

Dear editor and reviewers,

Thank you for offering us an opportunity to improve the quality of our submitted manuscript (Manuscript Number: 88927). We appreciated very much the reviewers' constructive and insightful comments. In this revision, we have addressed all of these comments/suggestions. We hope the revised manuscript has now met the publication standard of your journal.

We highlighted all the revisions in yellow color.

On the next pages, our point-to-point responses to the queries raised by the reviewers are listed.

Reviewer #1

Specific Comments:

Comment 1: The manuscript is disorganized and has been poorly written. It should be elaborated to reach scientific writing. The text should also be checked for the English language.

Response: Thank you for your valuable feedback on our article. We have carefully considered and revised it based on your comments. We acknowledge your concerns and assure you that we have taken your comments seriously to improve the manuscript. We have carefully revised the organization of the manuscript to enhance its clarity, coherence, and scientific writing standards. Additionally, we have thoroughly reviewed and edited the text to ensure that it meets the required standards of scientific writing and language proficiency. We sent our revised manuscript to a professional English language editing company to polish the manuscript further. And we have provided a new language certificate along with the manuscript. We are committed to addressing the issues you have raised and have made every effort to enhance the quality and readability of the manuscript. We sincerely appreciate your input, and we are grateful for the opportunity to improve our work based on your valuable feedback.

Comment 2: The abstract section is descriptive and not statistically informative. The

key points of the results section should be addressed in this section.

Response: Thank you for your helpful suggestions regarding our article. We appreciate your professional input. We acknowledge the importance of ensuring that the abstract provides a clear and concise summary of the key findings and statistical information from the results section. We have revised the abstract to include the essential statistical information and key findings, ensuring that it effectively represents the results of the study (Lines53-59). Thank you for your insightful comments and constructive feedback.

Comment 3: The results section is busy and exhausting and all the findings of the tables are repeated in it. Tables 5 and 6 would be deleted and replaced by tables containing univariate and multivariate analyses for disease-free survival and overall survival. The components of SIRI and AFR such as neutrophil count, monocyte count, lymphocyte count, albumin, and fibrinogen serum levels should be included in the univariate and multivariate Cox regression analyses to determine whether SIRI and AFR are independent variables or not. Additionally, the components of SIRI and AFR should be included in Table 4.

Response: Thank you for your helpful suggestions regarding our article. We appreciate your professional input. After careful reflection and research, we have carefully considered your feedback and suggestions and have made significant improvements to the manuscript. Specifically, we have reorganized and consolidated the follow-up data, resulting in the acquisition of five-year OS and DFS information for the patients. Additionally, we have conducted further follow-up to obtain missing data for some patients. Subsequently, we performed survival analysis for the included patients and have generated Table 5 and Table 6 and removed the original table. Moreover, we have incorporated the components of SIRI and AFR, such as neutrophil count, monocyte count, lymphocyte count, albumin, and serum fibrinogen levels, into the single-factor and multi-factor Cox regression analysis, as per your recommendation. Additionally, the components of SIRI and AFR have been reanalyzed and added to Table 4. The specific results can be found in the revised manuscript. Your feedback is invaluable, which will improve the quality and clarity of the results section and tables.

Comment 3: Minor comments: The authors should precisely use the words "recurrence" "relapse" and "metastasis". Recurrence and relapse may be locoregional or distant (metastasis). The authors used "recurrence" and "relapse" as local recurrent diseases. So, it is better to use "locoregional recurrence" instead of "recurrence" and "relapse" in the text.

Response: Thanks for your constructive feedback on our manuscript. We have replaced the term "recurrence" or "relapse" with "locoregional recurrence" throughout the manuscript, as your suggestion. We believe that this change has significantly improved the clarity and accuracy of our manuscript.

Reviewer #2

Specific Comments:

Comment 1: In the abstract section, it is necessary to add background information (see the format of the journal). In addition, the period of time related to study should be added. Please describe the three groups of patients mentioned in this section. The main statistical methods should also be included as well as the main results with statistical values. There are some words with grammatical errors and some typos.

