

Dear Editors and Reviewers:

We are so appreciated for your letter on our manuscript entitled “Clinical features of intracerebral hemorrhage in patients with colorectal cancer and its underlying pathogenesis” (Manuscript No: 69546).

We are also extremely grateful to the reviewers’ comments on our manuscript. Those comments are all valuable and very helpful for revising and improving our paper, as well as the important guiding significance to our researches. We have carefully considered every comment, and made cautious revision accordingly. Based on their suggestions, we have answered the questions in detail one by one, and the changes were highlighted in the manuscript with red colour. If you have any other questions about this revised manuscript, I would greatly appreciate it and make a further revision accordingly.

Yours sincerely

Zhijian Liang, PhD

Responses to Reviewers

Reviewer #1

The reviewer's comments: In this article, the authors attempted to investigate the clinical features and underlying pathogenesis of intracerebral hemorrhage in patients with colorectal cancer. However, your article is inadequately presented. Furthermore, there are many grammatical mistakes and spelling mistakes as well. Although the article has scientific rigor, several minor flows need to be improved before publication. Minor Comments: 1. The abstract section is worthy; just need to add a focus point in the abstract section. 2. Delete we, our etc. from the manuscript. 3. Change the sentence "Although the association between cancer and intracerebral hemorrhage (ICH) has attracted the interest of researchers, little attention has been paid to the clinical characteristics and mechanisms of specific cancer-related ICH". Need to make this lucid and clear. 4. Authors need to supplement the up to information related to Colorectal cancer with recent references. This is mandatory. 5. Originality of the work should be improved by the author (either in the conclusion or introduction section). 6. Write the objective/aim of the research clearly in the last paragraph of the introduction section. 7. To minimize the effects of CRC progression on physical activities, patients' functional prognosis on the 30th day after hemorrhage was measured using the modified Rankin Scale (mRS), and a mRS score > 3 was regarded as a poor prognosis. Where is the references? 8. Authors must need to explain figure 2 in the result section. 9. The discussion section is unclear and wordy. Many redundant sentences need to be deleted. 10. The flow of the discussion is still not perfect and unspecific. 11. Statistical analysis section is missing. Need to add precise information (whether mean or SD or SEM etc.). 12. Conclusion has to be improved by including more points (personal recommendation, limitation, etc.). 13. Spacing, punctuation marks, grammar, and spelling errors should be reviewed wholly.

Comment 1: The abstract section is worthy; just need to add a focus point in the abstract section.

Reply: The purpose of this study was to investigate the clinical features and the underlying pathogenesis of ICH in patients with CRC.

Comment 2: Delete we, our etc. from the manuscript.

Reply: Thank you for your constructive suggestion. We checked the words we, our etc. one by one, and deleted them from the manuscript. We adjusted the sentence structure when necessary.

Comment 3: Change the sentence “Although the association between cancer and intracerebral hemorrhage (ICH) has attracted the interest of researchers, little attention has been paid to the clinical characteristics and mechanisms of specific cancer-related ICH”. Need to make this lucid and clear.

Reply: Thanks for your valuable comment. Actually, it was our expressive mistake. We changed the sentence to “The association between cancer and intracerebral hemorrhage (ICH) has long been studied, however little attention has been paid to the hemorrhagic cerebrovascular events in patients with colorectal cancer (CRC)” in the Core Tip section.

Comment 4: Authors need to supplement the up to information related to Colorectal cancer with recent references. This is mandatory.

Reply: Thanks for your constructive suggestion. We have completed this work and added recent references No 10, 20, 21, 22, 25 and 26 related to colorectal cancer.

Comment 5: Originality of the work should be improved by the author (either in the conclusion or introduction section).

Reply: Thanks for your constructive comment. We have improved the originality of our work either in the conclusion or introduction section in the revised manuscript.

Comment 6: Write the objective/aim of the research clearly in the last paragraph of the introduction section.

Reply: Thank you for reminding me. we have written the objective of our study clearly in the last paragraph of the introduction section.

