PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below.

ARTICLE DETAILS

Title (Provisional)

Effects of Traditional Chinese Medicine massage therapy on pain, functional activity, muscle activation patterns, and proprioception in knee osteoarthritis: A randomized controlled trial protocol

Authors

Zhu, Bowen; Tang, Cheng; Zhou, Xin; Janice Hiew, Yuen Yee; Fang, Sitong; Fu, Yangyang; Zhu, Qingguang; Fang, Min

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VERSION 1 - REVIEW

Reviewer	**1**
Name	**Shepherd, Mark H.**
Affiliation	**Bellin College**
Date	**10-Apr-2024**
COI	**None.**

Thank you for your work on this manuscript.

ABSTRACT

Line 14 – define what KOA is before using acronym.

Line 28 – Should be (WOMAC)

RANDOMIZATION AND BLINDING

You mention that the assessor will be blinded for follow-up session outcome assessment, it may be appropriate to state this in this section as well.

INTERVENTION

It may be helpful to include any written health education given to study participants as an appendix to show what was included prior to randomization.

LINE 226 – state “3 times per week” vs. “third a week”.

CONTROL GROUP

It is unclear how long the control group last per session. It is noted that the experimental group will last approx. 30 minutes. There could be a confounding variable if the experimental group has more time with the clinician vs. the control group since they are only to get exercise. If deemed OK to have different treatment times per group, I suggest documenting mean treatment time per group and use as a covariate in your assessment to see if this has an effect on study outcomes.

The exercises described, while helpful having the figures showing pictures of what will be done, there is no comment on dosage of what appear to be isometric contractions. The reproducibility of the exercise program for this protocol is unclear and will limit true translation of the comparator and external generalizability. Furthermore, while there is reference to the ACSM guidelines on physical activity, there is no reference to guidance of the resistance training program. I do not think the exercise dosage is truly matched to what has been done in the previous published literature on knee OA (see https://www.nejm.org/doi/full/10.1056/NEJMoa1905877).

CONCOMITANT MEDICATIONS

Will telling patients not to take pain medication be part of the informed consent? This may be important to note before enrollment. How will you track adherence to not taking pain medication?

PATIENT AND PUBLIC INVOLVEMENT

LINE 338 – remove first 4 words.

STATISTICAL ANALYSIS

It is unclear to me what specific time points are being compared (i.e. group x time interaction). As this is a protocol, having specific detail of which time points being compared will be helpful. The statistics related to how each outcome will be assessed is unclear. The only mention of outcome assessment is Pearson correlation for strength and EMG.

Will a mixed-model ANOVA be performed or a linear mixed model approach? Will Bonferroni adjustments be made?

VERSION 1 - AUTHOR RESPONSE

- Reviewer: 1

  Dr. Mark H. Shepherd, Bellin College

  Comments to the Author:

  Thank you for your work on this manuscript.

  ABSTRACT

Line 14 – define what KOA is before using acronym.

We have completed the changes according to your comments. Details are in line 14 of the revised document.

Line 28 – Should be (WOMAC)

We have completed the changes according to your comments. Details are in line 27 of the revised document

RANDOMIZATION AND BLINDING

You mention that the assessor will be blinded for follow-up session outcome assessment, it may be appropriate to state this in this section as well.

Thank you for your valuable suggestions, which we have modified in the paper, as detailed in line 194.

INTERVENTION

It may be helpful to include any written health education given to study participants as an appendix to show what was included prior to randomization.

We uploaded health education in Appendix 1, line 214 in the article.

LINE 226 – state “3 times per week” vs. “third a week”.

We revisited to determine the frequency of the research intervention to be three times per week and made a change on line 246 in the paper.

CONTROL GROUP

It is unclear how long the control group last per session. It is noted that the experimental group will last approx. 30 minutes. There could be a confounding variable if the experimental group has more time with the clinician vs. the control group since they are only to get exercise. If deemed OK to have different treatment times per group, I suggest documenting mean treatment time per group and use as a covariate in your assessment to see if this has an effect on study outcomes.