Response: Thank you for the reviewer's suggestion, we have completed the background information. Responding to your comment is the Lines29-37. In addition, we have added the period of time related to study. Responding to your comment is the Lines45-46. In response to your suggestion, we have provided detailed descriptions of the three patient groups (Lines48-49) and have incorporated corresponding statistical information in this section of the manuscript (Lines53-59). Regarding your feedback on some words with grammatical errors and some typos, we acknowledge that our original manuscript contained inaccuracies in expression, which we have corrected. We sent our revised manuscript to a professional English language editing company to polish the manuscript further. And we have provided a new language certificate along with the manuscript. We sincerely appreciate your input, and we are grateful for the opportunity to improve our work based on your valuable feedback.

Comment 2: In the introduction section, please check the references 2 in order to correct the following phrase: “Gastric cancer is the second-highest cancer to be diagnosed and the secondary rate for gastric cancer compared to most developed countries2.” The authors should add some complications as examples in the next phrase: “Gastrectomy offers a substantial risk of postoperative complications.....”

Response: Thank you for your helpful suggestions regarding our article. We appreciate your professional input. We have re-read the cited literature carefully and found part of the misinformation, and changed the original sentence from “the secondary consideration of cancer-related death in China” to “the third leading cause of cancer-related deaths in China” (Lines79). According to your suggestion, we have added some complications as examples in the next phrase: “Gastrectomy offers a substantial risk of postoperative complications.....”. Responding to your comment is the Lines87-88. We have addressed these issues and have made the required revisions to improve the accuracy and comprehensiveness of the introduction section and references. We greatly appreciate your input.

Comment 3: In the following phrases it is necessary to add the original references because the reference 6 and 9 are not directly related to the phrases: “In actuality, postoperative complications following gastric surgery were reported to be 46%6.” and “Relevant evidence reveals that more than 70%gastric cancer can lead to a significant shortening of the time a patient survives9.”

Response: Thank you for the reviewer's suggestion, which we have incorporated after thorough discussion. Responding to your comment is the replaced References 6 and References 9, we have removed the original and rephrased them to enhance the precision and clarity of the expression in the text.

Comment 4: Please add the references appropriate to the next phrase: “A significant variety of studies have increasingly reported that SIRI is strongly associated with the prognosis of a multitude of tumors.” The acronym OS should be defined.

Response: Thank you for the reviewer's suggestion, which we have incorporated

relevant literature. Responding to your comment is the added References 15-17, to improve precision of expression. In addition, based on your suggestion, we defined the acronym OS. Responding to your comment is the Lines 112. Thank you for your careful review and valuable feedback on our manuscript.

Comment 5: The authors sometimes write albumin-fibrinogen ratio or fibrinogen-to-albumin ratio, please check and correct them.

Response: Thank you for the reviewer's suggestion and insightful comments. We appreciate your attention to detail and would like to address your query. We acknowledge your feedback regarding the use of both "albumin-fibrinogen ratio" and "fibrinogen-to-albumin ratio" in the manuscript. AFR = albumin/fibrinogen, FAR = fibrinogen/albumin, the components of these two indicators are the same. We would like to emphasize that these terms are indeed reciprocals of each other and can be used interchangeably based on the context of the discussion. Therefore, both terms are valid and convey the same concept, and their usage is consistent with the reciprocal relationship between the two ratios. When using ROC curve analysis, in order to comply with the application conditions and to facilitate the calculation of the predictive power of SIRI combined with AFR, we take the fibrinogen-to-albumin ratio as the calculation amount. The ratio of AFR (albumin-fibrinogen ratio) is essentially the inverse of the ratio of Fibrinogen-to-Albumin. This is in accordance with the principles of calculation. To clarify this concept and prevent reader confusion, we have provided a more extensive description in the manuscript (Lines 285-288). Additionally, we appreciate your understanding of the need for comprehensive literature review to support the research findings. We concur that the inclusion of both AFR and FAR in the literature search is essential for ensuring the accuracy and broad applicability of our study. We have used AFR and FAR interchangeably in the manuscript to reflect the comprehensive nature of our literature review and to ensure that our findings are robust and widely applicable. We appreciate the opportunity to address your concerns and provide clarification on this matter. We hope this explanation addresses your concerns. We appreciate the insightful comments of the reviewers and remain committed to

enhancing the precision and excellence of the article.

