

April 27, 2020

Name of Journal: World Journal of Gastrointestinal Surgery

Manuscript NO: 54569 **Column:** Observational Study

Title: Predictive significance of cancer related-inflammatory markers in patients with locally advanced rectal cancer receiving neoadjuvant chemoradiation

Authors: Kitinat Timudom, Thawatchai Akaraviputh, Vitoon Chinswangwatanakul, Ananya Pongpaibul, Pornpim Korpraphong, Janjira Petsuksiri, Suthinee Ithimakin and Atthaphorn Trakarnsanga

Dear Editors:

We thank the reviewers for their insightful comments and suggestions. Below are our responses to the reviewers' concerns. In addition, we have implemented corresponding changes within the manuscript, which are highlighted throughout the text.

Reviewer #1 (Comments to Author):

1- At what point is the blood taken for measurement of the NLR/MLR and PLR? Is it taken before chemo-radiotherapy, after chemo-radiotherapy just before surgery?

RESPONSE: The complete blood count examination was performed at baseline before starting nCRT in all patients. We have modified the text to reflect this (p.4, pp.26 and p.5, pp.11-12)

2- Was the timing of the blood test standardized for all patients?

RESPONSE: We took the blood sample in all patients at baseline before starting neoadjuvant chemoradiation. We have modified the text to clarify this (p.5, pp.11-12)

3- Do the authors consider the timing of the blood test to be relevant to their findings?

RESPONSE: The main objective of this article is to evaluate the correlation between ratios of these markers and pathological outcomes in term of pathological stages and NAR score

(predictive role). Therefore, we have used the pretreatment blood test (before starting chemoradiotherapy) instead of posttreatment blood exam. We have modified the text to clarify this (p.4, pp.23-25)

4- Indicate how the new results can help the clinic. If they were to perform a larger study and showed a statistical relevance to the NLR/MLR and PLR, how would that help clinicians treat the patients?

RESPONSE: We found restricted response to nCRT with high NAR score among patients with high ratios of these inflammatory markers. Although, the differences were not statistically significant, because the number of patients were limited. We plan to perform a further study of larger population by multicenter study. We have modified the text to reflect this (p.8, pp.17-19)

Another potential study, in patients with high level of pretreatment NLR, MLR, and PLR group, standard nCRT should be warranted. upfront chemotherapy or total neoadjuvant approach may play the important role in this patients. (p.8, pp.8-12)

Science Editor (Comments to Author):

1-Supplement the time for blood collection for NLR / MLR and PLR measurement.

RESPONSE: The complete blood count examination was performed at baseline before starting nCRT in all patients. We have modified the text to reflect this (p.4, pp.26 and p.5, pp.11-12)

2- Indicate when to take blood (before or after radiotherapy and chemotherapy).

RESPONSE: The complete blood count examination was performed at baseline before starting nCRT in all patients. We have modified the text to reflect this (p.5, pp.11-12)

3- Standardize blood test time for all patients.

RESPONSE: We took the blood sample in all patients at baseline before starting neoadjuvant chemoradiation. We have modified the text to clarify this (p.5, pp.11-12)

4- Supplement the relationship between blood test time and the findings of this article.

RESPONSE: The main objective of this article is to evaluate the correlation between ratios of these markers and pathological outcomes in term of pathological stages and NAR score (predictive role). Therefore, we have used the pretreatment blood test (before starting chemoradiotherapy) instead of posttreatment blood exam. We have modified the text to clarify this (p.4, pp.23-25)

5- Indicate how the new results can help the clinic. If they were to perform a larger study and showed a statistical relevance to the NLR/MLR and PLR, how would that help clinicians treat the patients?

RESPONSE: We found restricted response to nCRT with high NAR score among patients with high ratios of these inflammatory markers. Although, the differences were not statistically significant, because the number of patients were limited. We plan to perform a further study of larger population by multicenter study. We have modified the text to reflect this (p.8, pp.17-19)

Another potential study, in patients with high level of pretreatment NLR, MLR, and PLR group, standard nCRT should be warranted. upfront chemotherapy or total neoadjuvant approach may play the important role in this patients. (p.8, pp.8-12)

6- A total of 13 references are cited, including 1 references published in the last 3 years. The authors need to add more literatures.

RESPONSE: We have added 7 references to the manuscript, including 2 references published in the year 2019. (p.10-12)

7- I found the authors did not provide the original figures. Please provide the original figure documents. Please prepare and arrange the figures using PowerPoint to ensure that all graphs or arrows or text portions can be reprocessed by the editor.

RESPONSE: The original figure documents using PowerPoint were submitted.

8- I found the authors did not add the PMID and DOI in the reference list.

RESPONSE: We have added the PMID, DOI citation number, and list all authors in the reference list. (p.10-13)

9- I found the authors did not write the “article highlight” section. Please write the “article highlights” section at the end of the main text.

RESPONSE: We have added the “article highlight” section to the manuscript. (p.8-10)

We thank the editorial board for considering our work, and we thank the reviewers for their help in improving it. We hope you will find this revised manuscript suitable for publication in World Journal of Gastrointestinal Surgery.

Sincerely,

Atthaphorn Trakarnsanga MD.

Associated Professor of Surgery, Department of Surgery

Faculty of Medicine Siriraj Hospital, Mahidol University,

Bangkok, 10700, Thailand., Bangkok 10700, Thailand.

Email: atthaphorn.tra@mahidol.ac.th Telephone: +662-419-8006