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REVIEW

Tai chi for treating osteopenia and primary osteoporosis: a meta-analysis and trial sequential analysis

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Purpose: The aim of this meta-analysis was to evaluate the efficacy of Tai chi (TC) as an adjuvant treatment for osteopenia and primary osteoporosis.

Methods: We went through eight databases to identify relevant randomized controlled trials that compared TC with a control group. The primary outcome was osteoporosis-related fractures (fracture incidence). Meta-analyses and trial sequential analyses (TSA) were conducted using RevMan 5.3 and TSA 0.9.

Results: Fifteen randomized controlled trials involving a total of 857 patients were included in the analyses. No trials reported primary outcome; however, bone mineral density (BMD) values differed significantly in subgroup 1 (TC vs no treatment; weighted mean difference [WMD] =0.05 g/cm^2, 95% CI 0.03 to 0.07; $P<0.00001$; P for heterogeneity =0.22, I^2=22%) and subgroup 2 (TC vs conventional treatments; WMD =0.16 g/cm^2, 95% CI 0.11 to 0.21; $P<0.00001$; P for heterogeneity =0.008, I^2=75%). In addition, two trials compared TC with conventional treatments, which found a significant difference in bone gla protein (standardized mean difference =−1.18, 95% CI −1.66 to −0.70; $P<0.00001$; P for heterogeneity =0.58, I^2=75%). The results of the BMD were confirmed by TSA. Also, TC may have a certain effect on the relief of osteoporotic pain (WMD = −2.61, 95% CI −3.51 to −1.71; WMD = −1.39, 95% CI −2.01 to −0.77). However, it did not promote the quality of life, level of serum calcium, serum phosphorus, and also had no effect on bone turnover markers.

Conclusion: Although there is no study monitoring fracture incidence, TC may be beneficial for patients in improving BMD values, level of bone gla protein, and relieving osteoporotic pain. However, due to the low methodological quality, current evidence for treating osteopenia and primary osteoporosis through TC is insufficient.

Keywords: Tai chi, osteopenia, primary osteoporosis, evidence based medicine, trial sequential analyses

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Introduction

Primary osteoporosis (POP) is a worldwide health problem with a consequent increase in bone fragility and susceptibility to fractures.[1] It is characterized by low bone mass and microarchitectural deterioration of bone tissue.[2,3] Osteopenia is a condition of decreased bone density and a precursor of osteoporosis.[4] Osteoporosis affects about 200 million people worldwide and is a huge cost for the healthcare system. This cost is estimated to increase to $25.3 billion per year.[5]

Pharmacologic treatments for osteoporosis include bisphosphonates, estrogen, selective estrogen receptor modulators, and so forth.[6–8] The aim of most of these treatments is to prevent bone resorption. Dietary supplements, like calcium and vitamin D, are also

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used as basic treatment. However, because of the necessity of lifelong treatment and the potential negative side effects, like upper gastrointestinal symptoms and risk of venous thrombosis, research for alternative treatments remains pertinent.[9]

Physical activity is an important lifestyle factor for growth, development, and sustained health throughout life. In recent years, the benefits of physical activity have drawn more attention to its physiological effects on the body.[10] Considering the side effect of pharmacological treatment for osteoporosis, there is an increasing demand for nonpharmacologic therapy, such as physiotherapy and physical activity that are used appropriately and for long periods.[11] Previous experiments and/or clinical trials based on different types of physical activity such as aerobic exercise and/or resistance exercise have provided fundamental knowledge on this topic. In several studies, it has been demonstrated that both in human and in animal models, there is an increased expression of osteoprotegerin (OPG) consequent to a training program.[12] Exercise can also influence the secretion of some hormones involved in bone formation, such as parathyroid hormone, prostaglandin E2, and estrogen.[13] Moreover, some authors reported higher levels of anti-inflammatory cytokines such as IL-2 and IL-10, and lower levels of proinflammatory cytokines such as TNF-α and IL-6, as a consequence of moderate exercise, suggesting that exercise can also promote bone formation and inhibit bone resorption by OPG/RANKL/RANK-independent signaling pathways.[14] In addition to training programs, many studies support the effectiveness of the whole-body vibration training, and in particular, its positive effects on bone turnover in osteoporosis.[15–17]

Tai chi (TC) is a traditional systematic physical activity, which is widely practiced not only in China, but also has a large number of trainers worldwide.[18,19] TC employs precise regimens of physical movement, breathing techniques, and cognitive exercises (both visualization and focused internal awareness) to strengthen, relax, and adjust physical functioning and mental health.[20–22] Over the past 25 years, TC has grown in popularity and gained worldwide recognition for its health benefits. Aside from pharmacological methods, muscle strengthening and weight-bearing exercises, which prevent osteoporosis by increasing bone and muscle strength as well as coordination and balance, TC is often recommended to patients in addition to bisphosphonates administration. Previous studies have also focused on finding evidence of the effects of TC on pain relief and physical improvements in patients with illness like knee osteoarthritis and fibromyalgia.[23–25]

Moreover, clinical trials assessing TC treatment for osteopenia and osteoporosis have recently been published and may have strengthened the evidence base that TC is one of the nonpharmacological therapy treatments that are effective. However, treatment of osteopenia and POP by TC is not fully summarized based on the latest evidence. Therefore, we conducted an updated meta-analyses of randomized controlled trials (RCTs) to investigate the efficacy of TC treatment for regulating the bone mass, especially for the patients with osteopenia and POP and those at high risk of osteoporosis. Furthermore, we examined whether the current evidence was robust and conclusive by using trial sequential analyses (TSA).

