PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	Arthroscopic-assisted balloon tibioplasty versus open reduction internal fixation (ORIF) for treatment of Schatzker II–IV tibial plateau fractures: Study protocol of a randomized controlled trial
AUTHORS	Wang, Ji-Qi; Jiang, Bing-Jie; Guo, Wei-Jun; Zhang, Wei-Jiang; Li, A-Bing; Zhao, You-Ming

VERSION 1 – REVIEW

REVIEWER	David Metcalfe University of Oxford, U.K.
REVIEW RETURNED	28-Feb-2018

GENERAL COMMENTS	This is a protocol for a single centre RCT to compare balloon tibioplasty and open reduction internal fixation for the treatment of closed Schatzker II-IV tibial plateau fractures. It is reasonably straightforward but a few points should be clarified by the authors before the protocol is published. In particular, they should be clear about whether they are planning a pilot trial (e.g. to determine feasibility and inform a sample size calculation) or a full trial that is intended to answer the study question. The protocol also has some typos and grammatical errors that will require careful copyediting. -What is a “fresh” fracture in the inclusion criteria? Will there be a cut-off for patients that present or are treated late? -Can you use electronic randomisation rather than sealed envelopes, which are known to be open to manipulation? Cochrane considers “sealed envelopes” to be a randomisation technique that is at high risk of bias. -You are very specific about the techniques that each surgeon should employ. Will you report any deviation from these instructions to be a breach of protocol? Perhaps the technique could be described in outline but the protocol actually allow surgeons to perform the selected procedure in whatever way they think is best for that individual patient/fracture? -Will those involved in follow-up measurements be blinded to treatment allocation? -There is not currently a sample size calculation. If this is a pilot trial (as described in this paragraph of the protocol) then this should be stated earlier and ideally within the title. However there is also a line in the “Sample size” paragraph that reads: “the sample size is considered adequate to verify the research hypothesis”. If it is a pilot trial, then it would not usually be powered to answer the research question. If it is intended to answer the research question (and so is not a pilot trial), the protocol requires a proper power calculation. -Are you planning any particular sub-group or sensitivity analyses? -How will you treat patients that cross-over from one group to the other, e.g. satisfactory reduction cannot be achieved using balloon

	tibioplasty? The standard is an intention to treat analysis but this should be pre-specified. -How is the trial funded? Do any of the investigators have a proprietary interest in the product/technique? -How will complications be recorded? Which complications will you look for and how will they be defined/assessed? These seem likely to make the difference between the two interventions, e.g. wound infections/breakdown in the ORIF group. -If you are following up the patients, why not incorporate a health-related quality of life measure, e.g. the EQ5D or SF36 so that cost effectiveness can be considered later on? -An important limitation of the trial is going to be that early osteoarthritis is said to be the sequel of inadequate tibial plateau fracture treatment. This may well not manifest for patients within the 24-month follow-up. This isn't a problem if it is a pilot trial. Otherwise, can you make plans for long-term (e.g. 10-year follow-up) even if the main results will be published at 24 months? -Some of the protocol is written in the past tense as if the trial has already happened. Please confirm that the protocol is being published before the first patient has been randomised. If this is not the case, it does not make any sense to publish the protocol and full manuscript as separate items.

REVIEWER	Greg Robertson Edinburgh Orthopaedic Trauma Unit, Edinburgh, UK
REVIEW RETURNED	04-Mar-2018

GENERAL COMMENTS	Overall, this is reasonably well-presented study protocol for a randomised control trial that can provide useful information for clinicians involved in the management of tibial plateau fractures. However, there are a number of points that require addressing, prior for it being suitable for publication: Title: 1) The technique being assessed is 'arthroscopic-assisted balloon tibioplasty' - this should be adjusted in the title and the abstract. Abstract: 1) The authors state that 'the clinical outcomes of balloon tibioplasty and ORIF are insufficient' - the evidence for ORIF is relatively robust - I would rephrase this. Introduction: 1) P2 L43 - The reference provided for the 'acknowledged operative indication' is for lateral tibial plateau fractures only. Please provide one for medial tibial plateau fractures, given that this is included in the study cohort. 2) Please provide a better description of Schzatzker II to IV tibial plateau fractures - a diagram may be helpful. 3) In general, the language quality is poor - phrases such as 'internal joint injury' are unusual - please revise the language quality throughout the whole paper. 4) P3 L4 - Please better explain the meaning of 'biomechanical fixation'. 5) There are a number of studies in the literature which describe similar techniques to 'balloon tibioplasty', albeit not as randomised controlled trials. These should be discussed in the introduction. Similarly, the recent systematic review evidence on ORIF should be better discussed to provide a more comprehensive literature for the introduction.

