PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	Internal brace augmentation reconstruction versus standard anterior cruciate ligament reconstruction： A randomized controlled clinical trial study protocol
AUTHORS	Lu, Wenhao; Liu, Di; Cai, Zijun; Pan, Linyuan; Xie, Wenqing; Jin, Hongfu; Liu, Xu; Li, Yusheng; Xiao, Wenfeng

VERSION 1 – REVIEW

REVIEWER	Lizis, Pawel Coll Holy Cross
REVIEW RETURNED	09-Aug-2022

GENERAL COMMENTS	None.

REVIEWER	Cameron, Claire University of Otago, Dunedin School of Medicine
REVIEW RETURNED	17-Aug-2022

GENERAL COMMENTS	Thank you for the opportunity to review this protocol. It describes a two arm randomised control trial (RCT) to compare standard treatment for ACL rupture compared to internal brace technology. All conditions for participants (pre and post operative care and followup) are the same apart from the surgical treatment of their injury. I found it to be very well thought out and described. I have a few relatively minor queries and comments: 1. I notice that you do not refer to the CONSORT statement at any point. I would recommend using these guidelines as they lay out very clearly what is required in reporting an RCT (Moher, D., Hopewell, S., Schulz, K. F., Montori, V., Gøtzsche, P. C., Devereaux, P. J., ... & Altman, D. G. (2012). CONSORT 2010 explanation and elaboration: updated guidelines for reporting parallel group randomised trials. International journal of surgery, 10(1), 28-55.). 2. In your abstract, you have a list titled “Strengths and limitations of this study”. It is not clear why these are listed as strengths or limitations apart from, perhaps, the last point about generalisability. Could you please clarify the meaning of this list? 3. In the Study Setting (and elsewhere) you describe the recruitment as going from March 2022 until March 2023. Is that a 12-month period or 13 months? 4. In the Eligibility Criteria section (line 160), you say ‘satisfaction of 24 months follow-up’. What do you mean by that? 5. Line 163, you say, ‘inclusion criteria’ and I think you mean ‘exclusion’ because the inclusion criteria are described in the paragraph before (and these ones look like exclusion reasons).

	6. In Participant Setting you say people are assigned 'according to the time of admission according to the random number'. It is not clear what you mean by that. Do you mean people are randomly allocated to groups as they are admitted (and agree to take part)? 7. Line 189, you say 'playing with a tender leg', do you mean 'playing sport with a tender leg'? 8. Line 190, you have in parentheses 'not included in the total score'. I am not sure what you mean is not included – do you mean point 3? 9. Sample size: Great sample size statement – I appreciate being able to replicate your estimates. Three queries about it: • My replication of the calculation assumes that the quantities you are comparing from the IKDC are means. Is that the case? The protocol does not describe them as means. • You have used Greek notation for the difference (delta) and the type I and Type II errors (alpha and beta) without defining them. A statistician will know what you mean, but not necessarily anyone else. Either define them or find another way of describing those elements. • Allowing for a 20% lost visit rate gives a sample size of 32.4 and, strictly speaking you should round that sample size up to 33 (because you are allowing for slightly less than 20% by rounding down). However, possibly a minor point, all things considered. 10. The physicians collecting the data were blind to the groups participants were allocated to. Could you be more specific about the blinding in the trial (checkpoints 11(a) and 11(b) of the CONSORT statement)? 11. Under Secondary Outcomes/Endpoints, line 279, you have mentioned VAS. I think you have used a VAS to measure pain – but you should say that here. VAS scores can be used for many things (not just pain). 12. I like your summary of abbreviations at the end – very helpful! 13. Under Patient Withdrawal from the Trial, if they withdraw from the trail will they still get the follow-up care as usual and their data not recorded? 14. Line 346, what is the 'electronic questionnaire system of questionnaire star'? Minor points: 1. In the middle of your introduction (lines 103-105), you have a statement about a 41-year-old miner performing the world's first ACL surgery. It seems to be a statement out on its own – I don't understand its relevance to the rest of the paragraph. Maybe it belongs at the beginning of the description. 2. You have not defined the acronym ACLR at its first use (line 216) and you need to. 3. The tables need some realigning or something to make them easier to read. For example, a line between each phase. The label of Phase 2 is aligned to the top of that section and the rest are centred. Lines would help. 4. Line 285 and 406, you use 'Lysholm knee score' when you have defined it earlier as LKS. You should just use LKS.

REVIEWER	Mahapatra, Piyush West Hertfordshire Teaching Hospitals NHS Trust, Trauma and Orthopaedics
REVIEW RETURNED	13-Nov-2022

GENERAL COMMENTS	Error in wording when describing exclusion criteria. Overall this is a well written protocol and study design although I have concerns that study may not be adequately powered and would benefit from further statistical review.