Materials and methods

Eligibility criteria

This meta-analyses was reported in accordance with Preferred Reporting Items for Systematic Review and Meta-Analyses.[26] All the included studies would be critically appraised by using the tool from the *Cochrane Handbook for Systematic Reviews of Interventions*.[27] The protocol of this systematic review has been registered on PROSPERO (http://www.crd.york.ac.uk/prospero) on September 6, 2017 (registration number: CRD42017074663).

Types of studies

Only RCTs were included. There were no restrictions on language and setting. Quasi-experimental studies, animal experiments, duplicate studies, and studies for which the full text was not available to us were excluded. Review articles, case reports, editorials, letters, and comments were also excluded.

Types of participants

In this review, we paid close attention to the TC exercises for regulating the bone mass. The diseases we mainly focused on were osteopenia and POP so that the participants with osteopenia and POP or those at high risk of osteoporosis (mean age >50 years old) were included. The clinical diagnosis for osteopenia or POP should be in accordance with recognized international criteria, for instance WHO criteria: bone mineral density (BMD) of subjects, T-score ≤−2.5 could be defined as osteoporosis and T-scores in the range of −2.5 and −1 could be defined as osteopenia.[28] In addition, Chinese criteria (peak bone mass of subjects [mean ± standard deviation] >M − 1 SD ~2 SD could be defined as osteopenia and <M − 2 SD could be diagnosed as osteoporosis) were included as well.[29]

Types of interventions

In order to estimate the specific effect of TC, only the studies that had the TC as an intervention method were included.

TC compared with a control group including no intervention, placebo, and conventional treatments or TC plus conventional treatments compared with conventional monotherapy were taken into account. No limitation was imposed on the style of TC, the times of exercise, and the duration of the treatment.

Types of comparisons

In the control group, only placebo, no treatments, or conventional treatments recommended by the guidelines or internationally recognized treatments were included. Conventional treatments were mainly recommended by national guidelines, such as Clinical guidelines for diagnosis and treatment of postmenopausal osteoporosis (AACE/ACE),[30] Clinician's Guide to Prevention and Treatment of Osteoporosis (NOF),[31] and Guideline for diagnosis and treatment of primary osteoporosis (CSOBMR).[32] Usually, calcium and vitamin D supplements are also considered as conventional treatment. Other complementary and alternative treatments (eg, osteoporosis bone protective medication, physiotherapy, osteopathy, orthoses, herbal medicine, acupuncture, moxibustion, massage, yoga) have been excluded.

Types of outcomes

Osteoporosis-related fractures (fracture incidence) were the primary outcomes that we followed with interest. The secondary outcomes included changes in BMD value, serum calcium, serum phosphorus, and bone gla protein (BGP). Biochemical markers of bone turnover type I collagen carboxy-terminal peptide (CTX), quality of life,[33] and recognized pain scales were also included as the secondary outcomes.

Information sources and search strategy

A comprehensive search strategy was carried out including PubMed (1950 to September 2017), EMBASE (1974 to September 2017), the Cochrane Library (1996 to September 2017), ClinicalTrials.gov (from inception to September 2017), China Knowledge Resource Integrated Database (1979 to September 2017), Chinese Science and Technique Journals Database (1989 to September 2017), Wan Fang Database (1990 to September 2017), and the Chinese Biomedical Database (1990 to September 2017). The reference lists of studies meeting the inclusion criteria were analyzed to identify additional relevant studies.

The following search terms were used in separate or combined ways: "osteoporosis"; "primary osteoporosis"; "postmenopausal osteoporosis"; "senile osteoporosis"; "osteopenia"; "bone loss"; "Tai chi"; "Tai ji"; "Tai chichuan"; "Shadow Boxing"; "clinical trial". There were no restrictions on language, the types of publications, and participants' characteristics. Literature was managed by using Note Express 3.2.0 software.

Study selection

Two independent reviewers scanned the retrieved studies and decided whether or not to continue further analyses based on three criteria: titles, abstracts, and keywords. If the information met the inclusion criteria, full articles were retrieved for further assessment. We retrieved full content of articles if there was any doubt about these criteria from the information given in the title and abstract. Authors were contacted to obtain relevant missing data if necessary and where resources allowed. Any disagreements were settled by third party.

Data collection process

Data concerning details of participants, interventions, comparisons, and outcomes were extracted independently by two reviewers. The data extraction form included the following items: 1) general information: title, authors, and year of publication; 2) population: sample size, age, diagnostic criteria; 3) interventions: dose, duration, and frequency; and 4) outcomes: outcomes specified above.

Risk of bias in individual study

The methodological quality of RCTs was assessed independently using criteria from the *Cochrane Handbook for Systematic Review of Interventions*, Version 5.1.0.[27] Seven domains were considered, such as sequence generation (selection bias), allocation concealment (selection bias), blinding of participants and personnel (performance bias), blinding of outcome assessment (detection bias), incomplete outcome data (attrition bias), selective outcome reporting (reporting bias), and other biases. Three levels of "low risk", "high risk", or "unclear risk" marked the quality appraisal category. Any disagreements were resolved by mutual consensus.

Data analysis

Revman 5.3 software provided by the Cochrane Collaboration was used for the data analysis. All pooled outcome measures were determined using random effect models. For the dichotomous outcome, the pooled RR with 95% CI was used as the measure of effect. For the continuous outcomes with same units, weighted mean difference (WMD) was used when the units of outcomes were consistent, while standardize mean difference was performed as the effect measure if the units of the outcomes were different. If the number

of included studies was less than two or heterogeneity was apparent, meta-analysis was neither appropriate nor possible. Under these circumstances, the results of our systematic review were narratively reported. If the included studies had multiple arms, we identified the relevant intervention and control groups, and then combined the relevant groups into a single group before synthesizing the data.

Subgroup analysis and sensitivity analysis

Subgroup analysis was deemed necessary. In order to explore the potential sources of heterogeneity of the methodology, statistics, and clinical characteristics, sensitivity analyses were performed. When the results of the clinical trials varied widely and heterogeneity tests showed significant differences, we removed one trial that was significantly different from the other trials and then pooled the remaining studies to compare the results before and after.

