

Dear Editors and Reviewers:

We highly appreciate all of the insightful comments from the reviewers and editor of our work: Manuscript NO.: 78939, Review entitled " Predictive value of indirect bilirubin before neoadjuvant chemoradiotherapy in evaluating prognosis of local advanced rectal cancer patients". We have answered to each remark and altered the manuscript.

Reviewer #1:

Scientific Quality: Grade C (Good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Minor revision

Comments: Specify in the title of the work that the indirect bilirubin considered is the one before nCRT. Update, if possible, the bibliography (there are no works from 2021 and 2022).

Response: Thank you for reviewing our work and your valuable advice accordingly. We have revised our manuscript based on your suggestions. We have revised our title and added some recent relevant studies in 2021 and 2022 as references.

Reviewer #2:

Scientific Quality: Grade C (Good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Minor revision

Comment: Thank you so much for the opportunity to review this paper: Predictive value of the indirect bilirubin in evaluating the prognosis of local advanced rectal cancer patients treated with neoadjuvant chemoradiotherapy. I have some comments: Introduction: I understand the concept, but if you can, explain the pathophysiology of the indirect bilirubin and the rectal cancer.

Methodology: Why long course neoadjuvant treatment only? Exclusion criteria: please re-phrase. Also, the sentence: 3) malignant tumors occurred at other sites at the same time. Could be changed for synchronous tumor. How many weeks was the interval between the end of neoadjuvant treatment and surgery? Results: why the Pre-IBIL number was fixed in ≤ 6.2 $\mu\text{mol/L}$? Conclusion: Please rephrase, in your study, with the limitations and the retrospective nature, you found an association between a blood sample and oncological outcomes in patients with rectal cancer.

Response: Thank you for reviewing our work and your valuable advice accordingly. 1. We are sorry that no pathophysiology theory has been found to explain the pathophysiology of indirect bilirubin and rectal cancer, which is a direction for future research; 2. long-course neoadjuvant treatment was routinely performed in our center; 3. nCRT with a surgery interval is shown in Table 1; 4. the pre-IBIL number was fixed at ≤ 6.2 $\mu\text{mol/L}$ by using the median as the cutoff value; 5. we have revised our manuscript based on all of your suggestions.

Reviewer #3:

Scientific Quality: Grade B (Very good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Accept (General priority)

Comment: This topic is attractive for the oncological community. The manuscript is well written. In my opinion, the manuscript may be suitable for publication.

Response: Thank you for reviewing our work and your agreement with our work.