

Thessaloniki, May 4th 2020

Dear Editor,

We would like to thank you for accepting to reconsider our manuscript titled: "Tibial Tubercle Osteotomy in Revision Total Knee Arthroplasty: A Systematic Review" for publication in the World Journal of Orthopedics.

We would also like to thank the reviewers for their insightful comments. All points raised are addressed and the manuscript was revised according to their suggestions. All text changes in the manuscript have been highlighted. For reviewing purposes, the comments have been numbered and addressed one by one, and the text changes have been highlighted in the revised manuscript.

In more detail:

**Reviewer #1:**

COMMENT	RESPONSE	TEXT CHANGES
<p>1. The authors have mentioned the cut off dates for the articles for inclusion but not a time period.</p>	<p>Thank you for your comment. The literature search was performed in Medline, Scopus, and the Cochrane Central Register of Controlled Trials from inception to February 2020, with no date filters. After the selection process, 15 clinical studies were included in the review. The range of the publication dates of these 15 studies was 1998 to 2019. The details about the publication dates are included in the manuscript.</p>	<p>We added to the MATERIAL AND METHODS/Literature search section:            "Medline, Scopus, and the Cochrane Central Register of Controlled Trials were searched for studies from inception to February 2020. No database filters, language, or date restrictions were applied."</p> <p>The range of publication dates is reported in the RESULTS/Characteristics of the included studies section:            "Dates of publication ranged between 1998 and 2019."</p> <p>The specific publication years of each study are reported in Table 1.</p>
<p>2. Coleman methodology score less than 55 should not be included in the review as the authors have mentioned only the mean score of the included studies. Also, one study which was low quality using Modified Delphi technique by Moga should be excluded.</p>	<p>This is a fair comment. The range of the Coleman methodology score of the five comparative studies was 54-92%. The study by Zonnenberg et al. had a moderate score of 54%, while all other comparative studies had high quality scores. We decided to include the study by Zonnenberg et al. in the review, because the score is borderline acceptable, and the authors clearly reported all complications of TTO, thus improving the power of our review with the addition of their sample size.</p> <p>Also, the study by Hocking et al. was judged to have low quality according to</p>	<p>Addition to the RESULTS/Quality assessment section:            "The effect of the particular low-quality study was evaluated as a potential confounding factor; a stratified analysis of outcomes was repeated after excluding the study, and no substantial differences were noted (p=0.83). Therefore, the study was included in the review. The comparative trials</p>

	<p>the Moga score. Following your recommendation, we performed a stratified analysis excluding this study and we investigated the risk of bias introduced to our results. We did not detect any significant differences as compared to our primary analysis (p=0.83). Therefore, we decided to include this study as well, because the authors reported information about all outcomes assessed in our review, and that way the sample size and power of the review was increased.</p> <p>All these data including the stratified analysis on the risk of bias have been added to the results and limitations sections for transparency.</p>	<p>were rated with a mean Coleman Methodology Score[3,16–19] of 73.6% (range 54-92%).”</p> <p>Addition to the 4<sup>th</sup> paragraph of the DISCUSSION section:  “Another limitation was that the study by Zonnenberg et al. had a borderline moderate quality Coleman methodology score of 54%[15], and the study by Hocking et al. was of low quality according to the Moga score[1]. After accounting for the risk of bias introduced in the review by the latter study with a stratified analysis, no significant changes of the results were noted compared to the primary analysis. Therefore, both studies were included to increase the sample size and improve the power of this review.”</p>
<p>3. The previous similar systematic review in 2018, mentions the complication rates of 3.8 to 20%. So what is different in this analysis that shows the complication rates below 6.5%?</p>	<p>This is a fair comment. The recent systematic review (<i>Divano et al. Tibial tubercle osteotomy (TTO) in total knee arthroplasty, is it worth it? A review of the literature. Archives of Orthopaedic and Trauma Surgery, 2018</i>) aimed to analyze the outcomes of TTO in both primary and revision cases of TKA. Therefore, the major difference between this review and our study is that we only accounted for revision TKA cases, excluding primary TKAs. Twenty-six studies were included in the previous review, and 11 of them reported outcomes for revision cases. All of these 11 revision studies were included in our systematic review, along with another 4 studies not included in the previous article (although 3 of them were already published). A factor explaining the difference in complication rates can be explained by the fact that the previous review does not clearly distinguish the results of primary and revision cases.</p>	<p>No changes in the manuscript.</p>
<p>4. The article mentions the pre-operative and postoperative ROM</p>	<p>This is a fair point and thank you for your comment. The ROM values reported are pooled means using weights according to each study’s sample size.</p>	<p>Modifications in the ABSTRACT/RESULTS section:  “Knee flexion was</p>