Confidence in cumulative estimate

The quality of the evidence would be assessed by the GRADE tool.[34,35] High-quality evidence was considered as RCTs with low risk of bias, which could produce direct and precise results for the clinical outcome.[36] Based on five key domains (methodology quality, directness of evidence, heterogeneity, precision of effect estimates, and risk of publication bias), levels of quality of evidence were defined as high, moderate, low, and very low.[37]

Trial sequential analysis

TSA was conducted to obtain the primary result. Cumulative meta-analysis might result in false-positive results (type I error) because of an increased risk of random error from sparse data and repeated significance testing.[38] TSA could control the *P*-value and widen the confidence intervals.[39] Estimation of the required information size and trial sequential monitoring boundaries were the concepts and rationale combined by TSA. If the cumulative *Z* curve entered the futility area or crossed the trial sequential monitoring boundary, the anticipated intervention effect might reach a sufficient level of evidence, and further trials would not be necessary.

We calculated the required information size based on mean difference (Empirical) and variance (Empirical) in change of BMD value. The type I error (α) and power ($1 - \beta$) were set as 0.05 and 0.80, respectively. The TSA was conducted with the use of TSA version 0.9 beta software (http://www.ctu.dk/tsa).

Results

Study selection

In total, 785 records were identified. After removing 270 duplicates among different databases, the remaining 515 records were screened further by reading the title and abstract. Then, we excluded 436 records that did not meet the eligible criteria in title or abstract and the full texts of remaining 79 records were downloaded for careful assessment. Finally, 64 articles were excluded upon further scrutiny for non-RCTs (n=19); intervention measures did not meet the requirement of this review (n=11), participants were not suitable (n=12), study objectives different from the aim of this review (n=6), protocols (n=5), abstract (n=2), and review articles (n=9). There were 15 trials included in the review of which three trials[41,47,50] were published in English and the others[40,42–46,48,49,51–54] in Chinese. The detailed process of search and identification is shown in Figure 1.

Study characteristics

All trials included were conducted by a parallel design. The duration of trials ranged from 4 months to 12 months while only one trial did not report the duration.[45] Sample size was within the scope of 24–110, with a total of 857 participants included in this review. All included trials reported the outcomes we focused on and 14 trials referred to BMD values or index of quantitative ultrasound. Details of the 15 included trials are listed for characteristics of included trials (Table 1).

Methodological quality

There are five trials using random number table or other ways. Only two trials mentioned the allocation concealment through sealed envelope. Only one study protocol[50] was available at ClinicalTrials.gov. The quality criteria related to blinding of patients was not satisfactory. However, it should be noted that blinding patients or performers is difficult to realize in trials involving exercise as intervention.[55] Furthermore, three trials reported the dropout or withdrawal of patients. We also considered all included trials with "unclear" for the other bias, such as the sample size (Figure 2).

The effects of therapy

According to the different treatments, the studies were divided into three subgroups: TC vs no treatment (subgroup 1), TC vs conventional treatments (subgroup 2), and TC plus conventional treatments vs conventional treatments (subgroup 3). Among these subgroups, we assessed the primary and secondary outcomes separately for all participants (Table 2).

