


BMJ Open Effect of traditional Chinese exercise on abnormal lipid metabolism in patients with atherosclerosis: a protocol for meta-analysis of randomised controlled trials

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ABSTRACT

Introduction Atherosclerosis (AS) is an abnormal response within the vessel wall to endothelial dysfunction and inflammatory cellular processes. Taijiquan exercise as a moderate-intensity aerobic exercise can control or reverse AS by gradually reducing the deposition of cholesterol on the walls of blood vessels. Similarly, performing Baduanjin exercise, Liuzijue Qigong, Wuqinxi exercise and Yijinjing exercise has been found to have a positive effect on lipid metabolism in patients with AS. However, these studies focused only on middle-aged and older populations over 50 years of age and had short intervention periods, poor quality control and patient compliance, and no stratification by age and gender to observe the effects of traditional Chinese exercise (TCE) on patients with AS. Therefore, this meta-analysis will explore the specific effects of different TCE interventions on lipid metabolism in patients with AS through subgroup analysis of factors such as age, gender, intervention cycle and training method and lay the foundation of evidence-based medicine for the promotion of TCE in both clinical practice and the community.

Methods and analysis A systematic approach will be completed to search the literature published up to 30 September 2021 in the following databases: Web of Science, PubMed, Embase, Cochrane Library, EBSCO and CNKI. Other databases will also be searched manually. Lipid metabolism is the primary outcome indicator. Data synthesis, sensitivity analysis, regression analysis, subgroup analysis and risk bias evaluation will be performed using RevMan V.5.3 software. In addition, funnel plots generated by Begg's and Egger's tests will be used to assess reporting bias.

Ethics and dissemination Ethical approval and consent are not necessary as no primary data will be collected. The results of the study will be disseminated through carefully reviewed publications.

PROSPERO registration number CRD42022304283.

INTRODUCTION

According to preliminary statistics, the elderly population in China was expected to reach 264 million by 2020, accounting for 18.7% of the total population.¹ In addition, the incidence of cardiovascular disease (CVD), particularly coronary heart disease and atherosclerosis (AS), which are the most significant cardiovascular conditions, is

STRENGTHS AND LIMITATIONS OF THIS STUDY

- ⇒ Our analysis may offer a new complementary therapy derived from traditional Chinese exercise (TCE) for the rehabilitation of patients with atherosclerosis (AS).
- ⇒ The effectiveness and safety of TCE in improving lipid metabolism in patients with AS will be evaluated in this study. In addition, the effect of five different modes of TCE on lipid metabolism in patients with AS will be assessed through subgroup analysis.
- ⇒ It is unclear whether all patients had sufficient adherence, whether there were uncontrolled or unmeasured confounding factors and whether these factors will bias the results.
- ⇒ It is also unclear whether all studies distinguished between populations (eg, age, gender, region), which may introduce selection bias.

increasing each year in the middle-aged and elderly populations.² Most people choose to use medications to control or slow the development of CVD; although the treatment effect is evident, the long-term use of drugs not only has physical side effects but also contributes to the high cost of medical treatment. Hence, the exploration of how to effectively prevent and reduce the occurrence of chronic disease has become an urgent task, and AS has received significant attention as one of the most prevalent diseases in the middle-aged and elderly populations.

AS is a type of degenerative change in the arterial vessels caused by a number of factors. The deposition of lipids is the initiating factor of AS, which, along with the triggering of inflammatory cell infiltration under the internal membrane, causes endothelial damage and ultimately promotes the development of AS.³ The highest incidence of AS occurs in the elderly population, and timely diagnosis and treatment aimed at softening the blood vessels are important to prevent the occurrence of AS.⁴ Numerous studies have shown that a

combination of medication and exercise produces a more stable effect than either intervention alone in the prevention and treatment of AS.^{5,6} Domestic and international research has confirmed that aerobic exercise improves the body's metabolism and promotes the development of physical functions.⁷ It maintains blood lipids in a stable state, diminishes lipid abnormalities, protects the vascular endothelial cells and prevents and alleviates the development of AS.⁸ It has also been found that aerobic exercise can effectively reduce the extent of AS lesions, maintain the stability of plaques and decrease the incidence of embolic events.⁹

