Effect of Taijiquan assisted rehabilitation for breast cancer patients
A protocol for systematic review and meta-analysis

Sihua Zhao, MD\textsuperscript{a}, Rongna Lian, BS\textsuperscript{b}, Ruinian Zhang, BS\textsuperscript{b}, Fanghong Wang, MD\textsuperscript{c}\textsuperscript{*}, Hao Chen, MD\textsuperscript{d}, Run Wan, MD\textsuperscript{d}

Abstract

Background: Taijiquan, as a supplementary and alternative method, has attracted more and more attention in the treatment of breast cancer. But up to now, no systematic review has been performed to evaluate the efficacy of Taijiquan in the treatment of breast cancer. In this study, Cochrane systematic review method will be used to evaluate the effect of Taijiquan in the rehabilitation process of breast cancer patients after treatment.

Methods: PubMed, Embase.com, the Cochrane Central Register of Controlled Trials (CENTRAL), Web of Science, China National Knowledge Infrastructure (CNKI), Wanfang, and SinoMed will be searched to identify relevant studies up to May 31, 2021. We will include randomized controlled trials (RCTs) of the application of Taijiquan in post-treatment breast cancer patients. We will use the Cochrane bias risk assessment tool to assess the quality of included RCTs. We will use Stata 13.0 to perform pairwise meta-analyses using the inverse variance method. Subgroup analyses and sensitivity analyses will be conducted to investigate the sources of heterogeneity.

Results: The results of this study will be published in a peer-reviewed journal.

Conclusion: This study will comprehensively evaluate the efficacy of Taijiquan in the rehabilitation treatment of breast cancer. The results of this study will provide high-quality evidence to support clinical practice and guidelines development.

Abbreviations: CAM = complementary and alternative medicine, PRISMA = Preferred Reporting Items for Systematic Reviews and Meta-Analyses.

Keywords: breast cancer, comprehensive and alternative medicine, efficacy, rehabilitation, Taijiquan

1. Introduction

Breast cancer (BC) is the most common cancer in women all over the world and the second most common cause of cancer-related mortality.\textsuperscript{[1,2]} The overall incidence rate of breast cancer is increasing rapidly in the world, which is positively correlated with the level of regional development.\textsuperscript{[3]} Complementary and alternative medicine (CAM) is a group of medical and health care embodiment, practice and products different from traditional medical behavior, complementary to traditional medicine, and belongs to the category of general practice.\textsuperscript{[4,5]} Compared with the traditional model, CAM has the advantages of strong practicability, short treatment induction period, economic and practical, which can stimulate the rehabilitation potential and improve the overall quality of life of patients with breast cancer while carrying out traditional treatment.\textsuperscript{[6,7]} CAM has become the main treatment of pain, fatigue, dyspnea, and other symptoms in patients with advanced breast cancer.\textsuperscript{[8,9]} Taijiquan as a complementary alternative method in the treatment of breast cancer has attracted more and more attention.\textsuperscript{[10]} But up to now, no systematic review has been used to evaluate the efficacy of Taijiquan in the rehabilitation process of breast cancer patients after treatment. In this study, the Cochrane systematic review method will be used to evaluate the efficacy of Taijiquan in the rehabilitation treatment of breast cancer, to provide high-quality evidence to support guidelines development and clinical practice, and promote the development of personalized rehabilitation of breast cancer.

\textsuperscript{*}RL contributed equally to this work.

This work was supported by the Gansu Province Science and Technology Plan Funded Project (20CKX4ZA027).

The funders had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.

Ethical approval was not necessary, for this article does not contain any studies with human or animal subjects performed by any of the authors.

The authors have no conflicts of interest to disclose.

The datasets generated during and/or analyzed during the current study are publicly available.

\textsuperscript{a} Lanzhou University First Hospital Nursing Department (School of Nursing Lanzhou University).

\textsuperscript{b} The First Clinical Medical College of Lanzhou University.

\textsuperscript{c} Lanzhou University Second Hospital Oncology Center, \textsuperscript{d} Lanzhou University Second Hospital Nursing Department, Lanzhou, China.

Correspondence: Fanghong Wang, The First Hospital of Lanzhou University General Surgery Department, No. 1, Donggang West Road, Lanzhou City 730000, Gansu Province, China (e-mail: wfh126@sina.com).

Copyright © 2021 the Author(s). Published by Wolters Kluwer Health, Inc.