<p>and extension of the knee, but are these the mean values? Some studies in the table do not show pre-operative ROM or extension values, then is that justified to include them for the mean values?</p>	<p>Unfortunately, there was not a uniform reporting of ROM measurements by all authors. Therefore, we considered your comment and performed the analysis again after excluding the studies which did not report preoperative ROM values.</p>	<p>improved from 82.9 deg preoperatively to 100.1 deg postoperatively and total ROM was increased from 73.4 deg before surgery to 97 deg after surgery.”</p> <p>Modifications in the RESULTS/Synthesis of the results section:  “Total ROM improved from 73.4 deg preoperatively to 97 deg postoperatively and knee flexion increased from 82.9 deg before surgery to 100.1 deg after surgery.”</p> <p>Modifications in the 1<sup>st</sup> paragraph of the DISCUSSION section:  “Knee flexion and ROM were improved from 82.9 and 73.4 deg preoperatively to 100.1 and 97 deg postoperatively, respectively.”</p>
<p>5. Inclusion of Forest plot would definitely be helpful.</p>	<p>We agree with your comment. Although it was not feasible to conduct a meta-analysis with direct interventions between Groups, we included a forest plot of the incidence of non-union among studies to better illustrate the primary outcome. The markers of the forest plot are weighted according to the number of the cases of each study.</p>	<p>Figure 2 representing the forest plot has been added to the manuscript.</p>
<p>6. Page 8 mentions that Non-union is extremely rare. Kindly drop the word “extremely” as the non union rate is close to 2%.</p>	<p>Comment considered and we amended the text accordingly.</p>	<p>The word “extremely” in the 2<sup>nd</sup> paragraph of the DISCUSSION section has been omitted.</p>
<p>7. Did TTO help in eradication of infection in RTKA?</p>	<p>Thank you for your comment. All cases of reinfections were observed in septic RTKAs. We are aware that reinfections in such cases may be influenced by many other factors apart from the TTO procedure. Studies comparing TTO with other extensile approaches in cases of infected RTKAs could provide insights in that direction.</p> <p>When TTO was compared to rectus snip regarding re-infections after two-stage revisions in infected RTKA, Bruni et al. reported that the results showed no</p>	<p>Modification in the 2<sup>nd</sup> paragraph of the RESULTS/Synthesis of the results section:  “From all RTKAs that performed due to periprosthetic joint infection via TTO, 29 knees (9.8%) showed recurrence of infection.”</p> <p>Addition to the DISCUSSION section:  “Recurrence of</p>

	<p>difference (7% in the snip group and 5% in the TTO group, p=0.84).  <i>(Bruni et al. Tibial tubercle osteotomy or quadriceps snip in two-stage revision for prosthetic knee infection? A randomized prospective study. Clin Orthop Relat Res 2013;471:1305-1318.)</i></p> <p>Sun et al. also reported the incidence of reinfections in two-stage RTKAs; 4.8% in the TTO group and 7.4% in the snip group, without statistical significance (p=0.71).  <i>(Sun et al. Comparison of quadriceps snip and tibial tubercle osteotomy in revision for infected total knee arthroplasty. Int Orthop 2015;39:879–85.)</i></p>	<p>periprosthetic knee joint infection was identified in 9.8% of RTKA cases. The overall risk appears to be a complex and multifactorial issue involving patient and surgical factors. Tibial Tubercle Osteotomy should be considered a safe extensile procedure as so far there is no evidence that the technique may adversely affect the possibility of reinfection. When TTO was compared to rectus snip regarding re-infections after two-stage revisions in infected RTKA, Bruni et al. reported that the results were similar in both groups (7% in the snip group and 5% in the TTO group, p=0.84)[19]. Furthermore, Sun et al. in another comparative study found that the incidence of reinfection in two-stage RTKAs was 4.8% in the TTO group and 7.4% in the snip group. Nevertheless, this difference failed to reach statistical significance (p=0.71)[3].”</p>
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Once again, we would like to thank you and the reviewers for your time and effort. Please do not hesitate to contact me for any further clarifications and corrections regarding the submitted Manuscript.

Yours sincerely,  
Corresponding Author