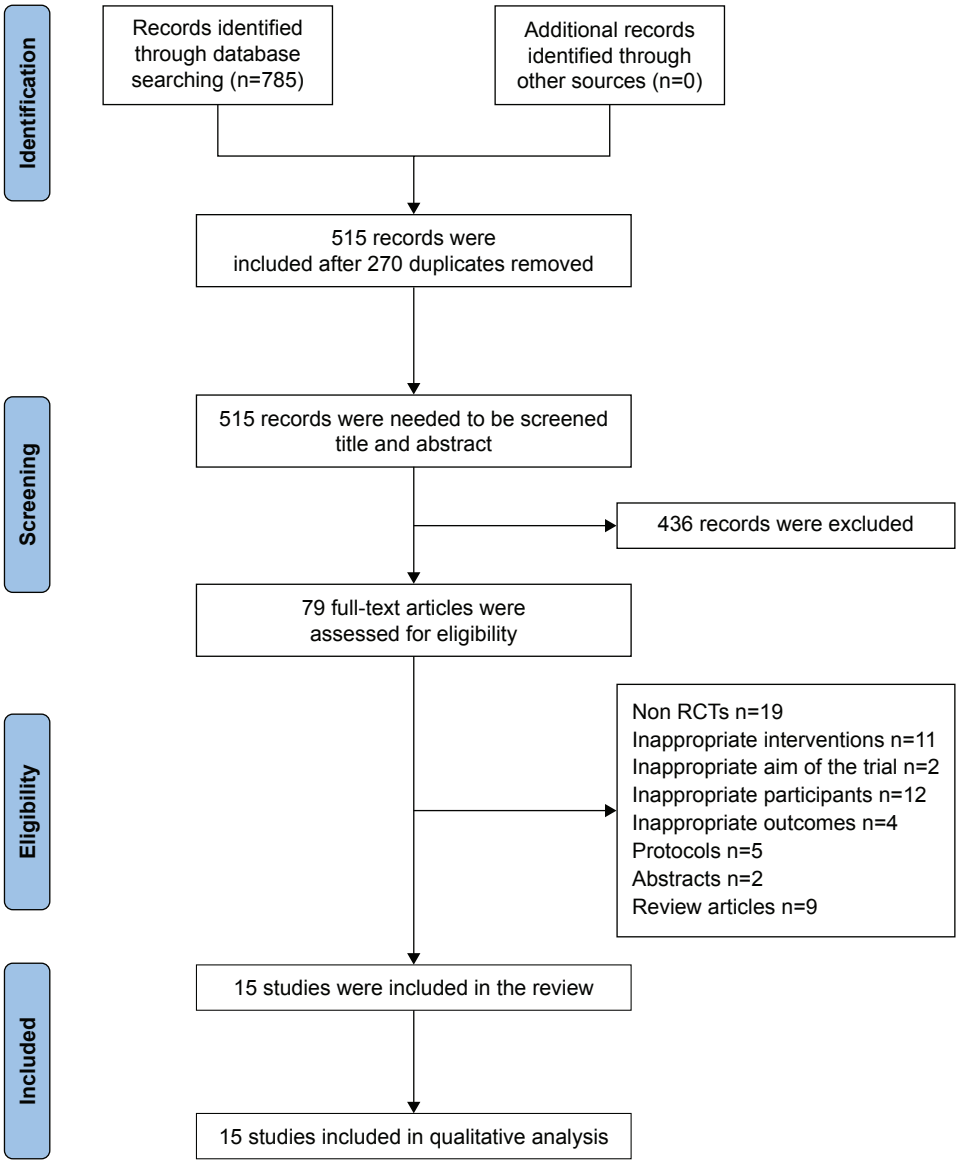

Figure 1 PRISMA flow diagram.
Abbreviations: PRISMA, Preferred Reporting Items for Systematic review and Meta-Analysis; RCTs, randomized controlled trials.

In addition, in order to explore the efficacy of TC in the treatment of osteopenia and POP, we conducted a separate analysis based on the included studies in which participants had confirmed osteopenia and POP (Table 3).

Although there is no study reporting primary outcome and no significant difference was detected in subgroup 3 on any outcomes, there was significant difference in BMD value in subgroup 1 (WMD=0.05 g/cm^2, 95% CI 0.03 to 0.07; $P<0.00001$; P for heterogeneity =0.22, I^2=22%) and subgroup 2 (WMD=0.16 g/cm^2, 95% CI 0.11 to 0.21; $P<0.00001$; P for heterogeneity =0.008, I^2=75%) which indicates that TC has a positive effect on BMD value and the therapeutic effect is higher than conventional treatments. TSA showed that the cumulative Z curves crossed both the conventional and the trial sequential monitoring boundaries and reached the significant area. Thus, it might be unlikely that further trials would change the conclusion (Figure 3). In addition, two trials compared TC with conventional treatments on BGP, which found a remarkable difference between the two groups (MD =−1.18, 95% CI −1.66 to −0.70; $P<0.00001$; P for heterogeneity =0.58, I^2=75%).

Meanwhile, TC was beneficial to the level of BGP and relieved patient's pain (Visual Analog Scale). However, TC did not promote the quality of life and levels of serum

Table 1 Characteristics of included trials

Study ID	Sample size (EG/CG)	Diagnostic criteria	Gender (male/female)	Mean age ± SD (years)	Types of participants	Experimental group	Control group	Duration of treatment	Outcomes
Zhou 2003[40]	EG:12 CG:12	Chinese criteria	EG:12 CG:12	EG:57.10±2.71 CG:55.96±2.84	PMOP	TC (no details provided)	No intervention	10 months	BMD (DEXA, lumbar spine, g/cm^2)
Chan et al 2004[41]	EG:67 CG:65	NR	EG:67 CG:65	EG:57.10±2.71 CG:55.96±2.84	Postmenopausal women without MBD	TC (50 minutes a day, five times a week)	Original lifestyle without any intervention	12 months	BMD (DEXA, spine and proximal femur, g/cm^2)
Zhou 2004[42]	EG:12 CG:12	NR	EG:12 CG:12	55.94±2.83	Postmenopausal women without MBD	TC (no details provided)	No intervention	10 months	BMD (DEXA, spine, and forearm distal, g/cm^2)
Zhou and Li 2005[43]	EG:16 CG:16	NR	EG:16 CG:16	57.21±3.41	Postmenopausal women without MBD	TC (45–60 minutes a day, five to seven times a week)	No intervention	6 months	BMD (DEXA, lumbar spine, g/cm^2)
Ma and Wang 2006[44]	EG:32 CG:35	NR	EG:32 CG:35	NR	Senile men without MBD	TC (40 minutes a day)	Calcium (600 mg/qd)	12 months	BGP, Hyp/Cr, BMD (DEXA, spine, Ward's triangle, femoral neck and femur, g/cm^2)
Song 2008[45]	EG:20 CG:20	Chinese criteria	EG:9/11 CG:10/10	EG:62.67±11.23 CG:63.81±13.07	Primary osteoporosis	TC (60 minutes/ session, six sessions per week)	Calcium preparations + calcitonin (no details provided)	NR	BMD (DEXA, lumbar spine, and femur, g/cm^2). BGP, ALP, Ca, P, Visual Analog Scale
Wang et al 2009[46]	EG:20 CG:20	NR	EG:20 CG:20	54.56±3.12	Postmenopausal women without MBD	TC (30–40 minutes/ session, four sessions per week)	No intervention	6 months	BMD (DEXA, forearm, g/cm^2), Ca, BGP
Chyu et al 2010[47]	EG:26 CG:27	BMD T-score at the spine and/or hip between 1 and 2.5 SD below the young, normal, sex-matched BMD of the reference database	NR	EG:72.4±6.2 CG:71.3±6.0	Postmenopausal osteopenia	TC (60 minutes/ session, three sessions/week)	Original lifestyle without any intervention	24 weeks	Computerized dynamic posturography, gait, "timed up and go", five-chair sit-to-stand and quality of life (SF-36)
Chen and Li 2011[48]	EG:20 CG:20	NR	EG:20 CG:20	Range: 55–65	Women without MBD	TC (60 minutes/ session, three to four sessions/week)	No intervention	20 weeks	Quantitative ultrasound, Ca, P, ALP
Zhang 2011[49]	EG:36 CG:36	WHO criteria	28/44	EG:58.4±3.0 CG:58.0±2.8	Primary osteoporosis	TC (30–60 minutes/ session, three to four sessions/ week) + Caltrate D (600 mg/qd)	Caltrate D (600 mg/qd)	24 weeks	BMD (DEXA, lumbar spine, and femur, g/cm^2)

