

## Peer Review File

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### Reviewer A

Thank you for the opportunity to revise this article. I have gone through the study thoroughly repeatedly; however, I have been more and more confused every time I get to write my points of revision. The Authors seem to have taken hospital data with GISTS and analyzed these data without a proper goal to bring about. However, I would Like to give a chance for the authors to revise the work, as the data provided might bring good discussion points. I want to re-evaluate this article after the changes and it would be an honour.

Comment #1: classifying stromal sarcomas as a subtype of GIST is an old classification. since the early 2000's GISTS are no longer defined as leiomyomas [1]. Please restate all your cases as GISTS and not stromal sarcomas.

**Reply 1:** All gastric stromal sarcoma in the paper have been replaced with gastrointestinal stromal tumors and marked with yellow.

Comment #2: please define the pathology immunohistochemistry of your cases DOG-1 and CD117 and compare that to the prognosis.

**Reply 2:** CD117 is the main diagnostic criterion for immunohistochemical diagnosis of GIST. DOG1 is a newly discovered protein selectively expressed in GIST. DOG1 has good sensitivity and specificity for the diagnosis of GIST. However, due to the long time span of the selected cases, the data of immunohistochemical CD117 and DOG1 in the cases were incomplete, and it was impossible to conduct statistics and then make a prediction model.

Comment #3: The authors did show the inclusion criteria in their study; however, what and how did they choose the validation cohort and the training cohort? Please give more details as to how you define these cohorts and what value is brought from this

**Reply 3:** Within the scope of inclusion criteria, we randomly select a part of people as the validation cohort and the training cohort to avoid selective bias.

**Changes in the text:** we have modified our text as advised (see Page 4, line 112-113).

Comment#4: prognostic factors of GIST according to NCCN guidelines [2], ESMO–EURACAN Clinical Practice Guidelines[3], and French clinical practice guidelines [4] are mitotic rate, tumor size, tumor site, histological type, depth of invasion, and grade. This is not discussed or considered at all in the study at hand. Rather the authors discussed the marital state!!!! What use is it?? Please state your key statement.

**Reply 4:** In this paper, tumor grade, tumor size, tumor site, and invasion depth (equivalent to T stage in TNM stage) were included into clinicopathological features for statistical and discussion (see Table and Figure). In the initial design, mitotic rate, depth of invasion may be related to the prognosis of GIST. They were intended to be used as Clinical characteristics, but the original data in SEER database did not contain these Clinical characteristics, so statistics

could not be made. Marital status's role in cancer prognosis has been underscored in various retrospective evaluations.(eg1:Krajc K, Mirošević Š, Sajovic J, et al. Marital status and survival in cancer patients: A systematic review and meta-analysis. *Cancer Med* 2023;12:1685-708. eg2:Zhou R, Yan S, Li J. Influence of marital status on the survival of patients with gastric cancer. *J Gastroenterol Hepatol* 2016;31:768-75.

**Changes in the text:** we have modified our text as advised (Page 8, line 242-244).

Comment #5: what is meant by local resection? did you mean partial gastrectomy? Furthermore there are many partial gastrectomies that can be done to GISTS please state in your study what type of GISTS partial gastrectomies were done. Sleeve gastrectomies, Central gastrectomies, Distal gastrectomies? please add this to your data and also discuss the surgical options that can be used in gastric GISTS with Citing the following article [5].

**Reply 5:** local resection means partial gastrectomy.

Comment#6: please add a paragraph discussing the limitations of this study.