This is an open access article distributed under the Creative Commons Attribution License 4.0 (CCBY), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

How to cite this article: Zhao S, Lian R, Zhang R, Wang F, Chen H, Wan R. Effect of Taijiquan assisted rehabilitation for breast cancer patients: a protocol for systematic review and meta-analysis. Medicine 2021;100:13(e25380).

Received: 11 March 2021 / Accepted: 12 March 2021
http://dx.doi.org/10.1097/MD.00000000000025380
2. Data and methods

We will conduct and report this meta-analysis according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement. The protocol of this study has been registered on the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY, INPLASY202130010).

2.1. Inclusion and exclusion criteria

2.1.1. Type of study. Randomized controlled trials (RCTs) about Tai Chi for breast cancer will be included. We will exclude research reviews, cross-sectional studies, conferences, observational studies, and case reports.

2.1.2. Type of participant. Women over 18 years old with breast cancer confirmed by pathology or cytology have received traditional western medicine treatment for breast cancer, including surgery, chemotherapy, radiotherapy, and hormone therapy, regardless of race and nationality.

2.1.3. Type of interventions. It can be any type of Tai Chi, such as simplified Taijiquan, simplified Yang’s Taijiquan, 19-style simple Taijiquan, and 24-style Taijiquan. It is not limited by the frequency, time, place, and intensity of intervention.

2.1.4. Types of controls. The control group should adopt one of the following treatment methods: no treatment, placebo, usual or standard care, health education, psychosocial therapy, and drug therapy.

2.1.5. Types of outcome measure. Physical function, quality of life, social function, mental status, grip strength, elbow flexion function, elbow extension, social well-being, and emotional health.

2.1.6. Exclusion criteria.

1. patients who did not meet the diagnostic criteria of breast cancer;
2. lymphatic drainage after breast cancer surgery;
3. physical function condition was not suitable for Taijiquan therapy;
4. psychiatric disorders or taking psychotropic drugs with the definite clinical diagnosis;
5. patients receiving a blood transfusion or steroid treatment;
6. patients with the second type of solid tumor who were not cured at the same time; and
7. the life span is less than 6 months.

2.2. Retrieval strategy

We will search English databases: PubMed, Embase.com, the Cochrane Central Register of controlled trials (CENTRAL) and Web of Science, as well as Chinese databases: China National Knowledge Infrastructure (CNKI), Wanfang, and Sinomed. The key words include: “breast cancer,” “breast tumor,” “breast cancer,” “breast tumor,” “breast cancer,” “TCC,” “Taiji,” “Taijiquan,” “Tai chi chuan,” “Tai-ji,” “TCC,” “Intention to Treat Analysis,” “Pragmatic Clinical Trials as Topic,” “Clinical Trials, Phase II,” “Clinical Trials, Phase III,” “Clinical Trials, Phase IV,” “Controlled Clinical Trials,” “Randomized Controlled Trials,” “Single-Blind Method,” “Double-Blind Method,” “random,” “blind,” “singleblind,” “doubleblind,” “trebleblind,” “tripleblind.” Taking PubMed as an example, the specific retrieval strategy is shown in Table 1.

2.3. Literature screening and data extraction

Two reviewers will independently screen the literature, extract the data, and cross-check the data. In case of disagreement, a third party will be consulted to assist in judgment, and the author will be contacted to supplement the missing data if possible. In the process of literature selection, we will first read the titles and abstracts. After excluding the unrelated literatures, we will further read the full text to determine whether they are included. Data extraction included: author, publication time, randomization method, grouping and sample size and sex of patients, intervention method (operation name, course of treatment), baseline comparison, distribution, whether to use the blind method, the outcome of interest, and follow-up time.

2.4. Risk of bias assessment of included studies

Two reviewers will assess the risk of bias of included RCTs using the “Cochrane bias risk assessment tool.” The evaluation items include:

