

Dear Dr. Leigheb and Editorial team,

We thank you for the helpful comments and suggestions for our article, “Association between tourniquet use and intraoperative blood loss during below-knee amputation”. Your insight has helped strengthen our manuscript. We have responded to the reviewer comments point by point in the text below their italicized comments and questions.

**Science Editor:**

*This manuscript explored whether tourniquet use is associated with differences in calculated blood loss without tourniquet use in orthopaedic patients with below-the-knee amputation (BKA). Please supplement a description of the literature describing the relationship between tourniquet use and blood loss during below-knee amputation in the orthopaedic population in Introduction. The manuscript mentions that some patients underwent surgery due to infection, please provide information on these patients and information on drug treatment. Please describe how to estimate blood volume in amputation and investigate hidden blood loss.*

*Language Quality: Grade B (Minor language polishing)*

*Scientific Quality: Grade C (Good)*

We thank you for your comments. Currently, there is a sparse amount of literature describing the relationship between tourniquet use and blood loss during below-knee amputation in the orthopedic population with some papers showing significant data that tourniquets reduce intraoperative blood loss and some showing no difference between the two cohorts. Most of these papers utilized an estimated blood loss at the end of the operation and we have decided to use an equation that is based off of hematocrit which was drawn one to three days postoperatively. Not only do we believe that this is a more accurate measurement of blood loss, but it also takes postoperative blood loss into account as well. We responded to the request to add more information on blood loss in the amputated limb in line 224. In response to the request to add more information to the patients with an infectious etiology, we have provided more information in the manuscript, adding that they are primarily of a diabetic etiology and that we did not specifically review the presence of peripheral vascular disease (line 245). We have also discussed how the use of anticoagulation and antiplatelet therapy may effect blood loss (line 228).

*Reviewer #1:*

***Scientific Quality: Grade B (Very good)***

***Language Quality: Grade B (Minor language polishing)***

***Conclusion: Accept (General priority)***

***Specific Comments to Authors: Title accurately reflects the topic and content of the paper.***

*Abstract: is appropriate, structured, 288 words. Key words: 4 key words, define the content of the paper. Core tip: is appropriate, 49 words. Introduction: is informative, 409 words, the reader is acquainted with the known facts about different surgical methods of limb amputations.*

*The reader is reminded of paucity of literature describing the association between tourniquet use*

*and blood loss during below knee amputation in orthopaedic populations. The primary and secondary goals of the study are clearly stated. Materials and methods: informative, 641 words, the methodology is accurately described, including patient selection, time period and calculation formulas. Statistical analysis is also recorded in detail. Results: informative, 336 words, the results are further presented in tables and figures (Fig. 1, 2, tables 1, 2 and additional supplemental table). The presentation of the results is transparent and clear. Discussion: interesting, 613 words. The discussion is clear, the authors provide answers to the questions posed by the research, but also point out some limitations in the interpretation of these results (academic center, small sample size,...) Conclusion: short, 90 words, the authors summarize the key findings of the presented research. The key message of the research is that tourniquet use during below knee amputation is associated with decreased calculated intraoperative blood loss and recommend this procedure. References: 16, time period 1962 (Surgery) - 2017 (World J Orthop 2017), references are appropriate. Conflict of interest: the authors declared no conflict of interest. Study ethics: the study was approved by the Institutional Review Board (STUDY00020406). Opinion of the reviewer The contribution is interesting, the content is clearly written. I suggest to accept the manuscript after minor language corrections.*

We thank the reviewer for the comments and suggestion to accept the manuscript.

#### **Reviewer 2 comments:**

*Thank you for the invitation! This study found that tourniquet use during BKA was associated with decreased calculated blood loss. However, the preoperative total blood volume is different with postoperative total blood volume in patients undergoing BKA. How did authors estimate the blood volume in amputated limb?*

We thank you for your comments. We agree that the preoperative total blood volume is different than the postoperative total blood volume. Our equation did not account for blood loss in the amputated limb, which would cause a slight tendency to overestimate blood loss because we used the pre-operative patient weight. However, we believe the impact of this is negligible and that the overestimation would be equal in each study group.

*Second, peri-operative total blood loss = intraoperative blood loss (visible) + postoperative hidden blood loss (invisible). To investigate the hidden blood loss seems to be more important in those patient population.*

We agree that postoperative hidden blood loss plays a significant role in total blood loss. The equation we used was based on timing of postoperative hematocrit levels that occurred on post op day 1-3, which would account for intraoperative blood loss as well as postoperative blood loss.

#### **Reviewer 3 comments:**

*Part of the patients underwent surgery due to an infection. Of what nature? Were they vascular or diabetic patients? Why was the presence of peripheral vascular disease not taken into consideration?*

Thank you for your comments. Most of the patients with infection in our study had an etiology of diabetes. We agree that peripheral vascular disease could affect blood loss among diabetic patients. However, we did not observe a statistical difference in blood loss in this population.

*Pharmacological therapies (especially anticoagulants and antiplatelet agents) why have they not been taken into consideration?*

Thank you for highlighting use of anticoagulation and antiplatelet therapy. We agree that their use could effect blood loss volume. Standard practice for patients undergoing elective BKA is reversal of medication effect with the availability of fresh frozen plasma or having patient stop the medication prior to the operation for effects to wear off.

*What are the variables used in the multivariate?*

We thank the reviewer for this question. The variables collected during data abstraction can be found in supplemental Table 1.