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Wayne et al 2012[50]	EG:42 CG:42	WHO criteria	NR	EG:60.4±5.3 CG:58.8±5.6	Postmenopausal osteopenic	TC (two classes/ week for the first month and one class/week for 8 months thereafter) (minimum class duration of one hour) + usual care	Usual care (including daily calcium, vitamin D, and regular exercise)	9 months	BMD (DEXA, femoral neck, total hip, and lumbar spine, g/cm^2) CTX, OSC, quality of life (SF-36, MENQOL), physical activity (PAR)
Fan 2013[51]	EG:20 CG:20	NR	EG:20 CG:20	EG:58.4±3.0 CG:58.0±2.8	Over 60 year-old women without MBD	TC (60 minutes/ session, three sessions/week)	No intervention	16 weeks	Quantitative ultrasound. Balance, and coordination
Shan and Kang 2015[52]	EG:54 CG:56	Chinese criteria	NR	EG:60.52±6.25 CG:61.12±5.87	Postmenopausal osteoporosis	TC (45–60 minutes/ session, one to two sessions/day) + calcitriol capsule	Calcitriol	6 months	BMD (DEXA, g/cm^2) quality of life (SF-36), therapeutic effect
Zhao et al 2015[53]	EG:30 CG:30	WHO criteria	EG:14/16 CG:12/18	EG:58.8±3.2 CG:61.1±2.8	Primary osteoporosis	TC (55 minutes/ session, six sessions/week)	No intervention	6 months	BMD (DEXA, femoral neck, Ward triangle, lumbar spine, g/cm^2), Visual Analog Scale
Yao et al 2016[54]	EG:17 CG:22	NR	EG:17 CG:22	NR	Healthy middle-aged women without MBD	TC (120 minutes/ session, three sessions/week)	Original lifestyle without any intervention	6 months	BMD (DEXA, femoral neck, Ward's triangle, lumbar spine, g/cm^2), quality of life (SF-36)

Notes: Chinese criteria: BMD of subjects, 2 SD (T-score ≤–2) or <75% of lower than young adult mean value; WHO criteria: BMD of subjects, 2.5 SD (T-score ≤–2.5) lower than young adult mean value.

Abbreviations: BMD, bone mineral density; BGP, bone gla protein; Ca, calcium; CG, control group; Cr, creatinine; CTX, C-terminal telo-peptide of type I collagen; DEXA, dual energy X-ray absorptiometry; EG, experimental group; Hyp, hydroxyproline; MBD, metabolic bone diseases; MENQOL, Menopause Quality of Life instrument; NR, not reported; OSC, osteocalcin; PAR, Seven-Day Physical Activity Recall; P, phosphorus; Pi, inorganic phosphorus; PMOP, postmenopausal osteoporosis; SF-36, 36-Item Short Form Health Survey; TC, Tai chi; WHO, World Health Organisation.

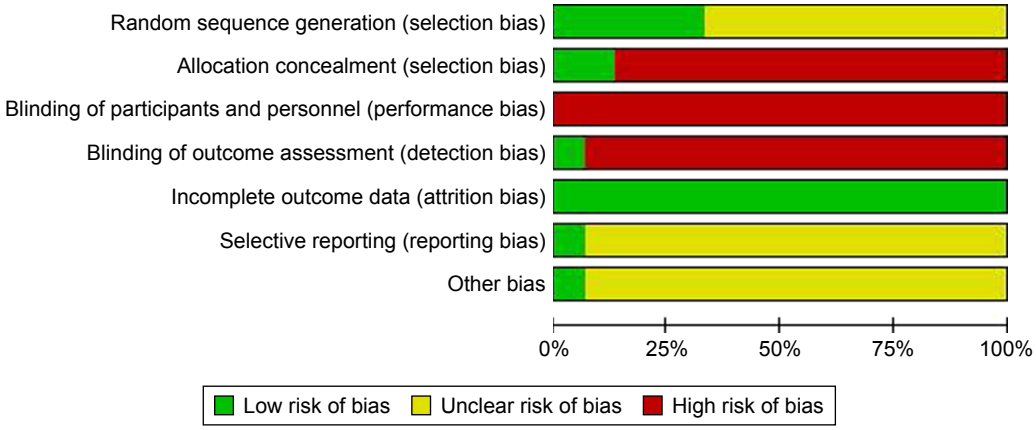

Figure 2 Risk of bias graph.

calcium, and serum phosphorus. According to the analysis, TC had no effect on CTX and osteocalcin.

Funnel plot analysis

Funnel plot analysis could not be conducted due to the small number of included studies (<10) for the same outcome in the meta-analysis.

Overall quality of evidence by GRADE

We graded the overall quality of available evidence with the GRADE approach. The quality of evidence for all outcomes was downgraded to "low" or "very low" mainly due to high risk of performance bias and imprecision (small number of total events or small sample size).

Discussion

This systematic review and meta-analysis, which was based on 15 RCTs including 857 participants, found that TC may have a positive effect on BMD values, both as a single treatment and in combination with others. The evidence was validated by TSA. In order to better guide clinical practice, we assessed the achieved evidence of the GRADE approach. Due to the low quality of included trials and the above outcomes from individual trials, we could not draw firm conclusions from current evidence. Thus, further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.