	6) P3 Line 9 - 'as' should be 'is'. 7) P3 L20 - Again the phrase' the application time of this surgical technique is short' is confusing- please rephrase. 8) P3 L34 - 'As we all know' - please avoid the use of colloquial language in the article. Methods: 1) P3 L51 - The sentence beginning 'The diagnosis of tibial plateau fracture...' should be re-phrased to improve comprehension. 2) P3 L55 - 'fresh' should 'acute' 3) P4 L24 - 'after the success continuous epidural anaesthesia' - poor English quality - please revise. 4) P4 L45 - 'reducted' should be 'reduced' 5) P4 L23 - I feel the description of the Balloon Tibioplasty technique would benefit from a series of figures to better explain this to the reader. Please also better describe the variations in technique between lateral and medial plateau fractures, and better describe the equipment that is planned to be used e.g. what contrast solution will be used for the balloon, what size of k-wires and locking plate are planned to be used. 6) P4 L47 - 'careffy' should be 'carefully' 7) P4 L47 - please explain how the fracture reduction will be held following balloon removal, prior to cement insertion. 8) P4 L53 - The description of ORIF should be more comprehensive. 9) P5 L6 - Does the post-operative rehab plan apply to ORIF alone, or to both techniques? 10) P5 L41 - power calculations should be added to this section. 11) P5 L51 - data relating to complications would likely be categorical instead of continuous - in which case Chi Squared testing should be used - please explain. 12) P5 L47 - please add normality testing for datasets to determine if the data is parametric or non-parametric - this will influence the choice of statistic. 13) P5 L47 - please add the chosen level of significance for the statistical tests. Discussion: 1) P6 L10 - 'posterior compressions' - again poor quality of English - please rephrase. 2) P6 L18 - 'identify' should be 'compare' 3) P6 L20 - surely the clinical outcome influences the residual disability, as opposed to the other way round - consider advising that the technique will improve fracture reduction and joint surface restoration, thus improving clinical outcome. 4) Again further discussion of the studies using a similar technique to 'balloon tibioplasty', as well as better reference to the existing literature of ORIF would improve the quality of the discussion.

REVIEWER	Tanguy Vendeuvre CHU de Poitiers (university hospital), FRANCE
REVIEW RETURNED	13-Mar-2018

GENERAL COMMENTS	Thank you very much for asking me to review this protocol. This protocol is interesting but has a future interpretation bias. The balloon appears interesting for reducing fracture depression, but schatzker 4 fractures do not have depression. Depression is present in types 2 and 3, so it seems interesting to study these two types of depression in a 40:40 study. The inclusion of types 4 risks modifying the results especially if their number is not the same in both groups.

	With regard to the main criteria, types 4 are known to have less good functional prognosis and therefore risk modifying the results. If we consider the balloon as an ARIF and that the control group is an ORIF then the literature seems already clear on the difference in functional recovery in favour of the ARIF group and thus the study loses relevance. In the same way, the protocol specifies the interest of the scanner to evaluate the reduction and the durability of the reduction over time. The literature agrees with the interest of reduction in functional prognosis. It is therefore unfortunate to perform 6 ct scan and that the first one is at 1 month when the patient will resume support. The date of the handover seems about the same time "The patients were allowed to bear no weight within 4 weeks". Indeed, it would be essential to have an earlier ct scan or to be sure that it is done before reloading, if not we do not study the quality of the reduction by the balloon but already the mechanical properties of the assembly. In total the protocol is interesting but the inclusion of schatzker fractures 4 risks to make the interpretation of future results difficult (interpretation of the Rasmussen score and ct scan). It is very interesting to have a follow-up with ct scan for 24 months but this will allow a discussion on the nature of calcium phosphate vs bone graft filling and their mechanical properties over time. To discuss the interest of reduction by the balloon it seems essential to have a CT scan before resuming walking with patient support

