	L	L	H	U	L	L	U

*, Domains of quality assessment based on Cochrane tools for assessing risk of bias.
†, Two domains referring to 'incomplete outcome data' in the Cochrane tools for assessing risk of bias.
Abbreviations; L: low risk of bias; H: high risk of bias; U: Unclear (uncertain risk of bias).

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Tai chi for the treatment of osteoarthritis:

a systematic review and meta-analysis

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License statement

Article focus

- Tai chi is a form of physical exercise and may offer physiological and psychological benefit to osteoarthritis (OA) sufferers.

Key messages

- This systematic review offers encouraging evidence suggesting that tai chi may be effective for pain control in patients with OA.

Strengths and limitations of this study

- The strength of this systematic review is its extensive, unbiased search of various databases without language restriction.
- Our systematic review pertains to the potential incompleteness of the evidence reviewed, including publication and location bias, poor quality of the primary data and poor reporting of results.

Abstract

Objectives: To summarise and critically evaluate the evidence from randomised clinical trials (RCTs) of tai chi as a treatment for patients with osteoarthritis.

Design: Eleven databases were searched from their inception through July 2010. RCTs testing tai chi against any type of controls in human patients with osteoarthritis localised in any joints that assessed any type of clinical outcome measures were considered. The selection of studies, data abstraction and validations were performed independently by two reviewers. The risk of bias was assessed using Cochrane criteria.

Results: Nine RCTs met our inclusion criteria. Most of them had significant methodological weaknesses. Six RCTs tested the effects of tai chi compared with attention control program, a wait list, routine care or self-help programs in patients with osteoarthritis in the knee. The meta-analysis suggested favourable effects of tai chi on pain (n=256; standard mean difference (SMD), -0.79; 95% CI, -1.19 to -0.39; P=0.0001; I^2=55%), physical function (n=256; SMD, -0.86; 95% CI, -1.20 to -0.52; P<0.00001; I^2=38%) and joint stiffness (n=256; SMD, -0.53; 95% CI, -0.99 to -0.08; P=0.02; I^2=67%).

Conclusion: There is some encouraging evidence suggesting that tai chi may be effective in controlling pain and improving physical function in patients with osteoarthritis in the knee. However, due to the small number of RCTs with a low risk of bias, the evidence that tai chi is effective in patients with osteoarthritis is limited.

Introduction

Osteoarthritis (OA) is the most common degenerative joint disease and affects the knees, hips, hands and spine. It is characterised by degradation of the joints including cartilage surfaces and subchondral bone, causing joint space narrowing, pain, stiffness, swelling, tenderness and reduced physical function.[1 2] About 5% and 10% of adults aged 60 years or older suffer from OA of the hip[1] and knee[2], respectively. Because there is no known cure for OA, the main therapeutic strategy is symptomatic. Treatment includes analgesics, nonsteroidal anti-inflammatory drugs (NSAIDS), COX-2 inhibitors, glucocorticoids, topical analgesics and cartilage protective agents (e.g., diacerein, glucosamine, and chondroitin). Exercise is often recommended for managing OA,[3-5]and there is some evidence of its effectiveness.[2 6 7] However, total hip or knee replacements may often be the most effective treatments. [1 2]

Tai chi (TC) is a form of complementary therapy with similarities to aerobic exercise. It involves relaxation, deep breathing techniques and slow movements.[8] There are two systematic reviews of tai chi for OA[9] or musculoskeletal pain.[10] One of them included five randomised clinical trials (RCTs) and 7 controlled clinical trials (CCTs) compared with several types of controls. This review suggested that TC may be beneficial for pain control in patients with knee OA.[9] However, this review is now out-dated. Recently, another review was published in 2009; this review was based on the same 4 RCTs for OA as well as 1 for arthritis, 1 RCT for tension headache and 1 RCT for rheumatoid arthritis.[10] This review also showed some favourable effects of tai chi for musculoskeletal pain. However, this review pooled the trials regardless of clinical heterogeneity, and it also now out-dated.
Therefore, the aim of this article is to update, complete and critically evaluate the evidence from RCTs of tai chi as a method of treatment for patients with OA of any joint.