A previous study showed that during Taijiquan exercise (TJQE), subjects' mean heart rate was maintained at approximately 60% of their maximum heart rate with little variation in intensity of approximately 4 metabolic equivalents (METs), suggesting that TJQE is a form of low-intensity to moderate-intensity aerobic exercise.¹⁰ A randomised controlled trials (RCTs) found that 16 weeks of TJQE significantly improved total cholesterol (TC) and low-density lipoprotein cholesterol (LDL) levels in patients with AS between 50 and 60 years of age.¹¹ Another study showed that TJQE significantly reduced lipid levels in people with AS, though the long-term effects could not be confirmed due to the short intervention period.¹² An RCT studying traditional fitness qigong found that performing Baduanjin exercise (BDJE), Wuqinxi exercise (WQXE), Yijinjing exercise (YJJE) and Liuzijue Qigong (LQG) had a positive effect on lipid metabolism in a middle-aged and elderly cardiovascular population.¹³ Similarly, a 6-month RCT found that LQG significantly reduced TC, LDL and triglyceride (TG) levels in middle-aged and older men aged 55–60 years with AS compared with the control group.¹⁴

Although each of these RCTs demonstrated the clinical effectiveness of traditional Chinese exercise (TCE) in improving lipid metabolism in patients with AS, these studies focused only on middle-aged and elderly populations over 50 years of age and had short intervention periods and poor quality control and patient compliance, resulting in findings that were less convincing than expected. Furthermore, these studies did not stratify the results by age and gender nor did they conduct follow-up assessments to further observe the effects of TCE on patients with AS. Therefore, this meta-analysis will explore the specific effects of different TCE interventions on lipid metabolism in patients with AS through subgroup analysis of factors such as age, gender, intervention cycle and training method and lay the foundation of evidence-based medicine for the promotion of TCE in both clinical practice and the community.

METHODS AND ANALYSIS

Design

The programme is registered with PROSPERO under registration number CRD42022304283 and has been prepared in accordance with the guidelines of the

Systematic Review and Meta-Analysis Programme Preferred Reporting Project.¹⁵

Inclusion and exclusion criteria

Studies will be included if they meet the following criteria: (1) the study is an RCT on the effects of TCE on lipid metabolism in patients with AS published in Chinese or English; (2) the study includes a study population of patients with a clear diagnosis of AS; (3) the intervention group was treated with TCE (eg, TJQE, BDJE, WQXE, LQG and YJJE) combined with medication or TCE alone, with exercise intervention durations of ≥ 8 weeks at a minimum of 60 min per week, and the control group was treated with medication only without an exercise intervention. Studies will be excluded if they are any of the following: (1) studies for which the full text is not available; (2) studies published in abstract form with incomplete information even after contacting the authors; (3) studies without outcome indicators of lipid metabolism; (4) articles that are reviews, study protocols, case reports or animal studies.

Intervention/control

The control groups of included studies will undergo conventional medication treatment or be provided health education for daily life maintenance. The intervention groups will receive TCE, such as TJQE, BDJE, WQXE, LQG and YJJE, at different durations and frequencies.

Outcome measures

Measures of lipid metabolism will be used as the primary outcome indicators, including TC, TG, high-density lipoprotein cholesterol (HDL), LDL and adiponectin.

Search strategy

Electronic search

The search terms “Taijiquan, Taijiquan exercise, Qigong, Liuzijue, Wuqinxi, Yijinjing, Baduanjin, Traditional Chinese exercise” and “atherosclerosis, peripheral artery disease” and “randomised, randomised controlled, randomised study, randomised controlled trial, blinded, blank control, clinical study, clinical trial” will be employed in the search strategy. PubMed, Embase, Web of Science, Cochrane Library, EBSCO and CNKI databases will be searched for studies published from January 2000 to September 2021 to collect RCTs studying the effects of TCE on lipid metabolism in patients with AS. The specific search strategy that will be used to search PubMed is detailed in [table 1](#) as an example. The specific search strategy is detailed in the online supplemental material 1.

Additional resources

We will also manually search the following resources to identify ongoing or completed clinical trials: Google Scholar (<http://scholar.google.com>), Baidu Scholar (<http://xueshu.baidu.com/>), ClinicalTrials.gov (<http://www.clinicaltrials.gov>) and the Chinese Clinical Trials Registry (<http://www.chictr.org/cn/>).

