Author’s response to reviews

Title: Prolonged Preoperative Treatment of Acromegaly with Somatostatin Analogs May improve Surgical Outcome in Patients with Invasive Pituitary Macroadenoma (Knosp grades 1–3): A Retrospective Cohort Study conducted at a Single Center

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Response to Reviewers' comments

Dear Dr. Koltowska-Haggstrom,

We thank you for your careful consideration of our manuscript. We appreciate your response and overall positive initial feedback, and made modifications to improve the manuscript. After carefully reviewing the comments made by the Reviewers, we have modified the manuscript to improve the presentation of our results and their discussion, therefore providing a more complete context for the research that may be of interest to your readers.
We hope that you will find the revised paper suitable for publication, and we look forward to contributing to your journal. Please do not hesitate to contact us with other questions or concerns regarding the manuscript.

Best regards,

Feng Gu

Reviewer #1

Firstly, the organization of the manuscript needs revision: some data (i.e., tumor invasiveness classification by MRI) described in Material and methods section should be transferred to the Results. The discussion is too long, and some information are repeated in introduction and discussion.

Response: We are sorry for this. We moved the results from the Methods section to the Results. We shortened the Discussion, as well as the overall manuscript.

Could you also discuss why some patients were qualified for SSAs therapy, and the others have been not?

Response: We thank the Reviewer for the comment. The decision about whether to take SSA was dependent on both the physicians and the patients. The physicians followed the Chinese diagnostic and treatment guidelines for acromegaly [1, 2]. For the patients, the main concern was the cost. Our hospital is located in Beijing and is considered to be one of the best centers for the treatment of hypophysoma in China. Therefore, the patients are from the whole country.

In addition, different medical insurance coverage is offered across different regions of China. SSA is very expensive (7000-10,000 RMB/month), and many patients cannot afford it without insurance coverage. On the other hand, most local patients from Beijing have coverage for SSA.
This was added to the manuscript.

Also, authors mixed gigantism with acromegaly- please, clarify.

Response: We are sorry for the confusion. Gigantism refers to abnormally high linear growth due to the excessive action of IGF-I while the epiphyseal growth plates are open during childhood. Acromegaly is the same disorder of IGF-I excess but occurs after the growth plate cartilage fuses in adulthood. Acromegalic gigantism refers to the same disorder but occurs around the time of growth plate cartilage fusion. In the present study, all patients were diagnosed with the disease at >18 years of age. The youngest age for symptom/disease onset was 15 (14 patients, three in the SSA group and 11 in the control group). Considering that all patients were diagnosed at >18 years of age, there should be no differences in disease management and efficacy assessment. It was nevertheless verified throughout the manuscript.

In abstract the information about the efficacy of preoperative SSAs therapy is contradictory to conclusions.

Response: We are sorry for the confusion. In the present study, invasive macroadenomas was defined as a Knosp grade >0. SSA appeared to be beneficial for patients with Knosp grades 1-3 (intermediate grade of severity). Longer pre-operative treatment also appeared to be beneficial for patients with macroadenoma, regardless of Knosp grade.

In the Results, the seemingly contradictory result was in fact for all patients, while the conclusion is only about patients with invasive macroadenoma. It was therefore edited as: "Among all patients (Knosp grades 0-4), preoperative SSA therapy did not significantly improve the curative effect of surgery [...]" and "The long-term preoperative SSAs treatment may improve the surgical curative rate in acromegalic patients with invasive macroadenomas (Knosp grades 1-3)."

The English language is poor and there are many grammas in the manuscript

Response: The manuscript was proofread.
1. different numbers of groups compared,

Response: We agree with the Reviewer. This was a retrospective study of all eligible patients treated at our center during the study period. In addition, many patients were from different parts of the country and referred to our center only for second opinion and/or treatments. Furthermore, many patients had no medical insurance and could not afford SSAs. Thus, the numbers of patients were different between the two groups. In addition, acromegaly is a complex disease and the different subgroups of patients cannot necessarily be analyzed together, hence the large number of subgroups. Nevertheless, we consulted a biostatistician for data analysis. This was stated as a limitation.

2. no clear information on the selection of the patients to the groups compared,

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3. the conclusions are not properly derived from the results obtained.

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improve the surgical curative rate in acromegalic patients with invasive macroadenomas (Knosp grades 1-3)."

In my opinion a manuscript is too long

Response: We shortened the Discussion, as well as the overall manuscript.

References