Methods

Searching

The following electronic databases were explored from their respective inceptions through July 2010: MEDLINE, AMED, EMBASE, CINAHL, five Korean Medical Databases (Korean Studies Information, DBPIA, Korea Institute of Science and Technology Information, KoreaMed, and Research Information Service System), Chinese Medical Databases (China National Knowledge Infrastructure: CNKI) and the Cochrane Library. The search terms used were as follows: [taichi OR tai adj chi OR tai chi chun OR Korean or Chinese language terms for (tai chi OR taiji OR tai chi chuan)] AND (osteoarthritis OR degenerative arthritis OR osteoarthrosis OR joint pain OR knee pain OR hip pain OR arthritis). The search strategies were shown in supplement 1. In addition, our own department files were manually searched. The references of all located articles and the proceedings of the First International Conference of Tai Chi for Health (December 2006, Seoul, South Korea) were also hand-searched for further relevant articles. No restrictions on years or publication status were imposed. We did not publish the protocol in advance.

Selection

All prospective RCTs of tai chi for OA (not just chronic pain of the knee, hip or back, etc.) were included. Trials comparing tai chi with any type of control intervention were also included. Dissertations and abstracts were also included. Any trials with tai chi as part of a complex intervention were excluded.

Data abstraction and study characteristics

Hard copies of all articles were obtained and read in full by two independent reviewers (MSL and JWK). The data from these articles were validated and abstracted according to predefined

criteria including authors information, origin of study, sample size, age of participants, site and duration of OA, regimen of experimental and control intervention, , main outcome, adverse events, author's conclusion (Table 1).

Validity assessment

The risk of bias was assessed using the Cochrane classification with four criteria: sequence generation, allocation concealment, blinding and incomplete outcome measurement.[11] Low risk of bias for assessor blinding was assumed if specified in the text regardless of the type of outcome measures (even for self-reported outcome measures). We assumed that the assessor was the person in charge of managing the outcome measures. Disagreements were resolved by discussions between the reviewers (MSL and JWK).

Quantitative data synthesis

Because there was no important clinical heterogeneity, we synthesised the results in a meta-analysis. The mean change of outcome measures between the ends of final intervention (post-treatment) and the baseline was used to assess the differences between intervention and control groups. Standardised mean differences (SMDs) were used because studies measured the outcomes on different scales (WOMAC and VAS). SMDs and 95% confidence intervals (CIs) were calculated using Cochrane Collaboration software (Review Manager Version 5.0 for Windows; Copenhagen: The Nordic Cochrane Centre). For studies with insufficient information, we contacted the primary authors to acquire and verify data when possible. For one trial, [12] we contacted the authors to check the standard deviations (SDs) of original raw data because they reported the same SDs for tai chi and control group. The original authors clarified their reported values does not different from the raw data. Summary estimates of the treatment effect were calculated using the random effects model to account for expected

heterogeneity. Differences between treatment and controls were considered relevant in the context of this study. For one trial, [13] the author did not report SD of changes for any outcomes. We therefore used the pre- and post-treatment means and SDs for each group, and assumed a conservative within-subject pretest-post-test correlation of 0.5,[14] to calculate the SDs of change of each group using the methods in Cochrane Handbook. [15] Cochrane's Q-test and I^2 were used to assess statistical heterogeneity. We determined that there was considerable heterogeneity when the Cochrane's Q-test result was determined with $P<0.10$ and I^2 was above 75%. If a sufficient number of studies (at least 10 studies) were available, we attempted to assess publication bias using a funnel plot or Egger's regression test, whereby effect estimates of the common outcome measures were plotted against the sample size. [16 17]