Three previous meta-analyses[56–58] have reported on the same topic, as presented in Table 4. Differences between the present meta-analyses and the previous ones are as follows: firstly, our analyses included four additional trials that were published in the past 2 years. As the latest and most comprehensively updated meta-analyses, the present study further reinforces the results of previous meta-analyses. Second, we focused on more representative and more specific outcomes, which might fully describe the effect of TC on patients with osteopenia and POP and strengthened the current body of evidence. Third, we registered the protocol of this study on PROSPERO. A registered protocol may increase the transparency and quality of meta-analyses. Finally, TSA was further applied to estimate the effect more conservatively.

Based on currently available literature, there are some limitations due to the flaws of design, measurement, and evaluation in original studies. First, the included RCTs in this meta-analysis were performed in different patient groups and various clinical settings. The risk of potential heterogeneity, therefore, is present. Second, TC is based on traditional exercises which could not be blinded for physicians and patients so that a performance bias may have been introduced. Meanwhile, the problem with the lack of blinded outcome assessment may have also introduced information bias. Third, patients may take a long time to practice TC in order to achieve the purpose of the treatment, but the trials included in this study were generally short in length of duration. This may reduce the apparent effectiveness of TC. Fourth, this study focused only on the efficacy of TC on regulating bone mass, though the safety or the impact of TC on muscle strength, functional mobility, balance, and coordination or fracture incidence are important. In addition, complete and transparent reporting in quality and methodology should be in accordance with well-known standards for further research. At the same time, different types of TC may produce different outcomes. The style of TC should be clearly defined in the trials. Participants that withdrew/dropped-out during the trials should be clearly described and intention-to-treat analysis could be performed in data analysis.

Previous studies indicated that vitamin D and calcium supplementation are the most widely used therapies for

Table 2 The results of all outcomes for three subgroups: all participants

Subgroups	Categories	Outcomes		Number of studies	Risk ratio or mean difference (95% CI)	*P*-value	*P* for heterogeneity	I^2 (%)	Quality
TC vs no treatment	Primary outcome	Osteoporosis-related fractures (fracture incidence)		None	–	–	–	–	–
	Secondary outcomes	BMD	Spine	6[40–43,53,54]	0.04 (0.02 to 0.06)	0.0006	0.47	0	Low
			Femur	3[41,53,54]	0.04 (0.01 to 0.06)	0.007	0.98	0	Low
			Forearm	2[42,46]	0.11 (–0.00 to 0.22)	0.06	0.11	61	Low
			Ward's triangle	2[53,54]	0.04 (–0.00 to 0.09)	0.07	0.85	0	Low
		Quality of life (score of physical component summary)		3[47,50,52]	2.39 (–1.62 to 6.40)	0.24	0.03	73	Low
		Quality of life (mental component summary)		3[47,50,52]	1.09 (–2.89 to 5.07)	0.59	0.05	66	Low
		Serum calcium		2[45,48]	–0.06 (–0.13 to 0.00)	0.06	0.65	0	Low
		Serum phosphorus		2[45,48]	0.02 (–0.04 to 0.08)	0.53	0.74	0	Low
		VAS		1[53]	–2.61 (–3.51 to –1.71)	<0.00001	–	–	Low
TC vs conventional treatments	Primary outcome	Osteoporosis-related fractures (fracture incidence)		None	–	–	–	–	–
	Secondary outcomes	BMD	Spine	2[44,45]	0.16 (0.09 to 0.23)	<0.00001	0.09	66	Low
			Femur	2[44,45]	0.16 (0.04 to 0.29)	0.009	0.003	89	Low
		Serum calcium		1[45]	–0.08 (–0.18 to 0.02)	0.11	–	–	Low
		Serum phosphorus		1[45]	0.01 (–0.07 to 0.09)	0.80	–	–	Low
		BGP		2[44,45]	–1.18 (–1.66 to –0.70)	<0.00001	0.58	0	Low
		VAS		1[45]	–1.39 (–2.01 to –0.77)	<0.0001	–	–	Low
TC plus conventional treatments vs conventional treatments	Primary outcome	Osteoporosis-related fractures (fracture incidence)		None	–	–	–	–	–
	Secondary outcomes	BMD		2[49,52]	0.07 (–0.02 to 0.15)	0.13	<0.00001	97	Low
		OSC		1[50]	–0.12 (–2.36 to 2.12)	0.92	–	–	Low
		CTX		1[50]	–0.06 (–0.18 to 0.06)	0.32	–	–	Low
		Quality of life (score of physical component summary)		2[50,52]	–1.13 (–3.60 to 1.35)	0.37	0.46	0	Low
		Quality of life (mental component summary)		2[50,52]	1.89 (–4.83 to 8.61)	0.58	0.02	82	Very low

Abbreviations: BGP, bone gla protein; BMD, bone mineral density; CTX, C-terminal telo-peptide of type I collagen; OSC, osteocalcin; TC, Tai chi; VAS, Visual Analog Scale; -, not applicable.

Table 3 The results of all outcomes for three subgroups: participants with osteopenia and osteoporosis