VERSION 1 – AUTHOR RESPONSE

Reviewer #1:
1. Response to comment: What is a “fresh” fracture in the inclusion criteria? Will there be a cut-off for patients that present or are treated late?
Response: We are very sorry for our incorrect writing of the inclusion criteria, “fresh” fracture should be modified to “Acute closed fractures less than 10 days old” (P3 line 14). We have a cut-off (fractures less than 10 days old) for patients that present or are treated late, we will exclude patients from our study who fractures more than 10 days because include this part of patients might cause bias and modify the results.
2. Response to comment: Can you use electronic randomisation rather than sealed envelopes, which are known to be open to manipulation?
Response: As Reviewer suggested that we use electronic randomisation to reduce the risk of bias (P3 line 35-36).
3. Response to comment: The problem of the description of surgical techniques.
Response: As Reviewer suggested that the technique could be described in outline and the protocol actually allow surgeons to perform the selected procedure which is best for that individual patient/fracture, we have made a corresponding revision (P3 line 40-44, P4 line 1-18). Futhermore, we will report any deviation from these instructions to be a breach of protocol.
4. Response to comment: Will those involved in follow-up measurements be blinded to treatment allocation?
Response: Researchers performing the follow-up measurements will be blinded to the group

allocations until the last questionnaires have been completed (P3 line 37-39).
5. Response to comment: Problems of the sample size calculation.
Response: We are very sorry for our negligence of this problem and we have made a sample size and power calculation in the manuscript (P5 line 23-30).
6. Response to comment: Are you planning any particular sub-group or sensitivity analyses?
Response: Yes, we are. We will carry out a sub-group analyse, which include some variables, such as age, sex, and injury mechanism etc. And this part of result also will be published.
7. Response to comment: How will you treat patients that cross-over from one group to the other, e.g. satisfactory reduction cannot be achieved using balloon tibioplasty?
Response: It is really true as Reviewer suggested that the standard is an intention to treat analysis but this should be pre-specified, and if satisfactory reduction cannot be achieved using arthroscopic-assisted balloon tibioplasty, patients will undergo ORIF and be excluded from the study (P4 line 19-20).
8. Response to comment: How is the trial funded? Do any of the investigators have a proprietary interest in the product/technique?
Response: This trail is funded by Clinical scientific research project of the Second Affiliated Hospital of the Wenzhou Medical University (SAHoWMU-CR2017-08-105). It's a Clinical scientific research project of our hospital, and the funders had no role in the design, execution or writing of the study (P7 line 1-2).
9. Response to comment: How will complications be recorded? Which complications will you look for and how will they be defined/assessed?
Response: We are very sorry for our negligence of this problem and we will record the complications by an electronic data capture system (P5 line 17-19), and complications including wound infection, reoperations, and posttraumatic arthritis (PTA) will be recorded (P4 line2-4).
10. Response to comment: If you are following up the patients, why not incorporate a health-related quality of life measure?
Response: It is really true as Reviewer suggested that a health-related quality of life measure should be carry out, and the health-related quality of life will be measured using the Short-Form Health Survey (SF-36) questionnaire during follow-up (P5 line 7-10).
11. Response to comment: Early osteoarthritis may well not manifest for patients within the 24-month follow-up.
Response: It is really true as Reviewer suggested that early osteoarthritis may well not manifest for patients within the 24-month follow-up, we will perform follow-up for at least 10 years in all patients (P5 line 5-6).
12. Response to comment: Please confirm that the protocol is being published before the first patient has been randomised.
Response: We are very sorry for our incorrect writing in the past tense, we cnofirm that this protocol is being published before the first patient has been randomised. This manuscript have been checked by two professional editors, both native speakers of English and made a revision (http://www.textcheck.com/certificate/r54ciS).
Special thanks to you for your good comments.