Comment 7: To minimize the effects of CRC progression on physical activities, patients' functional prognosis on the 30th day after hemorrhage was measured using the modified Rankin Scale (mRS), and a mRS score > 3 was regarded as a poor prognosis. Where is the references?

Reply: We are very sorry for our negligence. We have added the reference No 13 in the *Collection of clinical data* section.

Comment 8: Authors must need to explain figure 2 in the result section.

Reply: Thank you for reminding me. We have added the explanation of figure 2 to the end of the second paragraph in the result section.

Comment 9: The discussion section is unclear and wordy. Many redundant sentences need to be deleted.

Reply: It was a very constructive suggestion. We carefully revised the discussion section, deleted many redundant sentences, and made some modifications. The changes was marked in red in the revised manuscript.

Comment 10: The flow of the discussion is still not perfect and unspecific.

Reply: It was a constructive and meaningful advice to our study. We have optimized the flow of the discussion in the revised manuscript. In paragraph

1 to 3 in discussion section, we analysed the clinical characteristics of patients with colorectal cancer and intracerebral hemorrhage. The first paragraph mainly introduced that colorectal cancer could increase the incidence of intracerebral hemorrhage. The second paragraph described that patients with colorectal cancer and intracerebral hemorrhage were often found to have lobar hemorrhage, distant metastases and a poor prognosis. The third paragraph introduced that intracerebral hemorrhage might be the initial symptom of colorectal cancer. In paragraph 4 to 7, We analysed the possible mechanism. The 4th paragraph suggested that intratumoral hemorrhage and coagulopathy might be the main mechanisms. The 5th paragraph mainly introduced the possible mechanism of intratumoral hemorrhage in patients with colorectal cancer and intracerebral hemorrhage. The 6th paragraph mainly described the potential pathogenesis of coagulopathy. The 7th paragraph suggested the possible role of cancer markers in intracerebral hemorrhage. The 8th paragraph introduced some problems encountered in clinical practice and possible solutions. We put forward some deficiencies in our study in the last paragraph. By optimizing the discussion process, readers should be able to better understand.

Comment 11: Statistical analysis section is missing. Need to add precise information (whether mean or SD or SEM etc.).

Reply: We are very sorry for our negligence We have added the statistical analysis section to the end of materials and methods section, and added precise information of quantitative data and qualitative data.

Comment 12: Conclusion has to be improved by including more points (personal recommendation, limitation, etc.).

Reply: Thanks for your constructive advice. We have added personal recommendation in the conclusion section.

Comment 13: Spacing, punctuation marks, grammar, and spelling errors should be reviewed wholly.

Reply: Thanks for your suggestion. We made cautious revision in these respects; besides, MedE Editing Service have edited our manuscript twice.

Responses to Science editor

Science editor's comments: Evaluation Report of First Decision Name of journal: World Journal of Gastrointestinal Oncology Manuscript NO: 69546 Title: Clinical features of intracerebral hemorrhage in patients with colorectal cancer and its underlying pathogenesis 1 Scientific quality: The manuscript is a retrospective study of the clinical features underlying intracerebral hemorrhage in patients with colorectal cancer. The topic is within the scope of the WJGO. (1) Classification: Grade B Summary of the Peer-Review Report: Name of journal: World Journal of Gastrointestinal Oncology Manuscript Type: ORIGINAL ARTICLE Manuscript Number: 69546 Clinical features of intracerebral hemorrhage in patients with colorectal cancer and its underlying pathogenesis In this article, the authors attempted to investigate the clinical features and underlying pathogenesis of intracerebral hemorrhage in patients with colorectal cancer. However, your article is inadequately presented. Furthermore, there are many grammatical mistakes and spelling mistakes as well. Although the article has scientific rigor, several minor flows need to be improved before publication. Minor Comments: 1. The abstract section is worthy; just need to add a focus point in the abstract section. 2. Delete we, our etc. from the manuscript. 3. Change the sentence "Although the association between cancer and intracerebral hemorrhage (ICH) has attracted the interest of researchers, little attention has been paid to the clinical characteristics and mechanisms of specific cancer-related ICH". Need to make this lucid and clear. 4. Authors need to supplement the up to information related to Colorectal cancer with recent references. This is mandatory. 5. Originality of the work should be improved by the author (either in the conclusion or introduction section). 6. Write the objective/aim of the research clearly in the last paragraph of the introduction section. 7. To minimize the effects of CRC progression on physical activities, patients' functional prognosis on the 30th day after hemorrhage was measured using the modified Rankin Scale (mRS),