VERSION 1 – AUTHOR RESPONSE

Responses to Reviewer's comments:

Reviewer: 1
Dr. Pawel Lizis, Coll Holy Cross
Comments to the Author:
None.

Response: Thank you for your review of the article

Reviewer: 2
Dr. Claire Cameron, University of Otago
Comments to the Author:
Thank you for the opportunity to review this protocol. It describes a two arms randomised control trial (RCT) to compare standard treatment for ACL rupture compared to internal brace technology. All conditions for participants (pre and post operative care and followup) are the same apart from the surgical treatment of their injury. I found it to be very well thought out and described. I have a few relatively minor queries and comments:

Response: Many thanks to Dr. Claire Cameron for your detailed review of our protocol, pointing out the problems and providing considerable substantive advice. Your comments will be responded to below.

1. I notice that you do not refer to the CONSORT statement at any point. I would recommend using these guidelines as they lay out very clearly what is required in reporting an RCT (Moher, D., Hopewell, S., Schulz, K. F., Montori, V., Gøtzsche, P. C., Devereaux, P. J., ... & Altman, D. G. (2012). CONSORT 2010 explanation and elaboration: updated guidelines for reporting parallel group randomised trials. International journal of surgery, 10(1), 28-55.).

Response: This research protocol was designed to follow the CONSORT statement, and due to an oversight in the writing, there was no mention of the CONSORT statement, which we have added in the revised version, as detailed in line 105 of the revised version.

2. In your abstract, you have a list titled “Strengths and limitations of this study”. It is not clear why these are listed as strengths or limitations apart from, perhaps, the last point about generalisability. Could you please clarify the meaning of this list?

Response: We have added this section at the request of the journal, and there were some problems with the description of the study in the initial manuscript. This study will fill an existing gap regarding the efficacy of the internal brace in ACL reconstruction by This study will fill an existing gap regarding the efficacy of the internal brace in ACL reconstruction by providing robust and high-quality evidence on its role and impact. After two years of follow-up to demonstrate the benefits of Internal Brace in clinical application, we have revised this section in the reworked version, in the

latest version, lines 49-54.

3. In the Study Setting (and elsewhere) you describe the recruitment as going from March 2022 until March 2023. Is that a 12-month period or 13 months?
Response: We plan to recruit subjects for 12 months from early March 2022 to the end of February 2023 and to follow all patients included in the study for 2 years until early March 2025, I apologise for any disagreement caused by the lack of specificity in the description. A change has been made to the exact timing, which can be found in line 107 of the returned version.

4. In the Eligibility Criteria section (line 160), you say ‘satisfaction of 24 months follow-up’. What do you mean by that?
Response: Thank you for pointing out the problem, we meant that the subjects to be included in the study should meet the 24-month follow-up, perhaps we used the terminology inaccurately, we have now changed it, see the revised version of line 116.

5. Line 163, you say, ‘inclusion criteria’ and I think you mean ‘exclusion’ because the inclusion criteria are described in the paragraph before (and these ones look like exclusion reasons).
Response: Yes, you are correct, and thank you for pointing out that this is indeed an "exclusion criterion", which has now been amended and can be found in line 119.

6. In Participant Setting you say people are assigned ‘according to the time of admission according to the random number’. It is not clear what you mean by that. Do you mean people are randomly allocated to groups as they are admitted (and agree to take part)?
Response: Yes, patients will be randomly allocated to the trial and control groups on admission (and consent to participate), the description of which has been amended and can be found in lines 128-131 of the amended version

7. Line 189, you say ‘playing with a tender leg’, do you mean ‘playing sport with a tender leg’?
Response: Our intention was to describe the clinical condition of "softening leg", which has been modified and can be seen in line 141.

8. Line 190, you have in parentheses ‘not included in the total score’. I am not sure what you mean is not included – do you mean point 3?
Response: This is to say that the pre-injury knee function score is not included in the total score; the description in the first version of the manuscript was objectionable and has now been revised, as seen in lines 141-144.