This is a very good suggestion and we have rewritten the statistical analysis methods section as per your valuable comments on lines 368-375.

The exercises described, while helpful having the figures showing pictures of what will be done, there is no comment on dosage of what appear to be isometric contractions. The reproducibility of the exercise program for this protocol is unclear and will limit true translation of the comparator and external generalizability. Furthermore, while there is reference to the ACSM guidelines on physical activity, there is no reference to guidance of the resistance training program. I do not think the exercise dosage is truly matched to what has been done in the previous published literature on knee OA (see https://www.nejm.org/doi/full/10.1056/NEJMoa1905877).

Thanks to the valuable references provided by the experts, we designed this study with the intention of simplifying as much as possible the content of exercise therapy for elderly patients with KOA, and therefore there were still parts of the writing of this section in the first draft where the description was lacking. In this revised version, we have revised this section in detail, taking into account the methodology you provided for writing the literature and the content of that literature (DOI: 10.7326/M22-2348), as detailed in lines 216-234 of the main text.

CONCOMITANT MEDICATIONS

Will telling patients not to take pain medication be part of the informed consent? This may be important to note before enrollment. How will you track adherence to not taking pain medication?

Telling patients not to take painkillers is part of the informed consent form, and we will be recording patients' use of painkillers in the study, as detailed on lines 255-257

PATIENT AND PUBLIC INVOLVEMENT

LINE 338 – remove first 4 words.

We have completed the changes according to your comments. Details are in line 347 of the revised document

STATISTICAL ANALYSIS

It is unclear to me what specific time points are being compared (i.e. group x time interaction). As this is a protocol, having specific detail of which time points being compared will be helpful. The statistics related to how each outcome will be assessed is unclear. The only mention of outcome assessment is Pearson correlation for strength and EMG.

Will a mixed-model ANOVA be performed or a linear mixed model approach? Will Bonferroni adjustments be made?

We have rewritten the section on analyzing statistical methods in accordance with your valuable suggestions (line 358).

Reviewer: 2

Dr. Kanda Chaipinyo, Srinakharinwirot University

Comments to the Author:

Overall:

The authors describe a parallel, single-centered randomized controlled trial comparing the effects of TCM massage and exercise to control who receive only exercise on WOMAC pain after 24 weeks. However, in the introduction, TCM was described to be effective for mobility and improved stiffness. In objectives the outcomes also included functional activity, proprioception, and muscle activation. Therefore, these outcome should be stated in the abstract as secondary outcomes.

Thank you for providing the corrections; we have added the secondary outcomes in the abstract (line 28).

There are some clarifications that are necessary to make this acceptable for publication.

1. Please check some typos and spelling such as WOMAC not WOMCA, functional activity not activity function, Material and methods not METHODS AND METHODS etc.

For grammatical and spelling errors in the text, we invited the magazine to recommend the English Language Editing Service and made extensive corrections. The proof of editing

service has been uploaded.

2. Rewrite objective 1 to To study the effect of TCM massage combined with exercise compared to exercise on pain, activity function, and proprioception in patients with KOA.

Thank you for the suggested changes, which have been made as requested (line 124).

3. Please check Objective 2 as there was no mention for sports in the protocol, is there any different in exercise and sports in this project?

The exercise and sports in this protocol is the same meaning and we have corrected this error in line 127, thank you for suggesting.

4. Objective 3 was not clear, please rewrite.

We have rewrited the Objective 3 in line 128.

5. In methods, please reconsider using an up to date guidelines for RCT such as CONSORT. See https://www.bmj.com/sites/default/files/attachments/resources/2018/05/BMJ-InstructionsForAuthors-2018.pdf

We have upped to date guidelines for RCT in methods (line136).

6. In Inclusion criteria, it would be better to show the full scale of WOMAC. May I suggest to change to: WOMAC pain subscale score of > 8/20.

