Efficacy and safety of tai chi for hyperlipidaemia: a protocol for systematic review and meta-analysis

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ABSTRACT

Introduction The prevalence of hyperlipidaemia is increasing, and patients with hyperlipidaemia are at increased risk of cardiovascular disease and atherosclerosis. In recent years, there has been a growing number of studies on tai chi for hyperlipidaemia. However, a systematic review on its efficacy and safety is not available. Therefore, this study aims to evaluate the efficacy and safety of tai chi for hyperlipidaemia.

Methods and analysis Four English databases and four Chinese databases will be searched from their inception to May 2021: PubMed, Embase, Cochrane Library, Web of Science, China National Knowledge Infrastructure, Chinese Biomedical Literature Database, VIP Database and Wanfang Database. Chinese and English randomised controlled trials related to tai chi for hyperlipidaemia will be included. Two reviewers should independently carry out study selection, data extraction and risk assessment of bias. The risk of bias in the study will be assessed by the Cochrane risk of bias tool. RevMan (V.5.4) statistical software will be applied for meta-analysis. The Grading of Recommendations Assessment, Development and Evaluation system approach will be employed to assess the quality of evidence.

Ethics and dissemination Ethical approval is not required because this protocol will not involve patients’ individual information and jeopardise the rights of patients. The meta-analysis result will be reported in peer-reviewed journals or disseminated at related conferences.

INTRODUCTION

Hyperlipidaemia is a common chronic metabolic disorder characterised by an increase in total cholesterol (TC), triglycerides (TG) or low-density lipoprotein cholesterol (LDL-C), and a decrease in high-density lipoprotein cholesterol.1 2 With the continuous development of economy, the improvement of living standards and the change of lifestyle, the prevalence of hyperlipidaemia is rising rapidly.3 There are over 3 million adults throughout the USA and Europe who currently have a diagnosis of hyperlipidaemia, and that number continues to rise at a drastic pace.4 Hyperlipidaemia has become an important public health problem.5 Previous studies have shown that the occurrence and development of hyperlipidaemia are related to gender, age, lifestyle, obesity, diabetes, dietary structure and other factors.6–8 Hyperlipidaemia is an important risk factor for atherosclerosis and cardiovascular disease.6 9–11 Related studies have shown that long-term hyperlipidaemia will cause accumulation of heart lipids, which will have a certain impact on the electrophysiological activities and functions of the heart.12 13 Patients with hyperlipidaemia are twice as likely to develop cardiovascular disease.14 Meanwhile, hyperlipidaemia can lead to chronic inflammation in the body; the release of inflammatory factors can increase the risk of atherosclerosis by damaging vascular endothelial cells and vascular walls.15 Chronic hyperlipidaemia in young people can increase the risk of atherosclerosis,3 so active prevention and treatment for hyperlipidaemia are particularly important.

Treatment for hyperlipidaemia can be divided into lifestyle changes and medication. Lifestyle changes, such as dietary adjustment, weight control and correction of poor lifestyle, are the basis of lipid-lowering therapy and are carried out throughout the treatment process.16 17 In terms of pharmacological treatment, lipid-lowering drugs in clinical practice include statins, fibrates, cholesterol absorption inhibitors and niacin.18 Among them, statins have always been the main drugs in the treatment of hyperlipidaemia,19 which
Long-term use of lipid-lowering drugs will increase the financial burden of patients. Therefore, the demand for non-pharmacological lipid-lowering treatment has grown stronger. In recent years, tai chi for hyperlipidaemia has attracted extensive attention from researchers.

Tai chi, as a representative of traditional Chinese martial arts, was listed on the Masterpiece List of Intangible Cultural Heritage of Humanity of UNESCO on 17 December 2020. It is a kind of physical and mental exercise, with soft and slow movements, natural breathing, dynamic and static combination, and integrity and unity. Tai chi can improve balance and cardiac functioning, and increase strength and flexibility. Up to now, tai chi, as an aerobic exercise, has been widely applied in knee osteoarthritis, Parkinson’s disease, rheumatoid arthritis, diabetes and other diseases. Nowadays, a large number of clinical studies show that aerobic exercise can not only increase energy consumption, but can also enhance the body metabolism and improve the activity of some body enzymes, thus enhance muscle uptake, use more free fatty acid, accelerate the metabolism of TC, TG and LDL, and help to reduce the lipid level. Existing studies have shown that tai chi is effective in treating hyperlipidaemia. Ding’s study shows that tai chi can reduce patients’ blood lipids and improve lipid metabolism, which is beneficial for the prevention and treatment of hyperlipidaemia. In China, tai chi has become a common method of prevention, healthcare and treatment in daily life.