Subgroups	Categories	Outcomes		Number of studies	Risk ratio or mean difference (95% CI)	*P*-value	*P* for heterogeneity	I^2 (%)	Quality
TC vs no treatment	Primary outcome	Osteoporosis-related fractures (fracture incidence)		None	–	–	–	–	–
	Secondary outcomes	BMD	Spine	2[40,53]	0.05 (0.02 to 0.08)	0.0008	0.95	0	Low
			Femur	1[53]	0.03 (–0.01 to 0.08)	0.16	–	–	Low
			Forearm	None	–	–	–	–	–
			Ward's triangle	1[53]	0.04 (–0.01 to 0.09)	0.13	–	–	Low
		Quality of life (score of physical component summary)		3[47,50,52]	2.39 (–1.62 to 6.40)	0.24	0.03	73	Low
		Quality of life (mental component summary)		3[47,50,52]	1.09 (–2.89 to 5.07)	0.59	0.05	66	Low
		Serum calcium		1[45]	–0.08 (–0.18 to 0.02)	0.11	–	–	Low
		Serum phosphorus		1[45]	0.01 (–0.07 to 0.09)	0.80	–	–	Low
		VAS		1[53]	–2.61 (–3.51 to –1.71)	<0.00001	–	–	Low
TC vs conventional treatments	Primary outcome	Osteoporosis-related fractures (fracture incidence)		None	–	–	–	–	–
	Secondary outcomes	BMD	Spine	1[45]	0.20 (0.13 to 0.28)	<0.00001	–	–	Low
			Femur	1[45]	0.23 (0.16 to 0.29)	<0.00001	–	–	Low
		Serum calcium		1[45]	–0.08 (–0.18 to 0.02)	0.11	–	–	Low
		Serum phosphorus		1[45]	0.01 (–0.07 to 0.09)	0.80	–	–	Low
		BGP		1[45]	–1.37 (–2.19 to –0.55)	0.001	–	–	Low
TC plus conventional treatments vs conventional treatments	Primary outcome	Osteoporosis-related fractures (fracture incidence)		None	–	–	–	–	–
	Secondary outcomes	BMD		2[49,52]	0.07 (–0.02 to 0.15)	0.13	<0.00001	97	Low
		OSC		1[50]	–0.12 (–2.36 to 2.12)	0.92	–	–	Low
		CTX		1[50]	–0.06 (–0.18 to 0.06)	0.32	–	–	Low
		Quality of life (score of physical component summary)		2[50,52]	–1.13 (–3.60 to 1.35)	0.37	0.46	0	Low
		Quality of life (mental component summary)		2[50,52]	1.89 (–4.83 to 8.61)	0.58	0.02	82	Very low

Abbreviations: BGP, bone gla protein; BMD, bone mineral density; CTX, C-terminal telo-peptide of type I collagen; OSC, osteocalcin; TC, Tai chi; VAS, Visual Analog Scale; –, not applicable.

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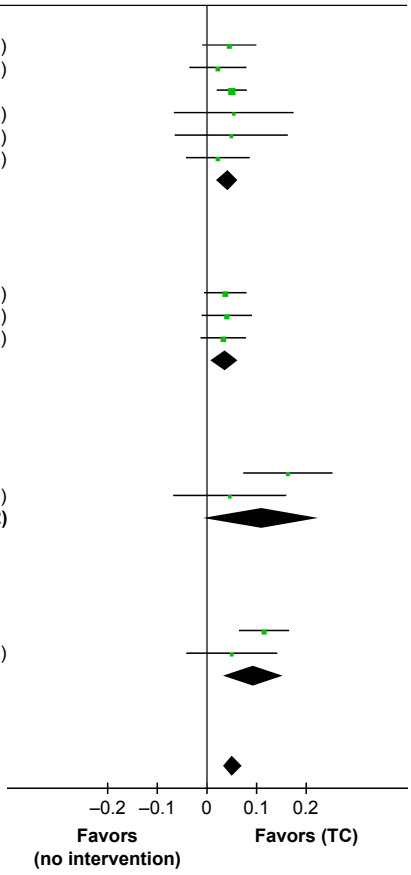
Study or subgroup	TC Mean	SD	Total	No intervention Mean	SD	Total	Weight (%)	Mean difference IV, random, 95% CI
BMD-spine								
Chan 2004	0.861	0.144	54	0.816	0.138	49	8.7	0.05 (–0.01 to 0.10)
Mao 2009	1.044	0.092	20	1.022	0.093	20	8.0	0.02 (–0.04 to 0.08)
Zhao 2015	0.723	0.037	14	0.673	0.041	12	18.8	0.05 (0.02 to 0.08)
Zhou 2003	1.049	0.137	12	0.995	0.149	10	2.2	0.05 (–0.07 to 0.17)
Zhou 2004	1.066	0.135	12	1.017	0.149	12	2.4	0.05 (–0.06 to 0.16)
Zhou 2005	1.043	0.092	16	1.021	0.093	16	6.7	0.02 (–0.04 to 0.09)
Subtotal (95% CI)			**128**			**119**	**46.9**	**0.04 (0.02 to 0.06)**
Heterogeneity: τ^2=0.00; χ^2=1.17, *df*=5 (*P*=0.95); I^2=0%								
Test for overall effect: *Z*=3.80 (*P*=0.0001)								
BMD-femur								
Chan 2004	0.74	0.116	54	0.703	0.105	49	12.4	0.04 (–0.01 to 0.08)
Ye 2016	0.73	0.08	17	0.69	0.08	22	9.7	0.04 (–0.01 to 0.09)
Zhao 2015	0.659	0.053	14	0.626	0.064	12	11.3	0.03 (–0.01 to 0.08)
Subtotal (95% CI)			**85**			**83**	**33.5**	**0.04 (0.01 to 0.06)**
Heterogeneity: τ^2=0.00; χ^2=0.04, *df*=2 (*P*=0.98); I^2=0%								
Test for overall effect: *Z*=2.69 (*P*=0.007)								
BMD-forearm								
Wang 2009	1.017	0.149	20	0.854	0.141	20	3.7	0.16 (0.07 to 0.25)
Zhou 2004	0.97	0.135	12	0.924	0.149	12	2.4	0.05 (–0.07 to 0.16)
Subtotal (95% CI)			**32**			**32**	**6.2**	**0.11 (–0.00 to 0.22)**
Heterogeneity: τ^2=0.00; χ^2=2.50, *df*=1 (*P*=0.11); I^2=60%								
Test for overall effect: *Z*=1.89 (*P*=0.06)								
BMD-Ward's triangle								
Ma 2006	0.567	0.105	32	0.452	0.105	35	9.8	0.11 (0.06 to 0.17)
Ye 2016	0.63	0.14	17	0.58	0.15	22	3.6	0.05 (–0.04 to 0.14)
Subtotal (95% CI)			**49**			**57**	**13.5**	**0.09 (0.03 to 0.15)**
Heterogeneity: τ^2=0.00; χ^2=1.49, *df*=1 (*P*=0.22); I^2=33%								
Test for overall effect: *Z*=3.10 (*P*=0.002)								
Total (95% CI)			**294**			**291**	**100**	**0.05 (0.03 to 0.07)**
Heterogeneity: τ^2=0.00; χ^2=15.20, *df*=12 (*P*=0.23); I^2=21%								
Test for overall effect: *Z*=5.52 (*P*<0.00001)								
Test for subgroup differences: χ^2=4.33, *df*=3 (*P*=0.23); I^2=30.8%								