Yes, we have changed to : WOMAC pain subscale score of > 8/20 (line 173).

7. In exclusion criteria, is any other treatment for KOA pain included medication? Please stated clearly. This was not coresponded to what described in Concomitant medications.

Thanks to your valuable suggestion, we have corrected the mischaracterization in the exclusion criteria by referring to the literature of similar studies, see line 175 for details.

8. Please consider rewrite Removed criteria: Misplacement or the inclusion this statement is not understandable.

The Removed criteria have been rewritten in line 185.

9. Please reconsider using the word “post hoc outcomes” because post hoc usually be used for statistical analysis. If satisfaction was evaluated, it can also be included in secondary outcomes.

We have taken your advice and modified the term “post hoc outcomes”and included satisfaction ratings in the secondary results (line 323).

10. For study protocol submitted, discussion section may not required as there was no results to to discuss.

Thank you for your patience in reviewing and guiding our article, we have removed the discussion section.

VERSION 2 - REVIEW

Reviewer	**2**
Name	**Chaipinyo, Kanda**
Affiliation	**Srinakharinwirot University, Division of Physical Therapy, Faculty of Health Science**
Date	**24-Oct-2024**
COI	

The authors have responded to all prior comments from the reviewers, There are still some points that required clarification/ corrections as follow,

1. There are some unclear statement in abstract. Not sure what is the intention for this sentence "This confirmed the feasibility of the proposed study", please clarify.

2. For statistical analysis, in line 367 as linear mixed-effects models, but later it was described interaction made it confusing, should it be Two-way Mixed ANOVA? Please check.

3. The authors stated that they used CONSORT but the checklist file submitted was SPIRIT, which one was correct?

VERSION 2 - AUTHOR RESPONSE

1. There are some unclear statements in abstract. Not sure what is the intention for this sentence "This confirmed the feasibility of the proposed study", please clarify.

Reply：Thank you very much for pointing out our mistakes. Yes, as you point out, the meaningful reference of the sentence is not clear. We have removed it from the revised manuscript.（line 21）

2. For statistical analysis, in line 367 as linear mixed-effects models, but later it was described interaction made it confusing, should it be Two-way Mixed ANOVA? Please check.

Reply：Thank you for your valuable suggestion, we have checked and corrected it to Two-way Mixed ANOVA.（line 368）

3. The authors stated that they used CONSORT but the checklist file submitted was SPIRIT, which one was correct?

Reply：We rechecked and found that it was more appropriate to apply SPIRIT to articles of type PROTOCOL, so we fixed the original error and made it consistent with the uploaded checklist file. The references to the index have also been corrected.（line136-137）

VERSION 3 - AUTHOR RESPONSE

- Please ensure abbreviations are defined at first mention in each of the following sections in your paper: title, abstract, main text, and in each figure/table legend.

Reply- Thank you for your tips. We reviewed the paper and the definitions of abbreviations in the titles, abstracts, text, and legends of each figure/table involved, and made corrections for errors. (line 100,358).

- Along with your revised manuscript, please include an updated copy of the SPIRIT checklist indicating the page/line numbers of your manuscript where the relevant information can be found (http://www.spirit-statement.org/). All items from the checklist should be included in your manuscript. Please do not leave blanks and indicate any items that do not apply to your study design as 'Not Applicable'.

Reply- We have re-uploaded the latest SPIRIT checklist and have indicated in the manuscript the page/line numbers where the relevant information can be found. It has been confirmed that all items in the checklist should be included in the manuscript.

- Along with your revised manuscript, please provide an example of the participant consent form as a ‘Supplemental Material’ file, as per item #32 of the SPIRIT checklist. This file should be cited in the main text where the informed consent procedures are described.

Reply- The example participant consent form has been submitted as a “Supplemental Materials” document with the revised draft in this revision.

Formatting Amendments (where applicable):

Reply- For some formatting errors, we have completed the fixes.