

Peer Review File

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Reviewer A

This study examined the influence of preoperative CrCl on the short-term prognosis of patients undergoing colorectal surgery. The analysis of 526 patients reveals that preoperative low-level CrCl and multi-organ combined resection stand out as salient prognostic factors, with an accentuated impact on elderly patients. These findings' implications for informed healthcare decision-making, particularly for CRC patients at an elevated risk of postoperative complications, are commendable and invaluable.

Comment #1 : In Table 3, complications are itemized in detail. Could you specifically highlight renal complications, such as acute kidney injury or acute tubular necrosis, particularly in patients with compromised CrCl?

Answer : Thank you for your valuable suggestion. Among the complications, there were 6 cases of urinary system related diseases, but only 1 case of renal insufficiency. His creatinine clearance is less than 70. However, because the number is too small, we believe that there is no statistical correlation. Therefore, it is not listed in detail in the table.

Comment #2 : Furthermore, as creatinine clearance is an evaluation tool and an indicator for CKD, could you elucidate the rationale behind choosing CrCl over eGFR? Including a discussion on their respective advantages and disadvantages would be enriching.

Answer : Thank you for your valuable suggestion. we have modified our text as advised (see Page 4, line 90-97).

Comment #3 : Could you also specify which variables were employed in the multivariate analysis? An elaboration on the selection criteria for inclusion in this analysis would be beneficial.

Answer : Thank you for your valuable suggestion. we have modified our text as advised (see Page 7-8, line 219-220).

Reviewer B

I have completed my review of your manuscript entitled "Effect of low-level creatinine clearance on short-term postoperative complications in patients with colorectal cancer" submitted to *Journal of Gastrointestinal Oncology*. I commend your efforts in conducting this detailed and valuable study exploring the relationship between preoperative creatinine clearance (CrCl) and postoperative complications in colorectal cancer (CRC) patients. This research significantly contributes to the existing literature by highlighting a potentially overlooked aspect of preoperative assessment and its implications on postoperative outcomes.

Your manuscript is well-organized, and the research methods and statistical analyses are generally sound. The findings are clearly presented, and the discussion provides insightful context about the implications of impaired renal function in the surgical prognosis of CRC patients.

Despite these strengths, I have several concerns that I believe should be addressed to enhance the quality and impact of the manuscript:

Comment #1: Justification of CrCl Threshold: The choice of a 70 mL/min cut-off for CrCl is not thoroughly justified in the context of the study population. The manuscript would benefit from an explanation regarding why this specific threshold was chosen and how it influences the categorization and outcomes of patients.

Answer: Thank you for your valuable suggestion. we have modified our text as advised (see Page 6, line 163-167).

Comment #2: Consideration of Muscle Mass: CrCl can be influenced by skeletal muscle mass, which is not discussed in the current manuscript. Given that creatinine production is related to muscle mass, variations in this parameter among the study population might affect CrCl levels, thereby influencing the interpretation of renal impairment and its consequences.

Answer: Thank you for your valuable suggestion. Creatinine is metabolized by muscle tissue. Measurements of muscle need to be determined by prospective collection of sarcopenia data. However, this study was a retrospective study, so data related to sarcopenia could not be included in the study. It is hoped that further studies will incorporate changes in muscle mass in the future.

Comment #3: Immune Function Assessment: While the manuscript suggests a connection between reduced CrCl and increased susceptibility to postoperative infections due to immune dysfunction, there is a lack of direct evidence supporting this within the study. Including preoperative immune status indicators, such as the neutrophil-to-lymphocyte ratio (NLR), could strengthen the understanding of the relationship between renal function, immune status, and postoperative outcomes.

Answer: Thank you for your valuable suggestion. we have modified our text as advised (see Page 7, line 198-199) and added some data (see Page 15).

Comment #4:

Introduction section:

The phrase "commonly seen malignancy" feels somewhat informal. "Common malignancy" or "prevalent cancer" would be more appropriate.

"Indicating a persistent pattern of expansion" is somewhat ambiguous. Clarifying what specifically is expanding (incidence rates, mortality rates, etc.) would make your statement more precise.

Instead of "influence pre-operative treatment decision-making," smoothing the sentence to "influence preoperative treatment and decision-making" would enhance the flow.

Answer: Thank you for your valuable suggestion. we have modified our text as advised (see

Page 3, line68\71\84).

Comment #5:

Methods section:

Instead of "Variables collected of patient clinicopathological characteristics included...," rephrasing to "Variables collected included patient clinicopathological characteristics such as..." would improve the sentence flow.

In the phrase "Variables including tumor location (rectum or colon), operative type ...," "including" should be changed to "included," reflecting that the list pertains to data collected in the past.

Answer: Thank you for your valuable suggestion. we have modified our text as advised (see Page 5, line126-127\140).

Comment #6:

Results section:

Starting a sentence with "And 250 patients had a low CrCl." is unnecessary. The sentence could begin with "In total, 250 patients..."

Repeating "significantly" in "patients with a low CrCl had a significantly higher NRS score ($p<0.001$), significantly lower BMI ($P<0.001$), and more comorbidities ($p<0.001$) than those with a high CrCl." is redundant. Smooth this to "patients with a low CrCl had significantly higher NRS scores and more comorbidities, along with lower BMI ($P<0.001$), compared to those with a high CrCl."

Answer: Thank you for your valuable suggestion. we have modified our text as advised (see Page 5, line191-192\196-197).

Comment #7:

Discussion section:

"The reason for this may be related to the relationship between kidney function and the immune system." can be made more concise with "This may be due to the relationship between kidney function and the immune system."

Instead of "In the meantime, the relevant literature demonstrates," you can modernize and make the expression more direct with "Concurrently, existing literature shows."

The repetition of "to" in "Therefore, when surgeons consider surgical treatment of CRC patients, special attention should be paid to patients with low CrCl." is clunky. Reframe this to "Therefore, surgeons should pay special attention to patients with low CrCl when considering surgical treatment for CRC."

Answer: Thank you for your valuable suggestion. we have modified our text as advised (see Page 8, line249-250\254\258-260).

Comment #8:

Conclusions section:

Avoid the repetition of "examined" and "after" in "This study examined the relationship between preoperative CrCl and short-term postoperative complications after CRC surgery." by rephrasing to "This study explored the relationship between preoperative CrCl levels and short-

term postoperative complications in CRC surgery."

Answer: Thank you for your valuable suggestion. we have modified our text as advised (see Page 8-9, line256-258).

Reviewer C

Comment #1:

In the methodology I suggest leaving the items measured in topics, including subdividing them into pre, intra and post-operative.

Answer: Thank you for your valuable suggestion. we have modified our text as advised (see Page 5, line126\140).

Comment #2: In lines 179 and 180, place percentages after the exact numbers

Answer: Thank you for your valuable suggestion. we have modified our text as advised (see Page 7, line191-192).