

Reviewer #1:

Scientific Quality: Grade C (Good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Major revision

Specific Comments to Authors:

Comments to the Authors Summary

The study aims to analyze the correlation between imaging findings and both the rupture and pathological risk grades of gastrointestinal stromal tumors (GIST). The results indicate associations between various factors like tumor diameter, tumor morphology, internal necrosis, and gas-liquid interface with GIST rupture. Similarly, gender and tumor diameter were found to correlate with the pathological risk of GIST.

Abstract

1. Methods: A sentence in the "Methods" section seems better suited for the "Results" section, as it discusses study outcomes. I suggest relocating this sentence for better structural clarity.

**Response: Thanks to your comments, we have revised this sentence.**

2. Results: The statement "gender was negatively correlated with the pathological risk grades of GIST" could be clearer. Could you specify whether male or female gender is associated with lower or higher risk grades?

**Response: Thank you very much for this professional advice. We have modified this statement.**

Introduction

1. On page 3, line 5, you state that needle biopsy is not recommended before surgery. Please include relevant references to substantiate this assertion.

Response: Thank you very much for your comment. According to Chinese consensus in diagnosis and treatment of gastrointestinal stromal tumor, GIST tumors are soft in texture, and inappropriate preoperative biopsy may cause tumor seeding, dissemination and bleeding. Most primary GISTs can be completely resected, so routine biopsy before surgery is not recommended. We have added citations to this document.

2. The study's aim is briefly outlined but could be enhanced by the addition of specific research questions or hypotheses, which would lend more clarity and focus to the introduction.

Response: We are very grateful to the reviewers for their excellent suggestions. We have added content on specific hypotheses.

## Methods

1. Table 1: Is the table original? Although references are cited, it might be helpful to also mention established risk classifications like the Miettinen or AFIP systems.

Response: Thank you for your comment. The contents of this table are the standards for pathological risk grades after primary GIST resection that we formulated based on the results of many similar studies.

2. Patient Selection and Radiological Techniques: The absence of detailed criteria for these elements may compromise the study's replicability. Providing this information is recommended.

Response: Thank you very much for your professional suggestion. Patients were selected based on inclusion and exclusion criteria, which can be seen in the "Subjects" subsection. We have added the specific content of CT detection methods in the "CT indicators" section (modified to "CT detection methods and indicators").

3. Statistical Analysis: Pearson's correlation is designed to measure linear relationships between quantitative variables. The method is applied here to a mix of factors, some of which are not quantitative. Consulting a statistician and potentially using logistic regression may offer a more appropriate analytical approach.

Response: Thank you very much for your professional comments. After consulting statistical a statistician, we revised this part and re-used logistic regression for analysis. The modified results can be seen in Tables 3 and 4 and Sections 2.3 and 2.4.

## Results

1. Table 2: Categorizing continuous variables may affect the study's conclusions, especially given Pearson's correlation's sensitivity to outliers and limitation to linear relationships. Providing additional statistics like median, 25th, and 75th percentile values could offer a more comprehensive understanding of data distribution.

Response: Thank you very much for your professional suggestions, which are very helpful for us to improve the quality of the manuscript. Based on your suggestions and combining data types, we re-presented and compared the relevant indicators of the ruptured group and the unruptured group.

2. Table 2: Were cases of rectal GIST, which generally have higher malignant potential, not included in this study? Additionally, the lack of information on treatment modalities and presence of metastases is a noticeable omission.

Response: Thank you very much for your comments. Based on the inclusion and exclusion criteria, rectal GIST was included in this study. In addition, the main purpose of this study was to study the correlation of imaging findings with the rupture and pathological risk of GIST, and the lack of information on treatment modalities and

presence of metastases is a shortcoming of this study, which we have added in the discussion.

3. Table 2: Please change the column header from "Factors, grades" to "Grades."

Response: Thanks for the advice. To avoid confusion, we have deleted "factors" here.

4. On page 8, lines 3-4, the statement "tumor diameter was inversely related to the pathological risk grades of GIST" warrants verification. Is this accurate?