Table 1

| Search strategy of PubMed. |
|---------------------------|
| #1 | Breast Neoplasms[Mesh] OR Breast Carcinoma In Situ[Mesh] OR Breast Neoplasms, Male[Mesh] OR Carcinoma, Ductal, Breast[Mesh] OR Carcinoma, Lobular[Mesh] OR Inflammatory Breast Neoplasms[Mesh] OR Triple Negative Breast Neoplasms[Mesh] OR Unilateral Breast Neoplasms[Mesh] OR Breast neoplasm[Title/Abstract] OR breast tumor[Title/Abstract] OR breast carcinoma[Title/Abstract] OR breast cancer[Title/Abstract] OR breast tumour[Title/Abstract] OR mammary neoplasm[Title/Abstract] OR mammary tumor[Title/Abstract] OR mammary carcinoma[Title/Abstract] OR mammary cancer[Title/Abstract] OR mammary tumour[Title/Abstract] OR breast adenocarcinoma[Title/Abstract] OR breast carcinogenesis[Title/Abstract] OR breast carcinoma[Title/Abstract] OR phyllodes tumor[Title/Abstract] OR intraductal carcinoma[Title/Abstract] OR lobular carcinoma[Title/Abstract] |
| #2 | *tai ji*[Mesh] OR *Tai-ji*[Title/Abstract] OR *tai chi*[Title/Abstract] OR *tai jiquan*[Title/Abstract] OR *Tai* OR *Tai jiquan*[Title/Abstract] OR *tai chi chuan*[Title/Abstract] OR *Tai-ji*[Title/Abstract] OR *TCC*[Title/Abstract] |
| #3 | Clinical Trials, Phase II as Topic[Mesh] OR Clinical Trials, Phase III as Topic[Mesh] OR Clinical Trials, Phase IV as Topic[Mesh] OR Controlled Clinical Trials as Topic[Mesh] OR Randomized Controlled Trials as Topic[Mesh] OR Intention to Treat Analysis[Mesh] OR Pragmatic Clinical Trials as Topic[Mesh] OR “Clinical Trials, Phase II”[Publication Type] OR “Clinical Trials, Phase III”[Publication Type] OR “Clinical Trials, Phase IV”[Publication Type] OR Controlled Clinical Trials[Publication Type] OR Randomized Controlled Trials[Publication Type] OR Pragmatic Clinical Trials as Topic[Publication Type] OR “Single-Blind Method*[Mesh] OR “Double-Blind Method*[Mesh] OR random[Title/Abstract] OR blind[Title/Abstract] OR singleblind[Title/Abstract] OR doubleblind[Title/Abstract] OR trebleblind[Title/Abstract] OR tripleblind[Title/Abstract] |
| #4 | #1 AND #2 AND #3 |
1. random sequence generation (selection bias).
2. allocation concealment (selection bias).
3. blinding of participants and personnel (performance bias).
4. blinding of outcome assessment (detection bias).
5. incomplete outcome data (attrition bias).
6. selective reporting (reporting bias).
7. other sources of bias (other bias).

Each item will be judged as low risk, high risk, and unclear risk.

2.5. Statistical analysis
2.5.1. Data synthesis. We will use Stata (13.0; Stata Corporation, College Station, TX) for pooling data and statistical analysis. We will conduct a meta-analysis using the inverse variance method to compute relative risks (RRs) and their 95% confidence interval (CI) for dichotomous outcomes and mean difference (MD) and 95%CI for continuous outcomes. The statistical level of significance will be set at $P < 0.05$.

2.5.2. Assessment of heterogeneity. Chi$^2$ test will be used to analyze the statistical heterogeneity of the results, and $P$ value and $I^2$ will be used to quantitatively judge the heterogeneity. If the homogeneity of the included studies is low ($P > 0.1$ and $I^2 < 50\%$), the fixed-effect model will be used for meta-analysis; if there is heterogeneity between the included studies ($P < 0.1$ and $I^2 \geq 50\%$), the source of heterogeneity will be further analyzed. After excluding the influence of obvious clinical heterogeneity, the random effect model will be used for meta-analysis. Significant clinical heterogeneity will be explored by subgroup analysis and sensitivity analysis.

2.5.3. Subgroup analyses and meta-regression analyses. Univariate meta-regression analysis will be performed on the within-study factors (time, sample size, tumor pathological stage, previous treatment of breast cancer, intervention group scheme, intervention time) and between study factors (mean age, race) respectively to screen out the important factors leading to heterogeneity. Subgroup analysis will be performed on these significant factors.

2.5.4. Sensitivity analysis. We will perform sensitivity analyses by excluding low-quality studies to assess the robustness of our conclusions.

2.5.5. Publication bias. The publication bias will be explored using the funnel plot and Egger test for outcomes with studies no less than 10.