Reviewer #2:
1. Response to comment: The technique being assessed is 'arthroscopic-assisted balloon tibioplasty' - this should be adjusted in the title and the abstract.
Response: We have adjusted this problem in the title and the abstract (P1).
2. Response to comment: The authors state that 'the clinical outcomes of balloon tibioplasty and ORIF are insufficient' - the evidence for ORIF is relatively robust - I would rephrase this.
Response: We are very sorry for our incorrect writing the evidence for ORIF is relatively robust, in fact, arthroscopic-assisted balloon tibioplasty does not produce sufficiently beneficial clinical outcomes and we have modified it (P1 line 19-20).
3. Response to comment: The reference provided for the 'acknowledged operative indication' is for

lateral tibial plateau fractures only. Please provide one for medial tibial plateau fractures, given that this is included in the study cohort.
Response: We are very sorry for our negligence of this problem and we have made more detailed explanation for medial tibial plateau fractures (P2 line 6).
4. Response to comment: Please provide a better description of Schzatzker II to IV tibial plateau fractures - a diagram may be helpful.
Response: It is really true as Reviewer suggested that diagram may be helpful, and we provide a description of Schzatzker II to IV tibial plateau fractures in supplementary information, S1.
5. Response to comment: Please revise the language quality throughout the whole paper.
Response: It is really true as Reviewer suggested that there are numerous grammatical errors throughout the manuscript. The manuscript checked by two professional editors, both native speakers of English and made a revision (http://www.textcheck.com/certificate/r54ciS).
6. Response to comment: Please better explain the meaning of 'biomechanical fixation'.
Response: We are very sorry for our incorrect writing the biomechanical fixation, and we have made more detailed explanation in the introducation (P2 line 23-24).
7. Response to comment: Previous studies describe similar techniques to 'balloon tibioplasty', and the recent systematic review evidence on ORIF should be better discussed to provide a more comprehensive literature for the introduction.
Response: As Reviewer suggested that we made a detailed discussed in the introduction (P2 line 14-40).
8. Response to comment: 'as' should be 'is'.
Response: As Reviewer suggested that we have modified it (P2 line 26).
9. Response to comment: Again the phrase' the application time of this surgical technique is short' is confusing- please rephrase.
Response: As Reviewer suggested that we have modified it (P2 line 38).
10. Response to comment: 'As we all know' - please avoid the use of colloquial language in the article.
Response: We are very sorry for our negligence of this problem, and we have modified it (P2 line 41).
11. Response to comment: The sentence beginning 'The diagnosis of tibial plateau fracture...' should be re-phrased to improve comprehension.
Response: As Reviewer suggested that we have modified it (P3 line 10-12).
12. Response to comment: 'fresh' should 'acute'.
Response: As Reviewer suggested that we have modified it (P3 line 14).
13. Response to comment: 'after the success continuous epidural anaesthesia' - poor English quality - please revise.
Response: We think the technique could be described in outline, and we have removed some unimportant details in the interventions.
14. Response to comment: 'reducted' should be 'reduced'
Response: As Reviewer suggested that we have modified it (P4 line 9).
15. Response to comment: Description of the Balloon Tibioplasty technique would benefit from a series of figures to better explain this to the reader. Please also better describe the variations in technique between lateral and medial plateau fractures, and better describe the equipment that is planned to be used.
Response: It is really true as Reviewer suggested that a series of figures to better explain the Balloon Tibioplasty technique to the reader. We simulated the operation process with Mimics software in supplementary information (S2) to help reader understand. As Reviewer suggested that we have made a detail describtion of the variations in technique and the equipment that is planned to be used between lateral and medial plateau fractures (P3 line 42-44, P4 line 1-13).
16. Response to comment: 'careffy' should be 'carefully'
Response: As Reviewer suggested that we have modified it (P4 line 10).
17. Response to comment: please explain how the fracture reduction will be held following balloon removal, prior to cement insertion.

