

Respond to reviewers' comments

Reviewer #1: The authors looked back at 130 patients who were treated surgically for gastrointestinal GIST, intending to develop an innovative nomogram to predict recurrence. Major remarks:

Comment 1): The title is not informative at all. I would suggest changing it to: Development of an innovative nomogram of risk factors to predict postoperative recurrence of gastrointestinal stromal tumors.

Response: We thank the reviewer for raising this suggestion. We would gladly to change the title to: Development of an innovative nomogram of risk factors to predict postoperative recurrence of gastrointestinal stromal tumors.

Comment 2) Bottom of page 4: I would say that the prognosis of GIST "could" be improved. It remains to be seen how (see #5).

Response: Thanks to the reviewer for finding the problem. After discussion among the authors, we have consistently argued that the modification to the prognosis of GIST "could" be improved with more scientifically and rigorously.

Comment 3) I have failed to understand the nomogram itself as it has not been directly described in the text. At the bottom of page 8 we

read about 9 (?) factors that were calculated using the LASSO model and about 5 other factors. Please provide a clear description of the nomogram and clarify why it is innovative.

Response: We thank the reviewer for raising this question. First, nomogram, also known as Alignment Diagram, is based on multivariate regression analysis (this manuscript uses LASSO regression), integrates multiple predictors, and then uses scaled line segments to draw on the same plane according to a certain proportion, so as to express the relationship between the variables in the prediction model.

Second, the innovation lies in that the results of multi-factor regression are visualized, and each value level of each influencing factor is scored according to the contribution of each influencing factor in the model to the outcome variable. The total score is obtained by adding up each score, and finally the predicted value of the individual outcome event is calculated through the functional transformation relationship between the total score and the probability of the outcome event. Nomograms are visual and intuitive, not only providing a way for professional researchers to assess disease risk, but also helping the general population and health managers to more easily understand disease risk. We made appropriate changes in the results section (page 8 line 8).

Comment 4) It should be clarified in the methods whether all the patients had not received any neoadjuvant treatment.

Response: Thank you for this valuable feedback. First, none of our patients received neoadjuvant targeted therapy. We have added a sentence to the methods section (page 6 line 3) to clarify this point.

Comment 5) The discussion fails to describe how the nomogram could be useful in clinical practice. Can it be used to indicate neoadjuvant treatment and/or exclude patients from surgery with curative intents and/or indicate more stringent follow up?

Response: We are very sorry for our negligence of the explanation. In the discussion section, we briefly mentioned nomogram as a predictive tool for postoperative recurrence, but did not elaborate further on its use. In our study, for example, there is such a GIST patient, aged 66 years, the tumor is located in the stomach, the postoperative pathology shows that the tumor size is 11cm, the mitotic rate is 12/50HPF, the Ki-67 is 10%, there is no Intratumoral necrosis, and the total score of the patient is 155. The risk of recurrence after surgery is 59%. The nomogram established in our study is mainly based on postoperative pathological indicators as a reference factor, so it does not recommend neoadjuvant targeted therapy for GIST or

exclude patients from surgery with curative intent. However, the nomogram can give scores to postoperative patients and guide the frequency of postoperative follow up according to the scores. The higher the score, the higher the probability of postoperative recurrence and the higher the follow up frequency. We have carefully considered the reviewer's suggestion and made some changes in the discussion section (page 10 line 6) .

Comment 6) Page 12: In the sentence "Nomograms show that the highest risk of postoperative recurrence is for a tumor in the colorectal area, followed by the small intestine and finally the gastric region" are you referring to the current nomogram? If so, it should be better clarified and the past tense should be used.

Response: We thank the reviewer for raising this problem. We do mean the nomogram results of this manuscript. For better clarification, we made this point clear in the original text and changed it to the past tense (page 10 line 20) .

Minor remarks:

Comment 1) Page 5, last but one paragraph: what do you mean by "critical value"?

Response: We are very grateful to reviewer for reviewing the paper so

carefully. We are so sorry for not expressing this clearly. What we mean is that tumor size and mitotic rate are two key indicators. Our modifications in the manuscript are as follows: However, the use of a single grading method to predict the probability of postoperative recurrence in patients with GIST has certain limitations, especially for some GIST patients who only evaluate the two key indicators of tumor size and mitotic rate.

Comment 2) Page 5 last line: the aim should be in the past tense.

Response: We apologize for the language problems in the original manuscript. After revising the relevant grammar issues raised by the reviewers, we will further hand over the manuscript to a professional language editing company for language polishing.

Comment 3) Page 6, Patients: in the third criteria it should be specified "other gastrointestinal malignancy" as GIST are indeed a malignancy.

Response: We agree with the comment and re-wrote the sentence in the revised manuscript as the following: "third, patients presented with no other gastrointestinal malignancies" .

Comment 4) You can add the following reference: Catena F, Di

Battista M, Ansaloni L, et al. Microscopic margins of resection influence primary gastrointestinal stromal tumor survival. Onkologie. 2012;35(11):645-8. doi: 10.1159/000343585.

Response: We are grateful for the suggestion. After reading the recommended reference, we found it very useful to the manuscript and cite the findings of this reference in the discussion section of the manuscript (page 11 line 13).

All in all, we are very grateful to the reviewers for their constructive suggestions, and the revisions in the manuscript are marked in red font.

Reviewer #2: This is a useful overview of the topic and will be of use to the readership of the journal.

Response: Thank you very much for the reviewer's approval of the manuscript.