2.6. Certainty of evidence
We will create a “Summary of findings” table presenting our primary and secondary outcomes using the GRADEpro Guideline Development Tool (GDT) software. We will use the 5 Grading of Recommendations Assessment, Development, and Evaluation (GRADE) considerations (risk of bias, inconsistency, imprecision, indirectness, and publication bias) to assess the quality of the body of evidence for each meta-analysis.

Figure 1. Flow chart of literature screening.
Table 2
Characteristics of partially included studies.

| First author | Year | Country | Language | Taiji | Control | Sample | Age | Tumor staging | Previous treatment | Treatment cycle | Frequency |
|--------------|------|---------|----------|-------|---------|--------|-----|---------------|-------------------|----------------|-----------|
| Mustian et al | 2008 | USA     | English  | 11    | 10      | 52 (33–78) | 0-II | surgery, radiation, chemotherapy | 12 weeks | 3 times a week for 60 minutes |
| Sprod et al  | 2012 | USA     | English  | 9     | 10      | average 53 | average 53 | I-IIIb | surgery, radiation, chemotherapy, hormone therapy | 12 weeks | 3 times a week for 60 minutes |
| Robbins et al | 2013 | USA     | English  | 37    | 36      | 50      | 50  | I-IIIa | chemotherapy | 42 weeks | 3 times a week for 60 minutes |
| Janelins et al | 2011 | USA     | English  | 9     | 10      | average 54.3 | average 52.7 | I-IIIb | surgery, radiotherapy, chemotherapy | 12 weeks | 3 times a week for 60 minutes |
| Mustian et al | 2004 | USA     | English  | 11    | 10      | 52 (33–78) | 0-II | surgery, radiation, chemotherapy, hormone therapy | 12 weeks | 3 times a week for 60 minutes |
| Peppone et al | 2010 | USA     | English  | 7     | 9       | 53.8    | 52.9 | I-IIIb | surgery, hormone therapy | 12 weeks | Twice a day for 20 to 30 minutes |
| Larkey et al  | 2015 | USA     | English  | 42    | 42      | 57.7 (8.94) | 59.8 (8.93) | 0-II | surgery, radiation, and/or chemotherapy | 12 weeks | 60 minutes twice a week, followed by 60 minutes once a week |
| Irwin et al   | 2014 | USA     | English  | 45    | 45      | 59.6 (7.9) | 60.0 (9.3) | Not mentioned | surgery, radiation, and/or chemotherapy | 3 months | 2 hours a week |
| Mustian et al | 2006 | USA     | English  | 11    | 10      | 52 (33–78) | I-IIIb | surgery, radiation, chemotherapy, hormone therapy | 12 weeks | 3 times a week for 60 minutes |

We will rate the quality of evidence as high, moderate, low, or very low, and will justify decisions to downgrade or upgrade the quality of the evidence using footnotes where necessary.

3. Result

3.1. Screening results

We conducted a pilot literature search, and a total of 102 articles were retrieved, and 35 articles were obtained by endnote. By looking at the title and abstract of the literature, 12 unrelated literatures were excluded. We will show the screening process in the prism flow chart (Fig. 1).

3.2. General characteristics and quality of studies

We presented characteristics of some included studies in Table 2. All RCTs are in English,[17–25] publishing between 2006 and 2015. The details are shown in Table 2.

4. Discussion

CAM has become the main treatment of pain, fatigue, dyspnea, and other symptoms in patients with advanced breast cancer.[8,9] At present, the most effective method for the treatment of breast cancer is the comprehensive treatment based on radical surgery. We believe the results of our study will provide high-quality evidence to support clinical practice.

Author contributions

Conceptualization: Sihua Zhao, Rongna Lian, Ruinian Zhang, Fanghong Wang, Hao Chen, Run Wan.
Funding acquisition: Fanghong Wang.

Methodology: Sihua Zhao, Rongna Lian, Ruinian Zhang, Fanghong Wang, Hao Chen, Run Wan.
Writing – original draft: Sihua Zhao, Rongna Lian.
Writing – review & editing: Sihua Zhao, Rongna Lian, Ruinian Zhang, Fanghong Wang, Hao Chen, Run Wan.