Response: Thank you so much for your suggestion. We have revised this sentence.

5. Beyond statistical significance, the clinical relevance of the findings should also be discussed.

Response: Thank you very much for your professional advice. We have added this section to the Discussion.

## Discussion

1. Comparing your findings with existing research would add both depth and context. The current approach, which uses established risk factors for correlation analysis, could be perceived as lacking in novelty. Addressing this by discussing how your results align or differ from existing research could be beneficial.

Response: Thank you very much for your valuable comments. We have added a comparative analysis of similar research results to the discussion.

Reviewer #2:

Scientific Quality: Grade D (Fair)

Language Quality: Grade C (A great deal of language polishing)

Conclusion: Major revision

Specific Comments to Authors:

The manuscript is in general terms interesting, while very difficult to read due to major English problems and some inconsistencies, I will try to point some of the problems that I could face:

1. Title is not clear. In my understanding you are trying to predict risk of rupture and high risk tumors based on preoperative CT scans. The title should be changed as it is impossible to understand it without a full reading of the article.

**Response: Thank you very much for your suggestion, we have changed the title to "Analysis of factors associated with gastrointestinal stromal tumor rupture and pathological risk: a single-center retrospective study".**

2. " GIST biopsy samples are few and inconvenient, and easily lead to tumor metastasis" - while biopsy can indeed be difficult and many of us performe US guided fine needle biopsies, I cannot see why they would be incoveninet or lead to metastasis. Probably the author refers to open biopsies but they should pinpoint that. That is not a gold standard in clinical practice.

**Response: Thank you very much for your professional advice. During clinical biopsy, inappropriate biopsy can easily lead to tumor bleeding and rupture, leading to tumor dissemination. We further clarify this in the revised manuscript.**

3. "selected as the research objects" I believe it should be rephrased. Calling patients objects is not advisable.

**Response: Thanks to your suggestion, we deleted this word.**

4. Exclusion criteria: the lesion was tumor relapse - Probably in inclusion criteria you should point to primary tumors only.

**Response: Thank you very much for your professional advice. We accept this suggestion.**

5. Table 1 does not refer to your data and should be used as supplementary data if at all.

**Response: Thank you very much for your comments, we have revised Table 1 into Supplementary Table 1.**

6. CT indicators: - axial measurement of the diameter - why? why not coronal? I suggest using the maximum diameter. - Tumor morphology: Observe whether the shape of the tumor is regular - that is very unclear and very much observer dependent. Please define without so much subjectivity or do not use such a characteristic. - same for clear and unclear boundary - I am not used with such characteristics. Do you define a propensity to invade or is it invasion in adjacent organs? Again very subjective. If you use that please reevaluate with double or triple blinded readings and see if you have all the same results.

**Response: Thank you so much for your suggestion. In fact, the tumor diameter is measured by detecting the coronal image. We judge whether the shape of the tumor is regular based on whether it conforms to an ellipse or a circle. If the shape of the tumor tends to be elliptical or round, we consider its shape to be regular. As for boundary, unclear boundary means a propensity to invade. Your suggestions are great, and we plan to re-evaluate double-blind or triple-blind readings later to see if we get the same results.**

7. Criteria for rupture: bloody ascites - please check in literature if all agree with you. If the tumor is not opened intraoperatively it is hard to sustain. Microscopic infiltration of other organ - I disagree - that is not rupture; Intralesional dissection or segmental

resection are surgeon induced errors and I would not consider them as rupture in the sens of your paper, but intraoperative contamination based on bad surgery or impossibility to perform adequate surgery (in such cases no gesture is probably better + neoadjuvant therapy).

Response: Thank you very much for your professional advice. As mentioned in our discussion, the current standards for tumor rupture are not uniform. We specified this standard based on the information in relevant references. It may not be satisfactory to all researchers, but I believe that in the process of continuous improvement of research, This standard will definitely gain more and more recognition from everyone.