Comment 6: In the materials and methods section, specifically in Patients and Follow-Up, please add the numbers of patients analyzed, including mean age and percentage of sex.

Response: Thank you for the reviewer's suggestion, we have completed the corresponding information. Responding to your comment is the Lines135-137. We greatly appreciate your input.

Comment 7: In the following phrase add the reference of Dindo et al. ("Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey." or the reference related to a review that includes this information): "...and all complications were graded for severity according to the Clavien-Dindo complication grading system²⁶,"

Response: Thank you for your helpful suggestions regarding our article. We appreciate your professional input. We have completed the corresponding information. Responding to your comment is the added Reference 33.

Comment 8: The authors should include the complications according to the proposed classifications: "...with Grade I or II complications were categorized as minor complications, whereas Grade III and higher were characterized as major complications, whereas Grade III and higher were characterized as major complications."

Response: Thank you for your valuable feedback and comments on our manuscript. We understand your suggestion to include complications according to the proposed classifications, where Grade I or II complications are categorized as minor complications, and Grade III and higher are characterized as major complications. In our study, we categorized patients without postoperative complications and those experiencing Grade I-II complications into the "no or minor complications" group, while patients experiencing Grade III or higher complications were grouped as "major complications." We believe that this approach to grouping is appropriate in the context of our study. First, similar grouping methods have been used in other studies and have

been proven to be effective¹. Secondly, different severities of postoperative complications have varying impacts on patients. Severe complications may lead to longer hospital stays, higher mortality rates, and increased recurrence rates. Therefore, such a grouping would also better reflect the impact of different severities of complications on patients. Thirdly, grouping patients into no or mild and severe categories can simplify and clarify statistical analysis. In summary, we used subgroups that were more in line with our research aims. We are grateful to your constructive and valuable comments, but equally we appreciate your understanding.

1. Yildirim M, Koca B. Lymphocyte C-reactive protein ratio: A new biomarker to predict early complications after gastrointestinal oncologic surgery. *Cancer Biomark* 2021;31(4):409-17. doi: 10.3233/cbm-210251 [published Online First: 2021/06/22]

Comment 9: Please describe the method performed for immunohistochemistry (ki67, P53, and Her2), including the method for their determinations.

Response: Thank you for your helpful suggestions regarding our article. We appreciate your professional input. We have completed the corresponding information. Responding to your comment is the Lines143-152. We appreciate the reviewers' feedback, which fortified our article's accuracy and superiority.

Comment 10: What day is peripheral venous blood drawn after surgery?

Response: Many thanks to the reviewers for their inquiries. We appreciate the opportunity to address this query and provide clarification. We acknowledge your question about the timing of peripheral venous blood draw after surgery. In our study, we focused specifically on preoperative blood parameters and did not involve the collection of blood samples postoperatively. Therefore, the timing of peripheral venous blood draw after surgery was not a part of our investigation. We acknowledge that the timing of peripheral venous blood draw after surgery was not included in our investigation. This indeed represents a limitation of our study, and we appreciate your astute observation in this regard. We recognize the importance of considering postoperative blood parameters as part of a comprehensive analysis of the clinical

course and outcomes following surgery. Moving forward, we are committed to addressing this limitation and plan to explore the dynamics of peripheral venous blood parameters in the postoperative period in our future research endeavors. We believe that investigating the changes in blood parameters following surgery will provide valuable insights into the physiological responses and recovery processes in surgical patients. We ensure that this limitation is clearly articulated in the manuscript (Lines437-438), and we appreciate your understanding as we continue to refine our research focus in subsequent studies.

Comment 11: Were chronic inflammatory diseases excluded?