Response: We are very sorry for our negligence of this problem and we have made more detailed explanation in the Interventions (P4 line 9-13).
18. Response to comment: The description of ORIF should be more comprehensive.
Response: As Reviewer suggested that we have made more detailed description of ORIF (P4 line 14-18).
19. Response to comment: Does the post-operative rehab plan apply to ORIF alone, or to both techniques?
Response: We are very sorry for our negligence of this problem, and all patients will receive rehabilitation therapy regardless of the group to which they are allocated (P4 line 20-21).
20. Response to comment: Power calculations should be added to this section.
Response: We are very sorry for our negligence of this problem and we have made a sample size and power calculation in the manuscript (P5 line 23-30).
21. Response to comment: Data relating to complications would likely be categorical instead of continuous - in which case Chi Squared testing should be used - please explain.
Response: We are very sorry for our incorrect writing the statistical analysis, in fact, complications were categorical, and the chi-square test will be used to analyze it (P5 line 36).
22. Response to comment: Please add normality testing for datasets to determine if the data is parametric or non-parametric - this will influence the choice of statistic.
Response: We are very sorry for our negligence of this problem and we have made more detailed explanation in the statistical analysis. For continuous variables, the Shapiro–Wilk test will be applied to determine if they follow a normal distribution. For normally distributed variables, the means will be calculated and compared using the independent samples t test (Student's t test); otherwise, the Mann–Whitney U test will be used for group comparisons. (P5 line 32-36).
23. Response to comment: Please add the chosen level of significance for the statistical tests.
Response: We are very sorry for our negligence of this problem and $P < 0.05$ will be taken to indicate statistical significance in all analyses (P5 line 37).
24. Response to comment: 'posterior compressions' - again poor quality of English - please rephrase.
Response: As Reviewer suggested that we have modified it (P6 line 17-18).
25. Response to comment: 'identify' should be 'compare'
Response: As Reviewer suggested that we have modified it (P6 line 29).
26. Response to comment: Surely the clinical outcome influences the residual disability, as opposed to the other way round - consider advising that the technique will improve fracture reduction and joint surface restoration, thus improving clinical outcome.
Response: As Reviewer suggested that we have modified it (P6 line 30-32).
27. Response to comment: Again further discussion of the studies using a similar technique to 'balloon tibioplasty', as well as better reference to the existing literature of ORIF would improve the quality of the discussion.
Response : As Reviewer suggested that we made a detailed discussed in the discussion (P6 line 4-22).
Special thanks to you for your good comments.

Reviewer #3:
1. Response to comment: The problem of schatzker 4 fractures do not have depression, and he inclusion of types 4 risks modifying the results especially if their number is not the same in both groups.
Response：It is really true as Reviewer suggested that types 4 are known to have less good functional prognosis and therefore risk modifying the results, and we are very sorry for our incorrect writing the inclusion criteria before. In fact, we will include patients with Schatzker type II, III or IV with depression of the medial tibial plateau only (P3 line 14-15). According to the imaging data of our previous patients, we found that there were some types 4 fracture patient with the depression of the medial platform only, and without splitting or comminuting. The clinical data of our institution showed that the functional recovery of types 4 patients with depression of the medial tibial plateau only via

ORIF were usually satisfactory, so we want to include this part of patient. And as for types 4 with split or comminute fracture, we will exclude it from our study.
2. Response to comment: Whether consider the balloon as an ARIF and that the control group is an ORIF.
Response: We consider balloon tibioplasty as a minimally invasive technique to recover the depression of the articular surface, arthroscopy is an auxiliary technique in the process of operation, and balloon tibioplasty is different from ARIF.
3. Response to comment: It would be essential to have an earlier ct scan or to be sure that it is done before reloading.
Response: It is really true as Reviewer suggested that early ct scan is essential, and we have modified it (P4 line 22-23), postoperative CT scans will be performed immediately, and at 2 weeks and 1, 3, 6, 12, and 24 months.
If satisfactory reduction cannot be achieved using arthroscopic-assisted balloon tibioplasty, patients will undergo ORIF and be excluded from the study. In addition, if types 4 fracture patient with the depression of the medial platform only get good functional recovery via arthroscopic-assisted balloon tibioplasty, our results will be important for informing the scheduling and development of treatment options for Schatzker II–IV tibial plateau fracture surgery.
Please allow us to perform this RCT, and special thanks to you for your good comments.

