

Reviewer #1:

**Scientific Quality:** Grade C (Good)

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

**Conclusion:** Minor revision

**Specific Comments to Authors:** The authors build a predictive model based on machine learning and use it to predict the risk of stress ulcer in colorectal cancer patients underwent laparoscopic surgery, which is a powerful tool for the prognosis of patients. After reasonable grouping the patients, the authors showed that age, lymph node metastasis, and elevated HSP70, HSP90, and GAS are important risk factors to predict stress ulcer (SU). This result also draws a conclusion that the predictive model can be constructed by comparing the significant differences between SU and non-SU group. In short, the topic of this manuscript is timely and interesting. The authors have organized the manuscript rationally, with good methodology and well-written English. However, some important editing needs to be done before publication: 1) In this retrospective study, the authors selected 17 factors related to CRC for analysis and building the predictive model. So, what are the inclusion criteria to select the related factors? 2) Herein, 135 CRC patients was divided into SU and non-SU groups for analysis. However, only 23 patients underwent stress ulcer. Is such a data volume enough to build a reliable predictive model?

The author replies : Thank you very much for your valuable comments and corrections. For two questions, my answers are as follows : 1 ) The selection criteria of relevant factors. In this study, the relevant factors we selected included the patient 's general condition ( gender, age, smoking history, drinking history, etc. ), liver and kidney function, lymph node status, and more than a dozen routine laboratory test indicators. These indicators are closely related to the nutritional status, inflammatory response and immune function of patients. Studies have confirmed that they are related to the risk of stress ulcer. For example, CRP, TNF- $\alpha$ , IL-6 and IL-8 are associated with inflammatory response and immune function ; HSP70 and HSP90 are related to the body 's stress response. Low albumin is associated with malnutrition and so on. In summary, the relevant indicators we selected are based on existing research evidence and theoretical basis. These indicators can fully reflect the patient 's general condition, nutritional status, inflammatory immune response and stress status, and are closely related to the occurrence of stress ulcer, so they are selected as the influencing factors for constructing the prediction model.

2 ) Reliability of prediction model. We plotted the ROC curve and Calibration curve to evaluate the predictive performance of the model. The ROC curve and Calibration curve showed that the model had high prediction accuracy and calibration. The Hosmer-Lemeshow test showed that the model was stable. The DCA curve suggested that the model had strong clinical practicability. Secondly, we investigated the probability of stress ulcer in patients with colorectal cancer after laparoscopic surgery, and found that the probability was about 10 ~ 30 %. The incidence of SU in this study was 17.04 %, which was in the normal range, so we initially thought that the model had certain application reference value.

In summary, despite the limited sample size, we have ensured the good predictive performance and stability of the Nomogram prediction model through rigorous statistical

methods and multiple validation. Of course, further expanding the sample size will help to further improve the accuracy and stability of the model, which is also the focus of our future research.

Reviewer #2:

**Scientific Quality:** Grade C (Good)

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

**Conclusion:** Minor revision

**Specific Comments to Authors:** Laparoscopic surgery is a promising way for CRC treatment, which is still a traumatic treatment, as it can cause certain damage and mechanical stimulation, such as stress ulcer, in the patient CRC. In this study, the authors aimed at developing a predictive model to reduce mortality, accurately forecast CRC predisposition, and provide targeted treatment for high-risk groups. The authors used primary clinical data, multivariate logistic regression analysis, and nomogram to construct their model. The results showed that age  $\geq 65$  years, lymph node metastasis, and elevated HSP70, HSP90, and GAS are independent risk factors for postoperative SU in CRC patients. So, in my opinion, this paper is well-written. The model design is reasonable, and the results reflect the conclusion as well. I recommend its acceptance after the minor revision. The detailed comments are: 1. In the first paragraph of Discussion, the authors reviewed the background of this study again. In my opinion, this content can be integrated in the Introduction part. 2. It is always said that high salt diet is a potential risk leading to CRC. I wonder whether this factor can be added into the authors' new model?

The author replies: Thank you very much for the positive evaluation and valuable comments. In response to the above two questions, my answer is as follows :

1 ) We briefly describe the research background again at the beginning of the discussion section, which is not in line with the general article structure and is easy to cause repetition. According to the editor 's proposal, we will integrate the content of the beginning of the discussion in the revised draft, and directly enter the discussion of the research results and significance. This can avoid duplication and make the structure of the article more compact and reasonable. We thank the editor for his valuable correction. This helps us to further optimize the structure of the article and provide a more coherent and clear discussion. We must carefully study, in the revision of the draft to modify the perfect.

2 ) High salt diet is indeed one of the risk factors for colorectal cancer, whether it can be included in the prediction model is worth studying. Our considerations are as follows : high salt diet mainly increases the risk of colorectal cancer, but there is no study to confirm its association with postoperative complications such as stress ulcer. Therefore, there is no theoretical or research basis to support the inclusion of high salt into the prediction model of postoperative stress ulcer. Of course, if future studies confirm that the two are related, high salt can become the influencing factor of the subsequent research model, which deserves our further discussion.

Thank you again for the valuable suggestions and corrections of the editor. We will study

carefully and make corresponding revisions and supplements in the revised draft. Please continue to make valuable comments, we will strive to study and improve. We will continue to deepen and improve this work in the follow-up study.