9. Sample size:
Great sample size statement – I appreciate being able to replicate your estimates. Three queries about it:
• My replication of the calculation assumes that the quantities you are comparing from the IKDC are means. Is that the case? The protocol does not describe them as means.
• You have used Greek notation for the difference (delta) and the type I and Type II errors (alpha and beta) without defining them. A statistician will know what you mean, but not necessarily anyone else. Either define them or find another way of describing those elements.
• Allowing for a 20% lost visit rate gives a sample size of 32.4 and, strictly speaking you should round that sample size up to 33 (because you are allowing for slightly less than 20% by rounding down). However, possibly a minor point, all things considered.
Response: My replication of the calculation assumes that the quantities you are comparing from the IKDC are means. Is that the case? The protocol does not describe them as means.
Thank you for recognising the "sample size statement" and for your three comments on it.
Firstly, the comparison of IKDC is indeed the mean value, which has been added in the revised

version, as shown in lines 144-145; secondly, α and β are statistically defined, as shown in lines 149-150; and lastly, the sample size should indeed be set to 33, which has also been revised, as shown in line 151.

10. The physicians collecting the data were blind to the groups participants were allocated to. Could you be more specific about the blinding in the trial (checkpoints 11(a) and 11(b) of the CONSORT statement)?
Response: With regard to blinding, the rehabilitator and the follow-up data collector in this study plan were unaware of the patient grouping, the patient and the surgeon were aware of the subgroup grouping, and the relevant descriptions have been modified in accordance with checkpoints 11(a) and 11(b) of the CONSORT statement. Details can be found on lines 159-164.

11. Under Secondary Outcomes/Endpoints, line 279, you have mentioned VAS. I think you have used a VAS to measure pain – but you should say that here. VAS scores can be used for many things (not just pain).
Response: Thank you for pointing out that the VAS score, which is used to assess a patient's pain, is now labelled and can be seen on line 226

12. I like your summary of abbreviations at the end – very helpful!
Response: Thank you!

13. Under Patient Withdrawal from the Trial, if they withdraw from the trail will they still get the follow-up care as usual and their data not recorded?
Response: In the "Patient Withdrawal from Trial" column, follow-up care will no longer be provided for subjects who voluntarily withdrew from treatment and for whom no follow-up data were collected, but subjects who withdrew from the trial due to an adverse event or surgical failure must be followed until the adverse event stabilises or resolves or until, in the opinion of the investigator, further follow-up is no longer required. Details can be found on lines 278-283.

14. Line 346, what is the ‘electronic questionnaire system of questionnaire star’?
Minor points:
1. In the middle of your introduction (lines 103-105), you have a statement about a 41-year-old miner performing the world’s first ACL surgery. It seems to be a statement out on its own – I don’t understand its relevance to the rest of the paragraph. Maybe it belongs at the beginning of the description.
Response: Thank you for pointing out these problems with language and style, we had placed this description at the beginning, visible in line 60.

2. You have not defined the acronym ACLR at its first use (line 216) and you need to.
Response: Thank you for pointing out the problem, and the manuscript has been revised with regard to the abbreviation "ACLR".

3. The tables need some realigning or something to make them easier to read. For example, a line between each phase. The label of Phase 2 is aligned to the top of that section and the rest are centred. Lines would help.
Response: Thank you for your suggestions. The table in the manuscript has been modified.
4. Line 285 and 406, you use ‘Lysholm knee score’ when you have defined it earlier as LKS. You should just use LKS.
Response: Thanks to your suggestion, we had replaced "Lysholm knee score" with "LKS".

Reviewer: 3

Dr. Piyush Mahapatra, West Hertfordshire Teaching Hospitals NHS Trust
Comments to the Author:
Error in wording when describing exclusion criteria. Overall this is a well-written protocol and study design although I have concerns that study may not be adequately powered and would benefit from further statistical review.

Response: Many thanks to Dr. Piyush Mahapatra for his comment, the error regarding the description of the exclusion criteria has been corrected in the returned manuscript. Regarding the present study, as of now, our project is on schedule.

VERSION 2 – REVIEW

REVIEWER	Cameron, Claire University of Otago, Dunedin School of Medicine
REVIEW RETURNED	26-Sep-2023

GENERAL COMMENTS	Thank you for your clear and detailed responses to my queries. I notice, in your responses, you didn't answer my question 14, but when I look at the manuscript, you have taken out the terms I was questioning. I think that was an oversight and that point has been addressed. So, I am entirely happy with these revisions.

VERSION 2 – AUTHOR RESPONSE

Reviewer: 2
Dr. Claire Cameron, University of Otago

Comments to the Author:
Thank you for your clear and detailed responses to my queries. I notice, in your responses, you didn't answer my question 14, but when I look at the manuscript, you have taken out the terms I was questioning. I think that was an oversight and that point has been addressed. So, I am entirely happy with these revisions.

Response: Thank you very much for recognizing the changes we made to the manuscript! We apologize for our mistake in not answering question 14 about your previous question and take this opportunity to give you a response. The "electronic questionnaire system of questionnaire star" is a niche and not popular electronic questionnaire tool. To make it easier to understand, we have taken out the terms in the revised version.