VERSION 2 – REVIEW

REVIEWER	David Metcalfe University of Oxford, UK
REVIEW RETURNED	18-Apr-2018

GENERAL COMMENTS	Thank you for making these changes. I have now recommended publication.

REVIEWER	Greg Robertson Edinburgh Orthopaedic Trauma Unit, Edinburgh, UK
REVIEW RETURNED	22-Apr-2018

GENERAL COMMENTS	The raised points have been addressed satisfactorily. The only comment from the current version is that the sentence in the abstract: 'However, arthroscopic-assisted balloon tibioplasty does not produce sufficiently beneficial clinical outcomes.' does not reflect the evidence provided in the Introduction from the literature review: 'Primary data from Ollivier et al. [19] showed that depressed tibial plateau fractures treated with arthroscopic-assisted balloon tibioplasty had a high rate of anatomic reduction and good clinical outcomes. Similar results were also reported by Pizanis et al. [15] using arthroscopic-assisted balloon tibioplasty without classic fenestration of the tibia, which would minimize surgical trauma.' I think this is more a mis-judged choice of wording for the abstract. I would suggest re-wording that sentence.

REVIEWER	Tanguy Vendeuvre Service de chirurgie orthopédique, CHU Poitiers, France

REVIEW RETURNED	09-May-2018

GENERAL COMMENTS	Although all the clarifications requested have been provided, the protocol seems to present methodological biases that will make a conclusion difficult. Firstly, the choice to include fractures of the medial tibial plateau, the consequences of which are known to be less well tolerated, notably because of painful osteosynthesis under the skin. Moreover it had to be especially specified for this study of the type 4 of which one speaks which does not represent all the types 4. The other risk of this study is just to conclude ARIF versus ORIF and not on the use of the balloon. The conclusion is already in ARIF's favour. In fact, it is often the associated lesions that can be managed by arthroscopy that modify the functional prognosis, as well as the slightest skin decay. For all these reasons and despite the many clarifications made, we believe that the theme of the protocol is an excellent idea but that the conclusions will not necessarily be relevant.

VERSION 2 – AUTHOR RESPONSE

Reviewer #1:
Recommended publication.
Special thanks to you for your good comments.

Reviewer #2:
1. Response to comment: I think this is more a mis-judged choice of wording for the abstract. I would suggest re-wording that sentence. “However, arthroscopic-assisted balloon tibioplasty does not produce sufficiently beneficial clinical outcomes.”
Response: We are very sorry for our mis-judged choice of wording for the abstract, and we have rewritten this sentence (P1 line 19-21).
Special thanks to you for your good comments.

Reviewer #3:
1. Response to comment: The choice to include fractures of the medial tibial plateau, the consequences of which are known to be less well tolerated, notably because of painful osteosynthesis under the skin. Moreover it had to be especially specified for this study of the type 4 of which one speaks which does not represent all the types 4.
Response：The clinical data of our institution showed that the functional recovery of types 4 patients with depression of the medial tibial plateau only via ORIF were usually satisfactory. However, studies evaluating clinical outcomes after arthroscopic-assisted balloon tibioplasty of this type are sparse, so we want to include this type in our study. Moreover, it is really true as Reviewer suggested that “this study of the type 4 of which one speaks which does not represent all the types 4”, and we have especially specified in Abstract and Inclusion criteria section for this study (P1 line 22-23, P3 line 17-18).
2. Response to comment: The other risk of this study is just to conclude ARIF versus ORIF and not on the use of the balloon. The conclusion is already in ARIF's favour. In fact, it is often the associated lesions that can be managed by arthroscopy that modify the functional prognosis, as well as the slightest skin decay.
Response: Arthroscopic-assisted balloon tibioplasty is an emerging technology, and has shown advantages in recovering depression of the articular surface. It is not exactly the same as ARIF. It is really true as Reviewer suggested that associated lesions can be managed by arthroscopy, which

might influence our results. This is the advantage of this surgical method, and we will carry out a subgroup analysis to evaluate clinical outcomes between arthroscopic-assisted balloon tibioplasty group and traditional open reduction internal fixation group for the treatment of associated lesions. Special thanks to you for your good comments.