Results

Trial flow and study characteristics

The literature search revealed 117 articles, of which 108 studies were excluded. The reasons for article exclusion during the selection process are described in Figure 1. Key data regarding the 9 included RCTs are summarised in Table 1.[12 13 18-24] A total of 521 participants were included in these trials. Four RCTs originated in the US,[12 13 23 24] three RCTs were from Korea,[19-21] one RCT was from China[18] and one RCT was from Australia.[22] Six RCTs included patients with knee OA,[12 13 18-21] while the other three RCTs included patients with hip, knee or multiple-joint OA.[22-24] Yang-style tai chi was used in four trials, [12 13 18 23] Sun-style was used in three trials, [20-22] Wu-style was used in one trial[24] and one trial did not report the type of tai chi used.[19] All RCTs had a parallel-group design.

Most trials had a relatively small sample size, and only 5 trials were based on a sample size calculation.[12 13 20-22] All of the included trials employed appropriate sequence generation methods for randomisation (Table 2). The authors reported they employed assessor blinding in five RCTs[12 13 18 19 22] while blinding was unclear in the other 4 RCTs.[20 21 23 24] Five RCTs adopted an allocation concealment method,[12 18-20 24] two RCTs[13 22] failed to do so, and this parameter was unclear in two RCTs.[21 23] The risk of bias for reporting drop-out or withdrawal was low in all RCTs. Four RCTs had an intention to treat analysis.[12 19 22 24] Two trials had low risk of bias in selective outcome reporting,[12 22] and the other 2 studies are at high risk of bias.[20 23]

Quantitative Data Synthesis

Effects of tai chi on patients with knee OA

Six RCTs tested the effects of tai chi compared with attention control,[12 13 18] a waiting list, [19] routine care[20] or self-help programs[21] in patients with knee OA. The meta-analysis showed favourable effects of tai chi on pain (n=256; SMD, -0.79; 95% CI -1.19 to -0.39; P=0.0001; heterogeneity: χ^2=11.13, P=0.05, I^2=55%; Figure 2A), physical function (n=256; SMD, -0.86; 95% CI -1.20 to -0.52; P<0.00001; heterogeneity: χ^2=8.08, P=0.15, I^2=38%; Figure 2B) and joint stiffness (n=256; SMD, -0.53; 95% CI -0.99 to -0.08; P=0.02; heterogeneity: χ^2=15.28, P=0.009, I^2=67%; Figure 2C). A sub-analysis was performed to explore whether heterogeneity could be partially explained by the type of control intervention.

Tai chi versus attention control

Three RCTs[12 13 18] compared the effects of tai chi on pain, physical function and joint stiffness with attention control in patients with knee OA. All trials reported favourable effects of tai chi on pain reduction. The meta-analysis also showed superior effects of tai chi for pain

reduction compared with attention control (n=100; SMD, -1.18; 95% CI -1.82 to -0.54; P=0.0003; heterogeneity: χ^2=4.28, P=0.12, I^2=53%; Figure 2A).

Two RCTs showed favourable effects of tai chi on physical function, [12 18] while the other RCT failed to do so.[13] The meta-analysis showed the favourable effects of tai chi on physical function compared with attention control (n=100; SMD, -1.20; 95% CI -1.74 to -0.67; P<0.0001; heterogeneity: χ^2=2.99, P=0.22, I^2=33%; Figure 2B).

Three RCTs assessed the effects of tai chi on joint stiffness compared with attention control.[12 13 18] One RCT showed favourable effects of tai chi,[18] while the other two RCTs failed to do so.[12 13] The meta-analysis did not show positive effects of tai chi (n=100; SMD, -0.82; 95% CI -1.67 to 0.04; P=0.06; heterogeneity: χ^2=8.03, P=0.02, I^2=75%; Figure 2C).