In clinical randomised controlled trials (RCTs), tai chi includes different types of frequency and duration. The effect of different types of tai chi has not been synthesised. Despite a previously published paper entitled ‘Efficacy of Tai Chi and qigong for the prevention of stroke and stroke risk factors: A systematic review with meta-analysis’, its intervention included tai chi or qigong, and the diseases were limited to hypertension, hyperlipidaemia, diabetes, overweight or obesity, or metabolic syndrome. Meanwhile, only articles published in English and German were included. The Chinese articles were ignored. In short, there is no systematic review of tai chi for hyperlipidaemia. Therefore, this study aims to systematically evaluate the efficacy and safety of tai chi for hyperlipidaemia, and to provide strong evidence for clinical treatment.

**METHODS**

**Protocol and registration**

The protocol was drafted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analysis Protocols guidelines. The protocol has been registered with OSF (registration number: DOI 10.17605/OSF.IO/79D2S). If changes to the protocol are needed, the deviations from the original protocol and rationale will be reported transparently.

**Patient and public involvement**

No patient involved.

**CRITERIA FOR INCLUDING STUDIES IN THIS REVIEW**

**Types of studies**

All RCTs on tai chi for hyperlipidaemia will be included. Quasi-RCTs, non-RCTs, animal experiments, case reports and republished studies will be excluded. We will exclude studies in which exercise period was shorter than 3 months.

**Types of participants**

Patients diagnosed with pure high LDL-C and TG will be enrolled, and patients with mixed hyperlipidaemia will be excluded, regardless of gender, race, education level, economic status or nationality.

**Types of interventions**

Interventions in the treatment group will include different types of frequency and duration of tai chi therapy. Interventions in the control group will include no treatment, regular activity, aerobic exercise, western medicine treatment and other treatments.

**Types of outcome measures**

**Primary outcomes**

The changes in lipid levels after treatment, including LDL-C level and TG level.

**Secondary outcomes**

1. Long-term efficacy: measurements will be made from baseline to the last follow-up.
2. Quality of life score: measurements will be made at the end of treatment.
3. The changes of body mass index before and after treatment.
4. The safety of tai chi intervention including the incidence of adverse events.

**Search strategy**

The systematic search will comprise four English electronic databases and four Chinese electronic databases: PubMed, Embase, Cochrane Library, Web of Science, China National Knowledge Infrastructure, Chinese Biomedical Literature Database, VIP Database and Wanfang Database. Chinese and English RCTs related to tai chi for hyperlipidaemia will be included. Grey literature will be excluded. In addition, qualified study conference abstracts and reference lists of manuscripts will be retrieved to ensure that all relevant studies are acquired. A combination of Medical Subject Headings and free terms related to tai chi and hyperlipidaemia will be used to formulate a search strategy. The terms will be searched as follows: Hyperlipidemias, Lipidemia, Lipemia, Tai Chi, Tai Ji, Taijiquan. The search strategy will begin with PubMed and subsequently will be applied to other databases. The detailed search strategy is shown in box 1.
**Searching other resources**

Ongoing or unpublished trials will be searched in the WHO International Platform for Clinical Trials Registry, the US National Institutes of Health’s Ongoing Trial Registry, the China Clinical Registry and Clinical Trials.

**Data collection and analysis**

All articles systematically searched by the eight databases, grey literature and relevant articles retrieved from study conference abstracts and reference lists of manuscripts will be exported to the EndNote bibliographical software to manage all references. Duplicate articles will be removed after verification. Eligible studies will be carefully and independently screened and identified by two reviewers (WD and FZ) through the title and abstract’s initial reading. DL and XC will further review the full text to make selection. The entire screening process will be independently carried out by at least two reviewers. In case of no agreement, it will be resolved through discussion and consensus, if consensus cannot be reached, a third reviewer (CW) will be involved in making the final decision whether to include the article. The process of study selection is illustrated in the flow chart of the system review and meta-analysis (figure 1).

**Data extraction and management**

Based on a predefined data template, HZ and TG will independently extract the following items from eligible studies: title, country, year of publication, first author, participant, funding source, randomisation, blind method, different types of tai chi, duration of treatment, outcome measure, follow-up, outcomes and adverse events. The cross-check of the data will be carried out by XC and HZ. Any dispute will be resolved through discussion. If needed, a third reviewer will participate in arbitration. Finally, the data will be transferred to the Review Manager (RevMan) software.

**Assessment of risk of bias**

The risk of bias will be independently evaluated by three reviewers (WD, FZ and DL) using the Cochrane Collaboration tool V.2.0. Specifically, studies will be rated on the following six domains: random sequence generation, allocation concealment, blind method, selective outcome reporting, incomplete outcome data and other risks of bias. Ratings of risk of bias in each domain will be graded into three levels: low (all domains are rated as low), unclear (one domain is rated as unclear) or high (one domain is rated as high or two or more domains are rated as unclear). Any disagreement will be arbitrated by the fourth reviewer (CW) where required.

