

September 30, 2019

Re: Resubmission of manuscript, "Factors associated with trigger digit following carpal tunnel release," No. 46680

Dear Jin-Zhou Tang,

Thank you for the continued review of our manuscript, "Factors associated with trigger digit following carpal tunnel release." We are excited for the opportunity to publish in the *World Journal of Orthopedics*. We appreciate the thoughtful comments and suggestions from all of our reviewers, and we have given our best effort to enact these suggestions appropriately. We have listed each reviewer and their respective comments below; including the email comments from the first revision document, as well as our response underneath each respective comment. These changes are highlighted in our revision manuscript as requested. All coauthors have contributed to answering our reviewer's questions and have approved the revision manuscript.

Thank you for your consideration.

Sincerely,

Jacob Nosewicz

Reviewer's code: 02510721

Reviewer's country: Italy

Science editor: Ruo-Yu Ma

Reviewer's comments: "To Authors: The study explores a clinical problem of current feedback , carpal tunnel treatment and trigger digit. The introduction shows clearly the background of this clinical condition. The Materials and Methods are correctly organized, in particular for the very strict exclusion criteria. The results are believable. The Discussion shows and evaluate the various features of the disease and its treatment. Very interesting and worthy of clarification is the gender differences in the threshold for trigger digit occurrence after carpal tunnel surgery. The References are up-to-date. In summary the manuscript is well developed in all its sections."

1. The study explores a clinical problem of current feedback , carpal tunnel treatment and trigger digit. The introduction shows clearly the background of this clinical condition. The Materials and Methods are correctly organized, in particular for the very strict exclusion criteria. The results are believable. The Discussion shows and evaluate the various features of the disease and its treatment.

We would like to thank the reviewer for their thoughtful comments. We appreciate the thorough evaluation of our manuscript.

2. Very interesting and worthy of clarification is the gender differences in the threshold for trigger digit occurrence after carpal tunnel surgery.

We agree with the reviewer's curiosity regarding gender differences in the threshold for trigger digit occurrence after carpal tunnel surgery. To answer this, we evaluated how baseline morphological differences in the carpal tunnel between sexes may affect the threshold for trigger digit development. Furthermore, we examined if any current studies directly compared changes in postoperative carpal tunnel morphology either between surgical approach or between sexes.

*We used the most recent literature available in order to best examine these potential contributing factors: [Lakshminarayanan K, Shah R, Li Z. Sex related differences in carpal arch morphology. PloS One 2019; **14**(5): e0217425 [PMID:31116798 DOI: 10.1371/journal.pone.0217425] and [Peters BR, Martin AM, Memauri BF, Bock HW, Turner*

RB, Murray KA, Iskur A. Morphologic analysis of the carpal tunnel and median nerve following open and endoscopic carpal tunnel release. *HAND* 2019; 1558944719861711 [PMID: 31331208 DOI: 10.1177/1558944719861711].

Our response is as follows, which is addressed in our discussion section: "Current studies evaluating structural changes in the postoperative carpal tunnel do not make comparisons between genders. In contrast, imaging studies reveal gender differences in baseline carpal arch morphology. Females have a smaller cross-sectional area of the carpal tunnel and decreased palmar bowing of the carpal arch distally compared to males [16]. These baseline morphological differences may reduce the postoperative volar migration of the flexor tendons necessary for trigger digit development in females. Markedly, similar morphological changes of the carpal tunnel, including volar migration of the flexor tendons, occurs following both ECTR and OCTR [13,15,17]. Therefore, it may be expected that females are more likely than males to develop postoperative trigger digit given the smaller cross-sectional area of their carpal tunnel. This was not reflected in our study, which suggests that baseline morphological differences between genders may not contribute to postoperative trigger digit development. Gender differences in the postoperative carpal tunnel need to be further explored in order to support our findings."

3. The References are up-to-date. In summary the manuscript is well developed in all its sections.

We appreciate the thoughtful appraisal of our manuscript. In light of reviewer 2's comments, we further expanded our references to be more recent and robust in their coverage of the current discourse. See our response to comment #5 below.

Reviewer's code: 00646357

Reviewer's country: Egypt

Science editor: Ruo-Yu Ma

Reviewer's comments: "Add the unique of this study compared to other studies discuss the same issue. Add more on the basic of this disease in the introduction. Discuss role of advanced imaging in assessment using these ref -Razek AA, Shabana AA, El Saied TO, Alrefey N. Diffusion tensor imaging of mild-moderate carpal tunnel syndrome: correlation with nerve conduction study and clinical tests. *Clin Rheumatol* 2017;36:2319-2324. English language correction through the manuscript. Update of references as most of references are old."