References

[1] Bray F, Ferlay J, Soerjomataram I, et al. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin 2018;68:394–424.
[2] Gao Y, Liu M, Shi S, et al. Diagnostic value of seven biomarkers for breast cancer: an overview with evidence mapping and indirect comparisons of diagnostic test accuracy. Clin Exp Med 2020;20:97–108.
[3] Chen W, Zheng R, Baade PD, et al. Cancer statistics in China, 2015. CA Cancer J Clin 2016;66:115–39.
[4] International Office of Traditional Chinese Medicine, Department of International Cooperation, Ministry of Science and Technology. Complementary and alternative medicine in the United States, Asia Pacific traditional medicine. XIXXX 2006;5:28–38.
[5] Cheung CK, Wyman JF, alcon H, LL. Use of complementary and alternative therapies in community-dwelling older adults. J Altern Complement Med 2007;13:997–1006.
[6] Macpherson H, Thomas K. Short-term reactions to acupuncture—a cross-sectional survey of patient reports. Acupunc Med 2005;23:112–20.
[7] Hanje AJ, Fortune B, Song M, et al. The use of selected nutrition supplements and complementary and alternative medicine in liver disease. Nutr Clin Prac 2006;21:255–72.
[8] Garcia-P1anella E, Marin L, Damenech E, et al. Use of complementary and alternative medicine and drug abuse in patients with inflammatory bowel disease. Med Clin 2007;28:45–148.
[9] Liu Yan. Application and effect of Flos Daturae preparation in anesthesia of traditional Chinese medicine surgery. Seeking Med Adv 2011.
[10] Fan L, Strasser-Weippl K, Li JJ, et al. Breast cancer in China. Lancet Oncol 2014;15:279–89.
[11] Moher D, Liberati A, Tetzlaff J, et al. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. BMJ 2009;339:b2533.
[12] Higgins JPT, Altman DG, Sterne JAC. Higgins JPT, Green S, et al. Chapter 8: Assessing risk of bias in included studies. Cochrane Handbook for Systematic Reviews of Interventions Version 5. 1. 0 2011;The Cochrane Collaboration, Available at: www.cochranehandbook.org.

[13] McMaster University (developed by Evidence Prime, Inc.). GRADEpro Guideline Development Tool. McMaster University (developed by Evidence Prime, Inc.), 2015

[14] Guyatt GH, Oxman AD, Vist GE, et al. GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. BMJ 2008;336:924-6.

[15] Yao L, Sun R, Chen YL, et al. The quality of evidence in Chinese meta-analyses needs to be improved. J Clin Epidemiol 2016;74:73–9.

[16] Norris SL, Meerpohl JJ, Akl EA, et al. The skills and experience of GRADE methodologists can be assessed with a simple tool. J Clin Epidemiol 2016;79:150–8.

[17] Mustian K, Palesh O, Flecksteiner S. Tai Chi Chuan for breast cancer survivors. Med Sport Sci 2008;52:209.

[18] Sprod LK, Janelins MC, Palesh OG, et al. Health-related quality of life and biomarkers in breast cancer survivors participating in tai chi chuan. J Cancer Survivorship 2012;6:146–54.

[19] Robins JLW, Mccain NL, Elswick RK, et al. Psychoneuroimmunology-based stress management during adjuvant chemotherapy for early breast cancer. Evid Based Complement Altern Med 2013;2013:372908.

[20] Janelins MC, Davis PG, Wideman L, et al. Effects of Tai Chi Chuan on insulin and cytokine levels in a randomized controlled pilot study on breast cancer survivors. Clin Breast Cancer 2011;11:161–70.

[21] Mustian KM, Katula JA, Gill DL, et al. Tai Chi Chuan, health-related quality of life and self-esteem: a randomized trial with breast cancer survivors. Supportive Care Cancer 2004;12:871.

[22] Peppone LJ, Mustian KM, Janelins MC, et al. Effects of a structured weight-bearing exercise program on bone metabolism among breast cancer survivors: a feasibility trial. Clin Breast Cancer 2010;10:224–9.

[23] Larkey LK, Roe DJ, Wehs KL, et al. Randomized controlled trial of Qigong/Tai Chi easy on cancer-related fatigue in breast cancer survivors. Annals Behav Med 2015;49:165–76.

[24] Irwin MR, Richard O, Breen EC, et al. Tai Chi, cellular inflammation, and transcriptome dynamics in breast cancer survivors with insomnia: a randomized controlled trial. J National Cancer Inst Monogr 50:295.

[25] Mustian KM, Katula JA, Zhao H. A pilot study to assess the influence of Tai Chi Chuan on functional capacity among breast cancer survivors. J Supp Oncol 2006;4:139.