**Measures of treatment effect**

Data synthesis and analysis will be performed by the RevMan software (V.5.4). Dichotomous outcomes will be carried out to calculate using a risk ratio with 95% CI; OR and relative risk are frequently used. For continuous outcomes, weighted mean difference or standard mean difference will be used to calculate.

**Unit of analysis issues**

The analysis will be performed based on the aggregated outcome data.

**Dealing with missing data**

For missing or incomplete data in the study, XC and HZ will make efforts to contact the first author or corresponding author of the original trials to obtain the missing data by email or phone. If missing data are not available,
existing data will be analysed; meanwhile, sensitivity analysis will be applied to resolve the problem of missing data.

**Assessment of heterogeneity**

We will use χ² test and I² statistics to investigate heterogeneity, and the whole process of evaluating heterogeneity will be performed by RevMan (V.5.4). When I²<50% and p≥0.1 indicates no observed heterogeneity, the fixed-effects model will be adopted. On the other hand, when I²≥50% or p<0.1 indicates significant heterogeneity, the random-effects model will be used. Sensitivity analysis and subgroup analysis will be applied to explore the sources of potential heterogeneity.

**Assessment of reporting biases**

When more than or equal to 10 studies are included in the meta-analysis, we will use the RevMan (V.5.4) to generate funnel plots to evaluate potential reporting bias.

**Data synthesis**

Statistical analyses will be carried out based on the RevMan (V.5.4) software with random-effects model. Subgroup analysis and sensitivity analysis will be conducted for each subgroup. We will even provide a narrative, qualitative summary where necessary.

**Subgroup analysis and investigation of heterogeneity**

When the data of studies are available, subgroup analysis will be conducted to explore causes of potential heterogeneity. Subgroup analysis will be performed to explain heterogeneity on the basis of the frequency and duration of tai chi therapy and the type of control group. The type of control group will be separated into two parts. The control group in the first part included no treatment, regular activity and aerobic exercise. The second part included western medicine therapy and traditional Chinese medicine therapy.

**Sensitivity analysis**

If feasible, we will conduct sensitivity analysis in compliance with the recommendations of the Cochrane Handbook to monitor the robustness of the results during the review process. Consideration will be given to sample size, methodological quality and missing data from the study.

**Summary of evidence**

Two reviewers (DL and XC) will independently assess the quality of evidence for the main outcomes according to the Grading of Recommendations Assessment, Development and Evaluation system approach. Assessments of the quality evidence will be graded into ‘high’, ‘moderate’, ‘low’ or ‘very low’ in terms of heterogeneity, risk of bias, publication bias, indirectness and inaccuracy.

**DISCUSSION**

Hyperlipidaemia has become one of the most common pathological conditions in humans. Meanwhile, the high blood lipid is one of the main factors in inducing atherosclerosis and coronary heart disease and it seriously threatens the patient’s physical and mental health. Hyperlipidaemia can be divided into primary and secondary hyperlipidaemia, among which the primary hyperlipidaemia is related to congenital and genetic factors and the secondary hyperlipidaemia is induced by the metabolic disorder disease. Several factors are associated with an increased risk of hyperlipidaemia. Modifiable risk factors include a diet high in saturated or trans fats, physical inactivity, smoking and obesity. Lifestyle modification is the first step to improve the plasma lipid profile. At present, patients with hyperlipidaemia are intervened by the drugs in clinics; however, the side effects of drug treatment could easily damage the body organs. It has become an urgent need to seek a safe and economical green therapy without side effects. In the past 20 years, more and more clinical studies have found that tai chi has a good effect on people with hyperlipidaemia. Tai chi, as a traditional sport with a long history in China, is an aerobic exercise and its movement is slow. In the process of practising, it shows quiet movement in the posture, and the combined fast and slow movements are conducive to the regulation of practitioners’ physical and mental condition. It can be practised by people in any environment and is not limited by time or equipment, so it is very popular among Chinese people.

This systematic review will provide relatively convincing evidence for the efficacy and safety of tai chi for hyperlipidaemia. It can assist the patients with hyperlipidaemia and clinicians. However, we acknowledge potential limitations. For example, only Chinese and English studies are searched, and the diversity of tai chi methods may increase the risk of heterogeneity and thus affect the final results.

**Contributors**

WD and FZ will read the titles and abstracts to determine eligible studies. DL and XC will read the full text to make further selection. If there is disagreement about some studies, CW will make the decision. Data extraction will be performed by HZ and TG. WD, FZ and DL will assess the risk of bias. Any disagreement will be resolved after discussion with CW. DL and XC will use the Grading of Recommendations Assessment, Development and Evaluation (GRADE) system approach. WD conceived the review plan and drafted the manuscript. WC will supervise each process of the review. All authors have read and approved the publication of this protocol.

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**Competing interests**

None declared.

**Patient and public involvement**

Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

**Patient consent for publication**

Not required.

**Provenance and peer review**

Not commissioned; externally peer reviewed.

**Open access**

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