One RCT compared the effect of tai chi on the quality of life compared with attention control; it failed to show a favourable effect on this condition. [12]

Tai chi versus routine treatments, a waiting list or a self-help program

Three RCTs assessed the effectiveness of tai chi on pain caused by knee OA compared with routine treatments, a waiting list or a self-help program.[19-21] Two RCTs suggested a significant pain reduction compared with the waiting control[19] and the routine treatments,[20] while the other RCT did not.[21] The meta-analysis showed favourable effects of tai chi on pain reduction (n=156; SMD, -0.47; 95% CI -0.79 to -0.14; P=0.005; heterogeneity: χ^2=0.96, P=0.62, I^2=0%; Figure 2A).

Three RCTs tested the effect of tai chi on physical function compared with routine treatments, a waiting list or a self-help program.[19-21] Two RCTs showed significantly favourable effects,[20 21] while one RCT failed to do so.[19] The meta-analysis showed superior effects of tai chi on physical function compared with routine cares (n=156; SMD, -0.60; 95% CI -0.93 to -0.28; P=0.0003; heterogeneity: χ^2=0.79, P=0.67, I^2=0%; Figure 2B).

Three RCTs assessed the effects of tai chi on joint stiffness compared with routine treatments, a waiting list or a self-help program.[19-21] One RCT showed significantly favourable effects of tai chi,[20] while two RCTs failed to so.[19 21] The meta-analysis did not show significant effects of tai chi on joint stiffness (n=156; SMD, -0.30; 95% CI -0.79 to 0.19; P=0.23; heterogeneity: χ^2=4.39, P=0.11, I^2=54%; Figure 2C).

Effects of tai chi for patients with multiple-joint OA

Three RCTs tested the effects of tai chi compared with hydrotherapy, waiting list, routine treatments or participation in bingo games in patients with multiple joint OA.[22-24] One RCT with 3 parallel groups failed to show superior effects of tai chi on pain reduction, physical function, and quality of life compared with hydrotherapy or a waiting list control but did show improved physical function compared with the waiting list control.[22] The second RCT showed favourable effects of tai chi on the quality of life compared with routine treatments while failing to show pain reduction.[23] The third RCT did not show significant differences in pain reduction, physical function or joint stiffness between tai chi and participation in bingo games. [24]

Adverse effects

Four RCTs [12 13 18 22] assessed adverse effects while the other 5 RCTs [19-21 23 24] did not. None of the 4 RCTs reported serious adverse effects. Two RCTs reported minor muscle soreness and foot and knee pain in the early days of intervention.[13 18] One RCT reported increased knee pain and two cancer occurrences that were not related to the interventions.[12] The other RCT reported serious adverse effects that were not related to the intervention. [22]

Discussion

Overall, this systematic review suggests that tai chi may be an effective treatment for pain and physical function associated with knee OA compared with attention control or routine care. However, several caveats must be considered. For joint stiffness, the evidence was not robust. For a mixed population with hip or knee OA, the evidence is not sufficient to conclude whether tai chi was beneficial.

Our review aimed to update and complete the evidence by adding newly RCTs of tai chi as a method of treatment in patients with OA. Compared to 2 previous reviews,[9 10] we identified 4 new, low risk of bias RCTs[12 18-20] and successfully updated the evidence for therapy. The results of our review are similar to the other 2 reviews.[10 19] One previous review[19] showed that tai chi may be beneficial for pain control in patients with knee OA while the other review[10] also reported some favourable effects of tai chi for musculoskeletal pain. However, both reviews were concerned about the poor methodological quality of the included primary studies.

Previous systematic reviews have suggested that there are clinically important differences among various therapies compared with various controls in pain reduction and functional improvement in OA.[2] The effect size of pain reduction and function improvement in our review were higher than those of exercise, NSAIDs, and drug therapy, and this effect is

clinically significant.[2] However, these results are difficult to compare quantitatively due to the use of different assessment measures for evaluating pain and the use of different controls for evaluating the comparisons.