and a mRS score > 3 was regarded as a poor prognosis. Where is the references? 8. Authors must need to explain figure 2 in the result section. 9. The discussion section is unclear and wordy. Many redundant sentences need to be deleted. 10. The flow of the discussion is still not perfect and unspecific. 11. Statistical analysis section is missing. Need to add precise information (whether mean or SD or SEM etc.). 12. Conclusion has to be improved by including more points (personal recommendation, limitation, etc.). 13. Spacing, punctuation marks, grammar, and spelling errors should be reviewed wholly. (3) Format: There are 2 tables and 2 figures. (4) References: A total of 27 references are cited, including 10 references published in the last 3 years. (5) Self-cited references: There is 1 self-cited reference. The self-referencing rate should be less than 10%. Please keep the reasonable self-citations (i.e. those which are most closely related to the topic of the manuscript) and remove all other improper self-citations. If the authors fail to address the critical issue of self-citation, the editing process of this manuscript will be terminated; (6) References recommendations: The authors have the right to refuse to cite improper references recommended by the peer reviewer(s), especially those published by the peer reviewer(s) him/herself (themselves). If the authors find the peer reviewer(s) request for the authors to cite improper references published by him/herself (themselves), please send the peer reviewer's ID number to editorialoffice@wjgnet.com. The Editorial Office will close and remove the peer reviewer from the F6Publishing system immediately. 2 Language evaluation: Classification: Grade B. A language editing certificate issued by MedE Editing Service was provided. 3 Academic norms and rules: The authors provided the Biostatistics Review Certificate, informed consent form, and the Institutional Review Board Approval Form. The authors have not provided the signed Conflict-of-Interest Disclosure Form and Copyright License Agreement forms. No academic misconduct was found by the Google/Bing search. 4 Supplementary comments: This is an unsolicited manuscript. The study was

supported by Foundation of Prevention and Control of Chronic Diseases in Central-South China(Guangxi) and Foundation of Science and Technology Plan Projects of Qingxiu District of Nanning. The topic has not previously been published in the WJGO. 5 Issues raised: None 6 Re-Review: Required 7 Recommendation: Conditional acceptance

Reply: Thank you for your constructive suggestions. We carefully considered all the comments of the reviewers, and made cautious revision accordingly. Based on their suggestions, we have answered the questions in detail one by one. There is 1 self-cited reference in our manuscript, which meets the rules. We are very sorry for our negligence. Actually, the signed Conflict-of-Interest Disclosure Form and Copyright License Agreement forms had been ready before manuscript submission. We will submit the signed Conflict-of-Interest Disclosure Form and Copyright License Agreement forms together with the revised manuscript.

Responses to Company editor-in-chief:

Comments of Company editor-in-chief: I have reviewed the Peer-Review Report, the full text of the manuscript, and the relevant ethics documents, all of which have met the basic publishing requirements of the World Journal of Gastrointestinal Oncology, and the manuscript is conditionally accepted. I have sent the manuscript to the author(s) for its revision according to the Peer-Review Report, Editorial Office's comments and the Criteria for Manuscript Revision by Authors. Before its final acceptance, please upload the primary version (PDF) of the Institutional Review Board's official approval in official language of the authors' country to the system; for example, authors from China should upload the Chinese version of the document, authors from Italy should upload the Italian version of the document, authors from Germany should upload the Deutsch version of the document, and authors from the United States and the United Kingdom should upload the English version of the document, etc.

Reply: Thank you for your constructive suggestions. We will upload the primary version (PDF) of the Institutional Review Board's official approval to the system together with the revised manuscript.