Response: Many thanks to the reviewers for their inquiries. We acknowledge your observation that the exclusion of chronic inflammatory diseases was not explicitly stated in the manuscript, despite being an important aspect of our study design. We would like to confirm that during the data collection phase, we indeed excluded patients with chronic inflammatory diseases from our study cohort. We regret that this critical information was not adequately articulated in the manuscript. We understand the significance of transparently documenting the inclusion and exclusion criteria, and we apologize for any confusion that may have arisen from this oversight. We have ensured that the exclusion of chronic inflammatory diseases from our study cohort is clearly stated in the manuscript to provide a comprehensive understanding of our research methodology (Lines163). Thank you for bringing this to our attention, and we appreciate your understanding as we work to address this issue in the manuscript.

Comment 12: In the following phrase: “The average age of the population group was 60.29 ± 9.79 (25–87).” Is the age range correct? The acronym TNM should be defined in table 3. In the results header “3.6 Establishment of the SIRI-AFR Score.” The results, sensitivity, and specificity of the Youden index are unclear.

Response: Many thanks to the reviewers for their inquiries. After reviewing the age ranges reported in the manuscript, we found that the actual age ranges were correct, but there was an error in the presentation of the age ranges. The correct age range for the

population group should be 25–87 years. We apologize for this oversight and any confusion it may have caused. We have promptly made the necessary corrections to ensure the accurate reporting of the age range in the manuscript (Lines215-216). We acknowledge your suggestion to define the acronym "TNM" in Table 3 for the benefit of the readers. We have ensured that the meaning of "TNM" is explicitly defined in the table to enhance the clarity and comprehensibility of the information presented. Furthermore, we appreciate your valuable feedback, and we are committed to ensuring that the information presented in the manuscript is clear and accurate. We have revised the Results section to provide a more explicit explanation of the sensitivity and specificity calculations and their association with the Youden index (Lines296-298). Thanks again to the reviewers for their questions, which were very helpful in further refining our research.

Comment 13: The following phrase is incompleted: “Lymphocytes played a part in immunologic surveillance and were contributory to identification and destruction³⁷.” In addition, the reference 37 is not appropriate, please add the correct one.:

Response: Thank you for your helpful suggestions regarding our article. We appreciate your professional input. We have completed the phrase mentioned above. Responding to your comment is the Lines381. In addition, we apologize for the error in referencing and the inconvenience it may have caused. We have promptly corrected the Reference 37 and replaced it with the appropriate one in the manuscript. Responding to your comment is the added Reference 44. Thank you for bringing this to our attention, and we appreciate your efforts in ensuring the accuracy and quality of our manuscript.

Comment 14: The next phrase requires another reference to support the information: “Unlike other indicators of inflammation, inflammatory state of the patient after chemotherapy⁴⁰.”

Response: Thank you for your thoughtful review of our manuscript and for providing valuable feedback. We appreciate your attention to detail and your suggestion to include an additional reference to support the information presented in the manuscript. We have

carefully reviewed the relevant literature to identify an appropriate reference that aligns with the information in the specified phrase and provided the necessary citation to support the statement. Responding to your comment is the added Reference 48.

Comment 15: Change Mario for Schioetroma in the following phrase: “Recently, Mario and his colleagues confirmed that SIRI can be considered to potentially predict anastomotic fistulas after total gastrectomy⁵⁰.” Please correct the following “You's”: In accordance with You's findings,

Response: Thank you for your valuable feedback and your diligent review of our manuscript. We apologize for the error in referencing the name and the confusion it may have caused. We have promptly corrected the name "Mario" and replaced it with the correct name "Schioetroma" in the manuscript (Lines403). And corrected the name " You's " and replaced it with the correct name " You X " in the Lines409. We are grateful to the reviewers for their comments, which have helped to further improve the quality of the article.

Comment 16: GC needs to be corrected in the next sentence: “Subsequently, we lacked evaluation of postoperative SIRI and AFR dynamic changes in a relatively large cohort of GC patients,”

Response: Thank you for your insightful comments and your attention to detail in reviewing our manuscript. We acknowledge the typographical error in the sentence, and we have promptly corrected "GC" to the appropriate term “gastric cancer” in the manuscript (Lines438). We appreciate your efforts in ensuring the accuracy and quality of our manuscript.