Limitations of our systematic review and any systematic review in general pertain to the potential incompleteness of the evidence reviewed. The distorting effects on systematic reviews and meta-analyses arising from publication bias and location bias are well documented.[25-27] We are confident that our search strategy located all relevant data; however, some degree of uncertainty remains. Another possible source of bias is the fact that half of the included trials were carried out in China and Korea, where there have appeared to produce almost no negative studies.[28] Our review may be affected by the potentially poor quality of the primary data and poor reporting of results, which were highly heterogeneous in virtually every aspect.

The risk of bias in the studies was assessed based on the descriptions of sequence generation, allocation concealment, blinding, incomplete outcome measures, and selective outcome reporting. Based on these assessments, the risk of bias varied across the included studies. Only 3 RCTs had a low risk of bias,[12 19 22] and two studies had a moderate risk of bias.[18 24] The other 4 RCTs are at high risk of being biased.[13 20 21 23] Five RCTs employed allocation concealment,[12 18 19 21 24] and four RCTs used intention-to-treat analysis.[12 19 22 24] Inappropriate allocation concealment and lack of blinding exaggerate the results of outcome measures.[29 30] Only two RCTs are at low risk of bias in selective outcome reporting.[12 22] Even though the authors reported they employed assessor blinding,[12 13 18 19 22] some outcomes that they measured relied on patient's subjective reporting, due to which the patient's and assessor's blinding becomes unachievable and irrelevant. The main limitations of the included studies

were small sample sizes, inadequate control for non-specific effects and a lack of power calculations or adequate follow-up. Also, the fact that tai chi interventions cannot control for placebo effects limits generalisability. Second, adequate follow-ups of 6-12 moths are advisable for future studies of tai chi for OA.

One could argue the employment of the Cochrane risk of bias tool to assess the methodological bias in the clinical trial is not good. This tool was recently recommended for assessing methodological quality instead of scoring assessment tool including Jadad scale and others.[11] It has been proposed to using quality score for clinical trials are not good. [31 32] Even though the inter-rater disagreements across the domains were reported in the Cochrane risk of bias tool, their reliability was fair overall. [33 34] We also calculated our reliability for 9 included trials with Excel module (http://agreestat.com/agreestat.html). Our inter-rater agreement for the individual domains of risk of bias tool to 9 included trials ranged from substatial to almost perfect (0.88 for random sequence generation; 0.70 for allocation concealment; 1.00 for patient blinding; 0.85 for assessor blinding; 0.88 for reporting drop-out or withdrawal; 0.69 or intention-to-treat analysis; and 0.71 for selective outcome reporting). Therefore, the Cochrane risk of bias tool maybe the most comprehensive tool with fair reliability so far.

Proponents of tai chi claim that it improves flexibility, strength and balance, especially in the elderly. Clearly these claims need to be tested. The pooled results from 6 RCTs[12 13 18-21] suggested that pain intensity was reduced when patients used tai chi compared with attention control or routine care for knee OA. However, three RCTs found that tai chi had no significant effect on pain reduction compared with hydrotherapy, waiting list, routine treatments or participation in bingo games in multiple joint OA.[22-24] These results may be

explained in part through inadequate blinding and control for non-specific effects in some of the positive studies, among other sources of bias.

Assuming that tai chi was beneficial for treating OA, the possible mechanisms of action may be of interest. Regular tai chi has been postulated to improve balance and reduce the likelihood of falls by improving muscle flexibility and trunk rotation. Tai chi is a form of physical exercise combined with relaxation. Physical movement in tai chi can improve joint stability and aid in reducing excess weight, effectively decreasing joint pain, increasing function and reducing advancement of OA.[35 36] Furthermore, tai chi may also influence the psychosocial quality of life, which may have a positive influence on chronic pain.[35 37] The question about whether tai chi is superior to other forms of therapeutic exercise is currently unanswered and is thus a topic for further investigation.

Four of the reviewed studies reported minor adverse events related to tai chi.[12 13 18 22] Tai chi appears to be generally safe, and serious adverse effects have not been reported. Adverse effects were, however, not the focus of this review and may require further research.

