Author’s response to reviews

Title: Comparison of Outcomes of Unilateral Recession-Resection as primary surgery and reoperation for Intermittent Exotropia

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Version: 1 Date: 29 Dec 2016

Author’s response to reviews:

Dear Editor-in-chief

Thank you for providing us the opportunity to revise the manuscript, entitled "Comparison of Outcomes of Unilateral Recession-Resection as primary surgery and reoperation for Intermittent Exotropia" for consideration for publication in the BMC Ophthalmology.

A point-by-point response to the reviewers’ comments/requests and a detailed description of changes made to the manuscript are included below. We thank the reviewers for their valuable and constructive comments.

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Editor Comments:

Thanks to the authors' for an interesting manuscript. However, as suggested by esteemed reviewers' the authors' should address the issues to be considered for further consideration.

1) The basic mechanism for suggesting that R and R procedure might be more effective in patients with Recurrent exotropia is not clear. The authors' should try and explain it more clearly and suggest their hypothesis well.

According to their hypothesis, R and R procedure in reoperation might be expected to have a greater correlation, but it was not found to be true.

-> Thank you for your indispensable comment. According to Kim et al.’s report, (Korean J Ophthalmol. 2016;30:48-52), the exodrift changes after a second ULR muscle recession were smaller than those after a first URL muscle recession in small-angle (< 25 PD) exotropia patients. They explained that the stability of ULR recession as a second surgery is affected by several factors such as age at the time of surgery and the presence of latent exodeviation. In the same manner, our study results might have been affected by these factors. So, we added the additional explanations into the “Discussion” at page 11, lines 237-249.

2) It might be interesting to observe the effect in patients with only basic XT subgroup of patients, as suggested by our reviewers.

-> We are profoundly sorry to state that the count of patients with the pseudo-divergence excess type was incorrect. Initially, we planned to include both the basic and pseudo-divergence excess types. In fact, however, only patients with intermittent exotropia of the basic type were included. We revised the relevant sentence as follows: “All of the participating patients had been diagnosed as intermittent exotropia of the basic type according to Burian’s classification [6]” (“Methods”, page 5, lines 80-81).

3) It might be interesting to see if the dose-response relationship in two groups, was effected by: the presence/absence of the fusion and the difference in the amount of pre-operative deviation.

-> Thank you for your precious comment. We had a statistical review for the patients in each group. Please refer to our explanations mentioned below.

(1) presence/absence of the fusion
In the primary surgery group, the mean dose-effect ratio for the 22 patients with fusion was 1.96 ± 0.51 PD/mm, and for the 22 patients with no fusion, 1.80 ± 0.65 PD/mm (p=0.534, Mann-Whitney U test). In the reoperation group, the mean dose-effect ratio for the 22 patients with fusion was 2.21 ± 0.46 PD/mm, and for the 18 patients with no fusion, 2.03 ± 0.54 PD/mm (p=0.279, Mann-Whitney U test). The dose-effect ratio was not found to be significantly associated with the presence/absence of fusion. We inserted this paragraph into the “Dose-effect ratio of R&R” at page 9, lines 194-199.

(2) difference in the amount of pre-operative deviation

In general, the patients with large preoperative angle of deviation had undergone large amount of recess-resect. In this study, we evaluated the correlation between the dose-effect ratio and the amount of recess-resect in each group. The significant correlation between the dose-effect ratio and the amount of recess-resect was not found in each group (Figure 1) (p=0.093 in group A and p=0.693 in group B). In other words, there was no correlation between the dose-effect ratio and the preoperative angle of deviation. This explanation was already described in the “Dose-effect ratio of R&R” at page 9, lines 186-193.

4) Reclassify patients success according to more stringent criteria of post-operative deviation less than/equal to 8 PD, which is more physiological and commonly accepted in strabismus literature.

-> We redefined the surgical success criteria of post-operative deviation less than/equal to 8 PD and evaluated the success rate according to the new criteria. We changed the sentence “Surgical success was defined as ocular alignment within 10 PD. Overcorrection was defined as esodeviation over 10 PD, and undercorrection, as exodeviation over 10 PD.” to “Surgical success was defined as ocular alignment within 8 PD. Overcorrection was defined as esodeviation over 8 PD, and undercorrection, as exodeviation over 8 PD” in “Preoperative management” at page 6, lines 126-128. Also, the minor changes of success rate were observed and described in “Table 4” and “Surgical success” at page 8, line 173.