Table 1 PubMed search strategy

Number	Search terms
#1	"arteriosclerosis"[MeSH]
#2	(atherosclerosis[Title/Abstract]) OR (peripheral arterial disease[Title/Abstract])
#3	("arteriosclerosis"[MeSH]) OR ((atherosclerosis[Title/Abstract]) OR (peripheral arterial disease [Title/Abstract]))
#4	tai chi[MeSH Terms]
#5	(((((taiji[Title/Abstract]) OR (qigong[Title/Abstract])) OR (wuqinxi[Title/Abstract])) OR (baduanjin[Title/Abstract])) OR (traditional exercise[Title/Abstract])) OR (traditional chinese medicine[Title/Abstract])) OR(chinese traditional exercise[Title/Abstract]) OR(chinese exercise[Title/Abstract])
#6	(tai chi[MeSH Terms]) OR ((((((taiji[Title/Abstract]) OR (qigong[Title/Abstract])) OR (wuqinxi[Title/Abstract])) OR (baduanjin[Title/Abstract])) OR (traditional exercise[Title/Abstract])) OR (traditional chinese medicine[Title/Abstract])) OR (chinese traditional exercise[Title/Abstract]) OR (chinese exercise[Title/Abstract]))
#7	random[MeSH Terms]
#8	(((((allocation[Title/Abstract]) OR (random allocation[Title/Abstract])) OR (placebo[Title/Abstract])) OR (single blind[Title/Abstract])) OR (double blind[Title/Abstract])) OR (randomised controlled trial[Title/Abstract])) OR (RCT[Title/Abstract])
#9	(random[MeSH Terms]) OR ((((((allocation[Title/Abstract]) OR (random allocation[Title/Abstract])) OR (placebo[Title/Abstract])) OR (single blind[Title/Abstract])) OR (double blind[Title/Abstract])) OR (randomised controlled trial[Title/Abstract])) OR (RCT[Title/Abstract]))
#10	((("arteriosclerosis"[MeSH]) OR ((atherosclerosis[Title/Abstract]) OR (peripheral arterial disease[Title/Abstract]))) AND ((random[MeSH Terms]) OR ((((((allocation[Title/Abstract]) OR (random allocation[Title/Abstract])) OR (placebo[Title/Abstract])) OR (single blind[Title/Abstract])) OR (double blind[Title/Abstract])) OR (randomised controlled trial[Title/Abstract])) OR (RCT[Title/Abstract]))) AND ((tai chi[MeSH Terms]) OR ((((((taiji[Title/Abstract]) OR (qigong[Title/Abstract])) OR (wuqinxi[Title/Abstract])) OR (baduanjin[Title/Abstract])) OR (traditional exercise[Title/Abstract])) OR (traditional chinese medicine[Title/Abstract])) OR(chinese traditional exercise[Title/Abstract]) OR(chinese exercise[Title/Abstract])))

Study selection and data extraction

NoteExpress V.3.5 or Endnote V.X9 will be used to manage the literature and remove duplicates. Two researchers (CW) and (PZ) will first filter the studies based on their titles and abstracts to identify potentially eligible studies. Studies without relevant results and duplicates will be excluded. Two researchers (CW) and (PZ) will then independently assess the full texts of potentially eligible studies. After screening the eligible articles, two researchers will independently extract the data from the studies. Any disagreement during data extraction will be discussed with a third researcher (YY) if necessary. We will use an Excel spreadsheet to record information on the eligible articles, including study design, year of publication, study site, study period and authors. We will also

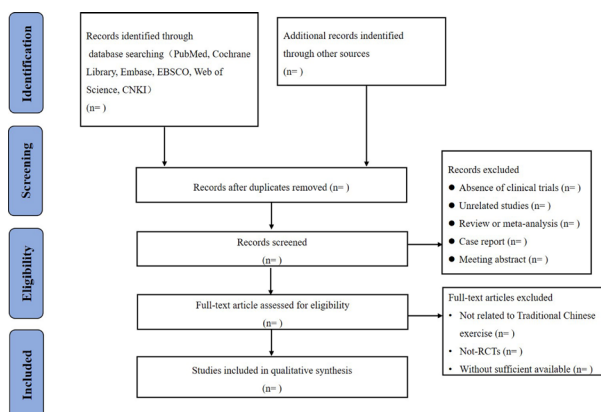
record participants, interventions and outcomes. Finally, all eligible studies will be included in a systematic review and those that meet the requirements will be selected for meta-analysis based on the quality of the included literature. We will map a flow chart based on the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) showing the number of articles identified, screened, included and excluded as well as the reasons for exclusion and the final number of eligible studies. The selection process will be described in a PRISMA flow chart (<http://www.prisma-statement.org>) (figure 1).¹⁵

Dealing with missing data or unclear measurement scales

If necessary, we will contact the first or corresponding author of an article by email to request missing data or additional information regarding the employed assessment scale. If sufficient information cannot be obtained in this manner, we will analyse the available data and discuss the potential impact of insufficient data on the study results.