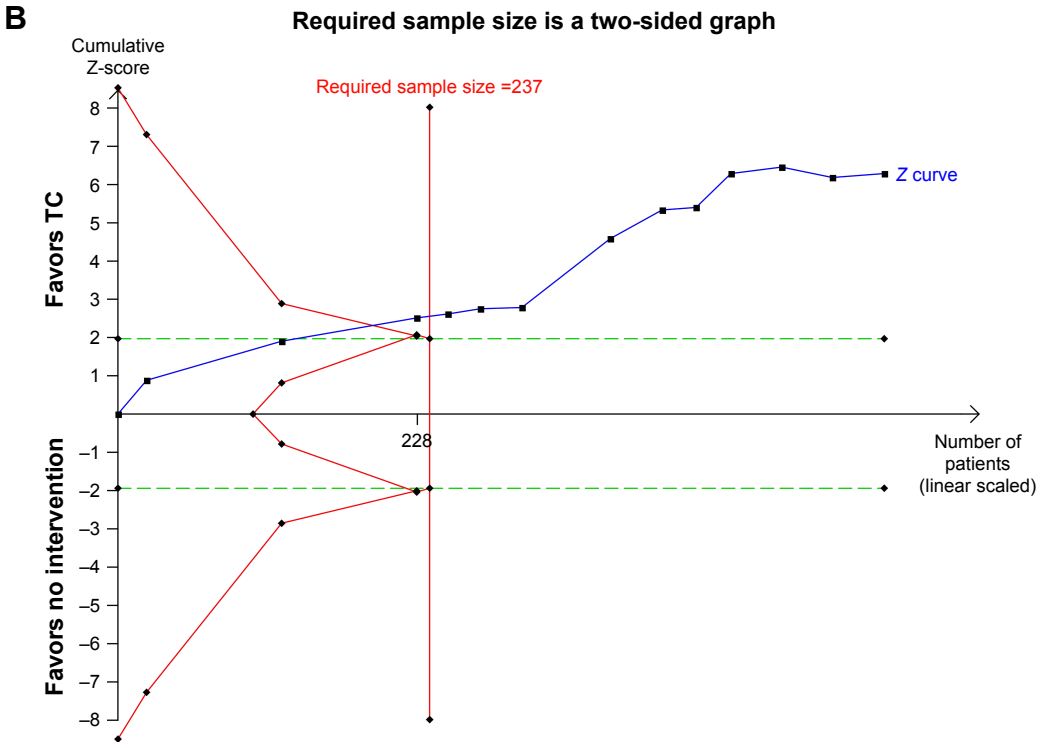


Figure 3 (**A**) TC vs no intervention: BMD value (all participants). (**B**) TSA for BMD value (TC vs no intervention) with an α of 5% (two-sided) and β of 20%.
Notes: The required information size was calculated as 237. *Z* curve has across-trial sequential monitoring boundary for benefit (all participants).
Abbreviations: BMD, bone mineral density; IV, inverse variance; TC, Tai chi; TSA, trial sequential analysis.

Table 4 Comparison with other previous meta-analyses

Author	Lee et al 2008[56]	Xu and Liu 2012[57]	Sun et al 2016[58]	The present meta-analysis
Number of RCTs	5	5	11	15
Participants	Osteoporosis	Postmenopausal women	Perimenopausal and postmenopausal women	Osteopenia and primary osteoporosis
Search strategy until (year)	2007	2012	2015	2017
Protocol registered	NA	NA	NA	Applied
Trial sequential analysis	NA	NA	NA	Applied
Outcomes	BMD	BMD	BMD, bone turnover markers	BMD, BGP, serum calcium, serum phosphorus, VAS, CTX, OSC

Abbreviations: BGP, bone gla protein; BMD, bone mineral density; CTX, C-terminal telo-peptide of type I collagen; NA, not available; OSC, osteocalcin; RCTs, randomized controlled trials; VAS, Visual Analog Scale.

osteoporosis.[59] Observational studies suggest that lower plasma levels of 25-hydroxy-vitamin D (25[OH]D) are associated with higher risks of osteoporosis[60,61] and fractures.[62] Also, calcium and vitamin D supplements have been recommended for older people to prevent fractures by practice guidelines. However, several meta-analyses recently showed that the use of supplements including calcium, vitamin D, or both was not associated with a low risk of fractures among patients with OP.[63–65] Therefore, in light of the need for safe and cost-effective treatments for POP, further research on nonpharmacological therapy treatments is needed.

Conclusion

In conclusion, there were positive results for TC to benefit for patients with osteopenia and POP. However, due to the low methodological quality and poor reporting quality, current evidence is insufficient. We need more information to firmly establish benefit–harm profile of TC for osteopenia and POP before we accept it as an evidence-based treatment option in our clinical practice. Furthermore, the quality of data must improve greatly if nondrug therapies are to assume a respected place in the contemporary health care.

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Disclosure

The authors report no conflicts of interest in this work.

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