5) Language can be improved by help from a natural English speaking person.

-> I’m sorry for your inconvenience. We revise the manuscript from a natural English speaking person.
Reviewer reports:

Reviewer 1:

1. Patients were either basic or pseudodivergence excess XT. Those are 2 different groups. This can create a selection bias.

   -> We are profoundly sorry to state that the count of patients with the pseudo-divergence excess type was incorrect. Initially, we planned to include both the basic and pseudo-divergence excess types. In fact, however, only patients with intermittent exotropia of the basic type were included. We revised the relevant sentence as follows: “All of the participating patients had been diagnosed as intermittent exotropia of the basic type according to Burian’s classification [6]” (“Methods”, page 5, lines 80-81).

2. Authors defined overcorrection as ET over 10 PD. A patient with intermittent exotropia and possible normal foveal near fixation who resulted in overcorrection may become monofixator. A range of 10PD +/- to define over and under correction is very soft criteria especially in patients with intermittent exotropia.

   -> Thank you for your precious comment. We redefined the surgical success criteria of post-operative deviation less than/equal to 8 PD and evaluated the success rate according to the new criteria. We changed the sentence “Surgical success was defined as ocular alignment within 10 PD. Overcorrection was defined as esodeviation over 10 PD, and undercorrection, as exodeviation over 10 PD.” to “Surgical success was defined as ocular alignment within 8 PD. Overcorrection was defined as esodeviation over 8 PD, and undercorrection, as exodeviation over 8 PD” in “Preoperative management” at page 6, lines 126-128. Also, the minor changes of success rate were observed and described in “Table 4” and “Surgical success” at page 8, line 173.

3. Although not significantly different (tendency 0.08), Group A patients postoperative follow up was almost 1 year longer than group B patients.

   -> As you mentioned, the postoperative follow-up period in group A was longer than in group B. However, this difference was not statistically significant, and furthermore, the postoperative follow-up periods in both groups were longer than 3 years. We considered that this minor difference was not a significant problem for interpretation of the results. Thank you for your meticulous review.
4. Groups were not different to begin with. There was a significant large angle of deviation in Group A patients.

-> We appreciate your valuable comment. Unfortunately, there was a difference of preoperative angle of deviation between the two groups. The reasons were as follows: (1) the patients with R&R as a reoperation had already undergone the primary surgery, which induced a relatively small angle of deviation, and (2) early detection of exotropia recurrence in the patients with R&R as a reoperation could be made, due to their steady follow-up after the primary surgery. As you mentioned, A discrepancy of preoperative angle of deviation would be likely to influence the postoperative angle of deviation and surgical success. We believe therefore that an additional, prospective study should be conducted to confirm our present results. We described this limitation in “discussion” at page 11, line 252-262.

5. Results. These 2 groups cannot be compared. Group B patients already had undergone another surgery for XT. The impact that first surgery had on the group is not known

-> Thank you for your indispensable comment. When we encounter patients who are to undergo reoperation for recurrent exotropia in clinical settings, they or their parents usually are concerned about the prognosis and the accuracy of the surgical dosage for avoidance of complications such as over- or undercorrection. These questions prompted us to compare the postoperative outcomes of the same surgical procedure (R&R) as primary surgery and reoperation for intermittent exotropia. To conduct the comparison of surgical outcome between primary surgery and reoperation, we enrolled recurrent exotropia patients who had previously undergone strabismus surgery for exotropia. To some degree, the impact that primary surgery had on the group would be likely to have acted as a bias affecting surgical outcomes such as postoperative angle of deviation and surgical success. However, our study design would remain a meaningful comparative case series in any event, given that we had concluded that we did not need to modify the surgical dose of reoperation by assessing the surgical success and dose-effect ratio of R&R as reoperation.