Our response:

We would like to thank the reviewer for their thoughtful comments. We appreciate the thorough evaluation of our manuscript.

1. Add the unique of this study compared to other studies discuss the same issue.

Thank you for this observation. We have revised our discussion to include the line: "One unique aspect of this paradigm was examining the interaction effect between surgical approach and gender." We believe that this helps focus the reader to the unique discoveries in our manuscript in the context of the previous line, "Strengths of this study include a large patient population size, stringent exclusion criteria for our sample population, and a study paradigm that explored the interaction between surgical approach to carpal tunnel release and patient comorbidities."

2. Add more on the basic of this disease in the introduction.

We agree with the reviewer that more background information on carpal tunnel and trigger digit should be included in the introduction and have added the following lines: "Carpal tunnel syndrome (CTS) is a common entrapment neuropathy of the hand that affects 3.8% of the general population [1]. Characteristic symptoms include burning pain, numbness, and tingling in the distribution of the median nerve distal to the wrist. CTS is diagnosed by a combination of clinical signs and median nerve conduction studies, with supportive diagnostic tools including ultrasonography, magnetic resonance imaging, and diffuse tensor imaging [2]. Surgical treatment, or carpal tunnel release (CTR), involves division of the transverse carpal ligament in order to release pressure on the median nerve. Surgical decompression of the median nerve of the can be accomplished via two different approaches: open carpal tunnel release (OCTR) and endoscopic carpal tunnel release (ECTR)."

3. Discus role of advanced imaging in assessment using these ref -Razek AA, Shabana AA, El Saied TO, Alrefey N. Diffusion tensor imaging of mild-moderate carpal tunnel syndrome: correlation with nerve conduction study and clinical tests. Clin Rheumatol 2017;36:2319-2324.

We agree and have added this reference in our introduction when discussing various imaging techniques for assessing and diagnosing carpal tunnel syndrome. The line added is: "CTS is diagnosed by a combination of clinical signs and median nerve conduction

studies, with supportive diagnostic tools including ultrasonography, magnetic resonance imaging, and diffuse tensor imaging."

4. English language correction through the manuscript.

We have reviewed our manuscript and made sure the writing is grammatically correct for the English language. Any changes made are highlighted in our revision document.

5. Update of references as most of references are old.

We have added newer references to our list, such as: [Aboonq MS. Pathophysiology of carpal tunnel syndrome. Neurosciences (Riyadh) 2015; 20: 4-9 [PMID: 25630774], [Lakshminarayanan K, Shah R, Li Z. Sex related differences in carpal arch morphology. PloS One 2019; 14(5): e0217425 [PMID:31116798 DOI: 10.1371/journal.pone.0217425], and [Peters BR, Martin AM, Memauri BF, Bock HW, Turner RB, Murray KA, Islur A. Morphologic analysis of the carpal tunnel and median nerve following open and endoscopic carpal tunnel release. HAND 2019; 1558944719861711 [PMID: 31331208 DOI: 10.1177/1558944719861711].

Reviewer: BPG Editorial Office

Our Response:

We would like to thank the editor for their thoughtful comments. We appreciate the continued evaluation of our manuscript.

1. Please add the ARTICLE HIGHLIGHTS in the manuscript.

We included the additional section, "ARTICLE HIGHLIGHTS," and answered each prompt accordingly.

2. You need to provide the grant application form(s) or certificate of funding agency for the Central Michigan University College of Medicine and the Number, or we will delete the part of "and the Central Michigan University College of Medicine".

We have deleted the part, “and the Central Michigan University College of Medicine.”

3. Notes in illustrations and tables: Data with statistical significance in a figure or table should be denoted using superscripted alphabetical lettering, such that ^a $P < 0.05$ and ^b $P < 0.01$. If there are other series of P values, the alphabetical subscripted denotation format is continued, such that ^c $P < 0.05$ vs control, ^d $P < 0.01$ vs control, ^e $P < 0.05$ vs group A, and ^f $P < 0.01$ vs group A. Data that are not statistically significant should not be denoted, *i.e.* $P > 0.05$ is not an allowed denotation.

We have reviewed every table with our statistician who confirms that our data with statistical significance is in accordance with the above guidelines.