8. I disagree with you statistical evaluation. It might be correct but it analyses wrong parameters. If you evaluate the risk of rupture based on imaging, than tumor morphology and Ki67 have nothing to do with it. These are postoperative data and have no place in here. Similar with evaluation of pathological grade - ou should only use imaging data in order to predict the type o tumor in the end.

Response: Thanks to your criticism, we re-used logistic regression analysis for evaluation and revised the title of the manuscript to go beyond imaging evaluation.

9. Page 8 - tumor diameter is inversely correlated with risk grades. I really do not believe. That means that small tumors have a high risk. I presume it is an error.

Response: Thank you very much for pointing out our error. In the revised manuscript we have made changes. In fact, the longer the tumor diameter, the higher the pathological risk of GIST.

10. Page 8 "In addition, the higher the Ki-67 expression index, the higher the pathological risk grades of GIST". while not essential in our discussion as you do not

discuss imaging data, I believe we all agree that Ki67 refers to rapid multiplying tumors and by definition should be correlated with high risk tumors. Plus it has nothing to do with your proposed research.

Response: Thank you very much for your comments and we have removed this statement in the revised manuscript.

11. Page 10: "The results showed that gender was negatively correlated with pathological risk grades of GIST" that is a nonsense. Do not know even what you mean. How can male/female correlate with anything.

Response: Thank you very much for your criticism. We clarified in the revised manuscript that males have higher pathological risk grades of GIST.

12. "Tumor diameter was positive correlated with pathological risk grades of GIST ( $r = 0.47$ ,  $P = 0.01$ )." that contradicts with observation 9 in my document.

Response: Thank you very much for your comment. We have deleted this part of the data and re-analyzed using logistic regression.

13. Discussion : We found that pathological risk grades, tumor diameter, tumor shape, internal necrosis, air-liquid interface and Ki-67 expression index were associated with the rupture of GIST, and gender, tumor diameter, tumor rupture, Ki-67 expression index were correlated with pathological risk grades of GIST. Our findings suggested that, in the GIST patients we screened, tumor diameter, tumor shape, internal necrosis, and gas-liquid interface were risk factors associated with the rupture of GIST, while gender and tumor diameter were associated with pathological risk grades of GIST." it looks like you repeat the sentence twice.

Response: Thank you very much for your suggestion, we have re-simplified this part in

the revised manuscript.

14. "Nonetheless, the definition of tumor rupture is controversial, with many surgeons arguing that tumor rupture is defined as not infiltrating adjacent structures at the time of surgical resection[17]" I do not understand that nor I believe it is correct. This statement should be made more clear. I believe is out of context.

Response: Thank you very much for your comment. We have revised this sentence in the revised manuscript.

15. Signs of malignancy on CT scans should not be in discussion. Maybe a table in supplementary data or appendix. Conclusion: I believe your data are interesting but very inconsistent analysis. Define better what you wish to study and reorganize your data.

Response: Thank you very much for your comment. We have revised the topic of the manuscript beyond imaging analysis, so here we propose to keep this part of the discussion.



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## Second round

Reviewer 1

The authors should follow the classic structure of a scientific article. This new version is chaotic and some chapters I do not understand. Introduction is a conclusion of the work while materials and methods starts with results of your work. In this form the paper can not be read.

**Response:** Thank you very much for your comment. In fact, we are not very familiar with the submission system, and the new version is automatically generated by the system. Here we provide the latest modified version as an attachment, hoping to meet your requirements.



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Reviewer 2

Comments to the Authors Thank you for your revisions and the comprehensive responses to the reviewer's queries. I have reviewed the amended manuscript and find it mostly acceptable. Nevertheless, there is one aspect that needs further clarification, as indicated below. In regard to my initial question about the Methods section (#1), your response suggests that the table presented sets the standards for pathological risk grades following primary GIST resection. This table is purportedly based on the synthesis of findings from multiple related studies. I recommend that you explicitly mention this in the Methods section and cite the relevant references to substantiate the originality of Table 1.

**Response: Thank you so much for your suggestion. We mention this explicitly in the Methods section and cite relevant references [8, 11, 12] to substantiate the originality of Table 1.**