Reviewer 2: The authors present a fascinating and interesting study about Unilateral Recession-Resection as a primary surgery and reoperation. This paper describes orthotic characteristics of these patients, evaluated during a follow-up ranging from 1 day to more of 24 months. Therefore it could offer useful information that could implement the current knowledge about type of surgical approach in patients with Intermittent Exotropia.
MAJOR REVISIONS:

1) It would be useful to know because it has been preferred the R&R surgery as primary surgery (group A).

-> The aim of this study was to compare the postoperative outcomes of primary surgery and reoperation for intermittent exotropia. According to Burian’s report, the R&R procedure was effective for exotropia of the basic type (Burian HM. Exodeviations: their classification, diagnosis, and treatment. Am J Ophthalmol. 1966;62:1161–6). Also, Kushner recommended R&R surgery for exotropia of the basic type (Kushner BJ. Selective surgery for intermittent exotropia based on distance/near differences. Arch Ophthalmol 1998;116:324-8). Accordingly, we usually utilize the R&R procedure (rather than BLR recession) as the primary surgery for correction of exotropia of the basic type.

2) It would be useful to know because it has been preferred the R&R surgery as reoperation technique (group B).

-> The surgical intervention for recurrent exotropia depends on the primary surgery. Bilateral or unilateral medial rectus resection might be performed on patients having previously undergone bilateral lateral rectus (LR) recession. Or, patients on whom R&R was previously performed might undergo, as reoperation, LR recession or R&R on the contralateral eye. In the present study, we included only patients who had undergone unilateral R&R on the non-dominant eye as a primary surgery for exotropia. The surgeon (Dong Gyu Choi) commonly performs the R&R procedure or LR recession on the unoperated eye as reoperation for recurrent exotropia. In this study, only patients who had undergone R&R surgery as reoperation were included.

3) It should explain better what are the benefits of this study. Is there any changes about surgical approach in patients with Intermittent Exotropia?

-> Thank you for your indispensable comment. When we encounter patients who are to undergo reoperation for recurrent exotropia in clinical settings, they or their parents usually are concerned about the prognosis and the accuracy of the surgical dosage for avoidance of complications such as over- or undercorrection. These questions prompted us to compare the postoperative outcomes of the same surgical procedure (R&R) as primary surgery and reoperation for intermittent exotropia. In our study, we have concluded that we do not need to modify the surgical dose of reoperation by assessing the surgical success and dose-effect ratio of R&R as reoperation. These results could serve as useful guidelines in the planning of surgical correction for primary and recurrent exotropia. We added some sentences into “discussion” at page 10, lines 206-211 and “conclusions” at page 13, lines 278-279.
4) It compares the same surgical approach on 2 different groups. It might be more interesting to compare two different surgical approaches for each group.

-> In our study, we would like to compare the postoperative outcomes of the surgical procedure (R&R) as primary surgery and reoperation for intermittent exotropia. We thought that this study would remain a useful comparative case series, given the distinct difference in dose-effect ratio between the two groups. Considering your comment, we also agree that it would be meaningful to investigate the comparison of two different surgical approaches for each group. In this light, the aforementioned additional prospective study will be suitable for comparison of the surgical outcomes between the R&R procedure and the other surgical methods. We added this limitation in “discussion” at page 12, lines 265-271.

MINOR REVISIONS:

1) A linguistic revision is desirable.

-> I’m sorry for your inconvenience. We revise the manuscript from a natural English speaking person.

2) Who has performed the orthotic assessments.

-> The corresponding author (Dong Gyu, Choi) performed the orthoptic assessments.

3) Are there amblyopic patients in groups A and B? If yes, what might be consequences on surgical outcomes.

-> There were 6 amblyopic patients in each group. Their proportions were not significantly different between groups A and B (p=0.806, Pearson chi-square test). In each group, the success rates at final follow-up did not differ between the amblyopic and non-amblyopic patients (p=0.745 in group A and p=0.851 in group B, Mann-Whitney U test). Likewise, the dose-effect ratio at postoperative 6 months did not differ (p= 0.107 in group A and p=0.668 in group B, Mann-Whitney U test). The surgical outcomes were not found to be significantly associated with amblyopia.