1. Zhao X, Yue C: Gastrointestinal stromal tumor. *Journal of gastrointestinal oncology* 2012, 3(3):189-208 doi: 10.3978/j.issn.2078-6891.2012.031.
2. Von Mehren M, Randall RL, Benjamin RS, Boles S, Bui MM, Ganjoo KN, George S, Gonzalez RJ, Heslin MJ, Kane JM: Soft tissue sarcoma, version 2.2018, NCCN clinical practice guidelines in oncology. *Journal of the National Comprehensive Cancer Network* 2018, 16(5):536-563.
3. Casali P, Abecassis N, Bauer S, Biagini R, Bielack S, Bonvalot S, Boukovinas I, Bovee J, Brodowicz T, Broto J: Gastrointestinal stromal tumours: ESMO–EURACAN Clinical Practice Guidelines for diagnosis, treatment and follow-up. *Annals of Oncology* 2018, 29:iv68-iv78.
4. Landi B, Blay J-Y, Bonvalot S, Brasseur M, Coindre JM, Emile JF, Hautefeuille V, Honore C, Lartigau E, Manton G: Gastrointestinal stromal tumours (GISTs): French Intergroup Clinical Practice Guidelines for diagnosis, treatments and follow-up (SNFGE, FFCD, GERCOR, UNICANCER, SFCD, SFED, SFRO). *Digestive and Liver Disease* 2019, 51(9):1223-1231.
5. Zidan M, Hassan E, Refaie M: A Successful Central Gastrectomy and Gastro-Gastric Anastomosis for a Large Gastric GIST. *Journal of Gastrointestinal Cancer* 2023 doi: 10.1007/s12029-023-00992-7.

**Reply 6:** It is stated in the article.( Page7- 8, line 231-253))

## **Reviewer B**

The category: “gastric stromal sarcoma” is not WHO/international sanctioned nomenclature. The correct nomenclature is “Gastrointestinal Stromal Tumor (GIST) of the stomach” or Gastric Gastrointestinal Stromal Tumor (GIS). The terminology needs to be updated.

**Reply:** Terms have been updated, see article highlighted in yellow.

The authors propose a novel nomogram for gastric GISTs. They do not comment on how their nomogram compares to existing nomograms such as the Memorial Sloan Kettering, which is

widely used in the West, and previously published nomograms from the East, such as the published by Li et al. (Front. Oncol. 2021; Volume 10 - 2020 | <https://doi.org/10.3389/fonc.2020.581855>)

**Reply:** The comments of the reviewers are very good, but because this study has not yet completed external validation, the nomogram needs further improvement and cannot be compared for the time being.

The authors appear to be confusing cause and effect in their analysis; resectable tumors have better prognosis because only early-stage tumors are resectable, not because surgery is a positive prognostic factor. Similarly, only unresectable, or recurrent tumors receive radiation, creating the association between radiotherapy and adverse prognosis. Association and causality are different.

**Reply:** Table 2 suggests that surgery is an independent prognostic factor.

The stratification of tumors in 4 histologic grades does not align with any of the histologic classifications used in GIST. Grading needs to be reconciled with existing reporting systems.

**Reply:** The grades downloaded from the database are classified as I-IV, and although inconsistent with the existing reporting system, there is nothing wrong with grading according to Grade I-IV.

The analysis contradicts all previous research on mesenchymal neoplasms, it does not show any effect of tumor size, but shows an outsized effect of marital status. These results are perplexing, and if correct would indicate that most of the existing literature on malignant mesenchymal tumors is wrong.

**Reply:** The conclusion of this paper does not show that the prognosis of GIST is related to tumor size, but it is considered to be related to the following two aspects: 1. The number of cases is not enough, and it is necessary to further increase the number of cases for verification in follow-up studies. 2. Follow-up studies also need external validation.

**Changes in the text:** we have modified our text as advised (Page 8, line 244-246).

Most parameters in the nomogram do not provide any useful information: it is obvious that advanced stage, high-grade tumors, affecting older individuals do worse than early stage, low-grade tumors, affecting younger individuals. The effect of gender and marital status is interesting. However, without information on the molecular subtypes of the GIST cohort, these results cannot be used to decide which specific type of adjuvant treatment should be given to a particular individual.

Nowadays, factors such as type of driver mutations, germline vs. sporadic, and variant mutations within specific exons, allow selecting the type of targeted therapy that would benefit the most patients with advanced disease or patients at increased risk for recurrence. The proposed nomogram ignores the most important advances in the prognostication and therapy of GISTs.

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nomogram ignores the most important advances in the prognostication and therapy of GISTs. This is a limitation of this study, and further research is needed. Due to the limited case information provided by the SEER database, further external verification is needed to improve the accuracy of the model.

**Changes in the text:** we have modified our text as advised (Page 8, line 246-251).