Risk of bias in included studies

This study will employ the Cochrane Risk Assessment Tool to evaluate the methodological quality of the included literature in six primary areas: selection bias, implementation bias, detection signal bias, loss to follow-up bias, information bias and other biases.¹⁶ Each domain is classified into three categories: low risk of bias, high risk of bias and unclear risk of bias. The overall quality of an individual study is considered good if more than two domains are low risk, fair if two domains are low risk and poor if less than two domains are low risk.


Figure 1 Preferred Reporting Items for Systematic Reviews and Meta-Analyses flow chart.

Data synthesis and analysis

Statistical analysis will be performed using the Review Manager V.5.3 software. The experimental data will consist of continuous variables. Standardised mean differences and 95% CIs will be used as the effect scales for combining effect sizes. $P > 0.05$ will indicate a statistically significant difference between the treatment and control groups and demonstrate that the results of the meta-analysis are statistically significant. The test of homogeneity (Q test at $\alpha = 0.1$) will be used to test for heterogeneity. After testing for heterogeneity, a fixed-effects model will be selected for meta-analysis for $I^2 \leq 40\%$ and a random-effects model will be selected for meta-analysis for $I^2 > 40\%$. Subgroup analysis, sensitivity analysis and one-way meta-regression analysis will then be conducted to identify the sources of heterogeneity, and Egger's test will be employed to detect the presence of publication bias in the included studies.

Additional analyses

Subgroup and meta-regression analyses will be conducted to explore the sources of heterogeneity based on the characteristics of the study, including participant age and gender, the type or timing of the intervention and other aspects of heterogeneity. For quality studies, individual studies that affect the primary outcome indicators will be excluded using sensitivity analysis to reduce their impact on the results.

Assessment of reporting biases

If at least 10 studies are included in an outcome indicator analysis, funnel plots may be used to assess for possible publication bias. Otherwise, Egger's or Begg's tests may be further used to assess for publication bias.

Patient and public involvement

This study is a systematic review and is only a generalisation and summary of previous studies. Therefore, patients and the public will not be involved the study.

ETHICS AND DISSEMINATION

Ethical approval and consent are not necessary, as no primary data will be collected. The results of the study will be disseminated through carefully reviewed publications.

DISCUSSION

Abnormal lipid metabolism is considered to be one of the primary mechanisms affecting AS.¹⁷ Two RCTs have confirmed that TCE, such as TJQE, stimulates the sympathetic nervous system to accelerate the secretion of catecholamines, increases the activity of TG oxidase, promotes the oxidative breakdown of TG and decreases TC and TG levels.^{18 19} Some studies have shown that TCE can increase the activity of apolipoprotein A, the primary component of HDL, converting a large quantity of cholesterol into cholesterol ester and improving AS.^{20 21} Another RCT found that performing BDJE, WQXE, YJJE and LQG had a positive effect on lipid metabolism in a middle-aged and elderly cardiovascular population. Similarly, a 6-month RCT found that LQG

significantly reduced TC, LDL and TG levels in middle-aged and older men aged 55–60 years with AS compared with the control group.¹⁴

Although the existing literature has demonstrated the clinical effectiveness of TCE in improving lipid metabolism in patients with AS,^{22–27} there are several limitations in the previous studies. First, most of these studies evaluated middle-aged and older populations over the age of 50 years. In addition, most of the studies employed group interventions conducted in the community instead of one-on-one individualised interventions. Second, these studies did not provide true real-time monitoring of the subjects' dietary control and lifestyle habits, and the subjects' compliance with the interventions and assessments was poor. Third, these studies did not provide stratification by age and gender, nor did they conduct follow-up assessments to further observe the effects of TCE on lipid metabolism in patients with AS. Therefore, this meta-analysis will explore the specific effects of different TCE interventions on lipid metabolism in patients with AS through subgroup analysis of factors such as age, gender, intervention cycle and training method and lay the foundation of evidence-based medicine for the promotion of TCE in both clinical practice and the community.

Contributors All authors conceived and designed the study. The manuscript of this protocol was drafted by all authors and revised by CW and PZ. CW and YY designed the search strategy and will independently perform the search, screening and assessment of risk of bias. CW and PZ will analyse and interpret the data. YY will arbitrate any disagreements during the review process. All authors approved the final version 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 applicable.

Provenance and peer review Not commissioned; externally peer reviewed.

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