Future RCTs of tai chi for OA should adhere to accepted standards of trial methodology. The studies included in this review show a number of problems that have been noted by other reviews of trials examining the efficacy of tai chi, such as the expertise of tai chi practitioners, the pluralism of tai chi, the frequency and duration of treatment, the use of validated primary outcome measures and adequate statistical tests, and heterogeneous comparison groups.[38 39] Furthermore, even though it is difficult to blind subjects to treatment, employing assessor blinding and allocation concealment are important for reducing bias. A clinical study is only truly useful if the intervention used can be replicated; hence, the type of

tai chi employed is important. There are significant differences among the numerous forms of tai chi, and a clear description of the tai chi intervention should be provided together with a description of the level of expertise of the instructors.

In conclusion, there is encouraging evidence suggesting that tai chi may be effective in controlling pain and improving physical function in patients with knee OA. However, due to the number of eligible RCTs and often poor quality of the available RCTs, the evidence is limited.

Competing Interest

The authors have declared that no competing interests exist.

Author Contributions

Jung Won Kang and Myeong Soo Lee designed the review, performed searches, appraised and selected trials, abstracted data, contacted authors for additional data, carried out analysis and interpretation of the data, and drafted this report.

Paul Posadzki and Edzard Ernst reviewed and critiqued on the review protocol and this report, assisted in designing of the review

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Data sharing

No additional data available

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Figure Legends

Figure 1. Flowchart of trial selection process. RCT: randomized clinical trial.

Figure 2. Forest plot of the effects of tai chi on (A) pain; (B) physical function; and (C) joint stiffness in patients with knee osteoarthritis.

Table 1. Summary of randomized clinical trials of tai chi for osteoarthritis

First author (year) Country	Sample size OA site Age (yrs) Duration of OA (yrs)	Experimental intervention (regimen)	Control intervention (regimen)	Main outcomes	Adverse effects	Author's conclusion
Ni (2010)[18] China	35 Knee 62.9; 63.5 ≥ 1 yrs	TC (30 min, 2 – 4 times weekly for 24 weeks, n=18) Yang-style (simplified 24 forms)	Attention control program (45 min, wellness and stretching, n=17)	1) Pain (WOMAC) 2) Physical function (WOMAC) 3) Joint stiffness (WOMAC) 4) Total WOMAC score	Not serious AE Minor muscle soreness, pain in foot and knee (n=5)	"[...] TC provide safe, feasible and useful exercise option for Chinese female patients with knee OA"
Brismee (2007)[13] USA	41 Knee 70.8; 68.8 n.r.	TC (40 min, 3 times weekly for 6 weeks plus home-based tai chi for 6 weeks, n=22) Yang-style (simplified 24 forms)	Attention control program (40 min, lecture, once weekly for 6 weeks, n=19)	1) Pain (VAS) 2) Physical function (WOMAC) 3) Joint stiffness (WOMAC)	Minor muscle soreness, pain in foot and knee (n.r.)	"[...] TC [...] provided significant knee pain reduction and physical function improvement in elderly subjects with knee OA"
Wang (2009)[12] USA	40 Knee 63; 68 n.r.	TC (60 min, twice weekly for 12 weeks, n=20) Yang-style (10 forms)	Attention control program (60 min, wellness and stretching, once weekly for 12 weeks, n=20)	1) Pain (WOMAC) 2) Physical function (WOMAC) 3) Joint stiffness (WOMAC) 4) Quality of Life (SF-36)	Increased knee pain (TC: 1); cancer (TC: 1; control: 1)	"TC reduces pain and improves physical function [...]"
Lee (2009)[19] Korea	44 Knee 70.2; 66.9 n.r.	TC (60 min, twice weekly for 8 weeks, n=29) n.r. (18 movements)	Waiting list (n=15)	1) Pain (WOMAC) 2) Physical function (WOMAC) 3) Joint stiffness (WOMAC) 4) Total WOMAC score 5) Quality of Life (SF-36)	n.r.	"TC appears to have beneficial effects [...]"
Song (2003)[20] Korea	72 Knee 64.8; 62.5 10.4; 9.2	TC (60 min, 3 times weekly for 12 weeks, n=22) Sun-style (12 forms)	Routine care (n=21)	1) Pain (WOMAC) 2) Physical function (ADL) 3) Joint stiffness (WOMAC)	n.r.	"[...] TC [...] was effective in improving [...]"
Song (2009)[21] Korea	82 Knee 62.4; 59.9 0.5 - 10	TC [(60 min, twice weekly for the first 3 weeks and once weekly for the next 6 months) plus 6 instances of self-help program, n=41] Sun-style (31 forms)	Self- help program (2 hr, once monthly for 6 months, n=39)	1) Pain (WOMAC) 2) Physical function (WOMAC) 3) Joint stiffness (WOMAC)	n.r.	"TC combined with self-help program was more effective than the self-help only program [...]"
Fransen (2007)[22] Australia	152 Hip or knee 70.8; 70.0; 69.6 n.r. (mean)	(A) TC (60 min, twice weekly for 12 weeks, n=56) Sun-style (modified 24 forms)	(B) Hydrotherapy (60 min, twice weekly for12 weeks, n=55) (C) Waiting list (n=41)	1) Pain (WOMAC) 2) Physical function (WOMAC) 3) Quality of Life (SF-12)	11 serious AE that are not related to intervention. Low back pain (hydrotherapy: 1; TC: 1)	"[...] TC [...] can provide large and sustained improvement in physical function [...]'
Hartman (2000)[23] USA	35 Multiple joint (hip, knee, ankles, foot) 68.6; 67.5 n.r. (mean)	TC (60 min, twice weekly for 12 weeks, n=19) Yang-style (9 forms)	Routine care (usual physical activity plus total of 3 group meetings and telephone discussion every 2 weeks, n=16)	1) Pain (AIMS) 2) Quality of life (AIMS)	n.r.	"TC is a safe and effective [...]"

