

Dear Editors and Reviewers:

Thank you for your letter and for the reviewers' comments concerning our manuscript entitled "Harnessing interventions during the immediate perioperative period to improve the long-term survival of patients following radical gastrectomy" (Manuscript NO.: 82318). These comments are all valuable and very helpful. I have studied the comments carefully. After reading these comments carefully, we revised our manuscript. The main responses to the reviewer's comments are as follows:

Reviewer #1:

Scientific Quality: Grade A (Excellent)

Language Quality: Grade A (Priority publishing)

Conclusion: Accept (High priority)

Specific Comments to Authors: It is a very interesting topic in radical gastrectomy, the negative effects of which have always been underestimated. Harnessing the immediate perioperative period to improve the oncological outcomes has attracted much attention in colorectal and breast cancer, however, less investigation in gastric cancer. In this review, the authors report the first summerizatoin of such topic in gastric cancer, may help guiding future direction in the field. In this review, the authors have discussed the possible interventions perioperatively to improve survival of patients following gastrectomy in detail. The results from these studies have been analysed and integrated into ERAS guidelines in various surgical arenas, including gastrectomy, therefore, it is advised to be discussed in this review.

Response:

Thank you for your valuable comment. We reviewed reports on ERAS in gastric cancer and added a paragraph to our manuscript to discuss the effects of ERAS on gastrectomy. However, we found that all studies on ERAS reported results in the immediate postsurgical settings, but none of them have reported the oncological outcomes, the aim of our manuscript, therefore, we recommended in our review to investigate the survival effects of ERAS in GC.

Reviewer #2:

Scientific Quality: Grade C (Good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Minor revision

Specific Comments to Authors: The article entitled Harnessing interventions during the immediate perioperative period to improve the long-term survival of patients following radical gastrectomy is a document of interesting subject matter.

1. Please try to add more Figure to more clarity your work.

Response:

Thank you for your valuable comment. However, the main content of our manuscript is the possible interventions to improve the survival of patients after radical gastrectomy, which were all depicted in Fig.1, and the mechanisms through which the perioperative events to increase the incidence of recurrence have been reviewed and comprehensively depicted in another figure previously, which was referred in the manuscript. Therefore, we suggest that there has no need to add more figures and hope that the reviewer may agree with us, thanks.

2. The objective or objectives should be clearly elucidated in the last paragraph of the introduction.

Response:

According to your suggestion, we have clearly elucidated the objective in the last paragraph of the introduction.

3. It is suggested to add one part on "challenges and opportunities" before conclusion part.

Response:

Thank you for your valuable comment. The challenges and opportunities have been discussed in the section "PERSPECTIVES AND CONCLUSIONS", as they are correlated, we think it is not necessary to separate them into two sections.

4. The authors should do the analysis the conclusion section must clearly establish a strong correlation with the proposed topic.

Response:

After have comprehensively reviewed related literature, we found that we cannot establish a strong correlation with the proposed topic as your suggestion. The peroperative period has been relatively unexplored therapeutically, robust evidence supporting the clinical application of these interventions is lacking at present. Therefore, we can only concluded that the majority of these interventions are already safely applied clinically for other indications, are cost-effective and can be administered conveniently, and some promising results have been reported, further studies are needed before they can be routinely applied during radical gastrectomy.

5. Please add the new references in the introduction part. I. Matzner, P., Sandbank, E., Neeman, E., Zmora, O., Gottumukkala, V., & Ben-Eliyahu, S. (2020). Harnessing cancer immunotherapy during the unexploited immediate perioperative period. *Nature Reviews Clinical Oncology*, 17(5), 313-326. II. Zhi, X., Kuang, X., & Li, J. (2022). The Impact of Perioperative Events on Cancer Recurrence and Metastasis in Patients after Radical Gastrectomy: A Review. *Cancers*, 14(14), 3496. III. Kanaoujiya, R., Porwal, D., & Srivastava, S. (2022). Applications of nanomaterials for gastrointestinal tumors: A review. *Frontiers in Medical Technology*, 2022; 4: 997123. IV. Gao, X., Pan, Y., Han, W., Hu, C., Wang, C., Chen, L., ... & Nie, Y. (2021). Association of systemic inflammation and body mass index with survival in patients with resectable gastric or gastroesophageal junction adenocarcinomas. *Cancer Biology & Medicine*, 18(1), 283.

**Response:**

Thank you for providing related new studies, and we have add them to our reference.

#### EDITORIAL OFFICE' S COMMENTS

Please provide the original figure documents. Please prepare and arrange the figures using PowerPoint to ensure that all graphs or arrows or text portions can be reprocessed by the editor. In order to respect and protect the author' s intellectual property rights and prevent others from misappropriating figures without the author's authorization or abusing figures without indicating the source, we will indicate the author's copyright for figures originally generated by the author, and if the author has used a figure published elsewhere or that is copyrighted, the author needs to be

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Response:

As the figure was created with BioRender.com, when it was transformed into ppt, only the text portions are editable, we hope such format will meet the requirement. In addition, the publication and licensing rights of the figure was obtained and has been submitted with the figure.

Authors are requested to send their revised manuscript to a professional English language editing company or a native English-speaking expert to polish the manuscript further. When the authors submit the subsequent polished manuscript to us, they must provide a new language certificate along with the manuscript.

Response:

The revised manuscript has been edited by AJE AI, and we hope that the language quality of our manuscript will meet the publication requirement.

We tried our best to improve the manuscript and made some changes in the manuscript. These changes will not influence the content and framework of the paper.

We appreciate for Editors/Reviewers' warm work earnestly, and hope that the correction will meet with approval.

Once again, thank you very much for your comments and suggestions.

Yours sincerely,

Linbo Liu, Jian Li, Jianxiong Lai, Sen Shi