Adler (2007)[24] USA	22 Hip or knee 70.8; 72.8 n.r.	TC (60 min, once weekly for 10 weeks, n=11) Wu-style (16 forms)	Bingo games (non-physical activity, n=11)	1) Pain (WOMAC) 2) Physical function (ADL) 3) Psychological symptoms	n.r.	"The current study will serve as a feasibility study for future TC research"

ADL: Activities of Daily Living; AE: adverse effects; AIMS: Arthritis Impact Measurement Scale; ITT: intention-to-treat; n.r.: not reported; NS: not significant; OA: osteoarthritis; TC: tai chi; VAS: visual analogue scale; WOMAC: Western Ontario and McMaster Universities Osteoarthritis Index

Table 2. Risk of bias of included RCTs*

*, Domains of quality assessment based on Cochrane tools for assessing risk of bias.
†, Two domains referring to 'incomplete outcome data' in the Cochrane tools for assessing risk of bias.

Study	Random sequence generation	Allocation concealment	Patient blinding	Assessor blinding	Reporting drop-out or withdrawal†	Intention-to-treat analysis†	Selective outcome reporting
Ni (2010) [18]	L	L	H	L	L	H	U
Brismee (2007) [13]	L	H	H	L	L	H	U
Wang (2009) [12]	L	L	H	L	L	L	L
Lee (2009) [19]	L	L	H	L	L	L	U
Song (2003) [20]	L	L	H	U	L	H	H
Song (2009) [21]	L	U	H	U	L	H	U
Fransen (2007) [22]	L	H	H	L	L	L	L
Hartman (2000) [23]	L	U	H	U	L	H	H
Adler (2007) [24]	L	L	H	U	L	L	U

Abbreviations; L: low risk of bias; H: high risk of bias; U: Unclear (uncertain risk of bias).