

## **RESPONSE TO REVIEWER'S COMMENTS:**

### **Review no. 03538879:**

1. In the second paragraph of INTRODUCTION, author mentioned "In another study, monocyte count was an independent factor correlated with survival in patients with metastasis from colorectal cancer". Previous study has demonstrated the clinical significance of monocyte count, so why did author choose a relatively complicated factor? What about the necessity?

**ANSWER:** We examined the MLR ratio because of both parameters can be easily calculated in the whole blood samples. Additionally, there is one of the first analysis such factor in colorectal cancer that can be specified and prognostic for those patients.

2. Authors employed the ROC to estimate the cut-off value. The description should be more detailed, not just give simple values. In addition, I noticed authors evaluate the prognostic value of selected factors in pre-operation and post-operation separately. However, only single cut-off value was given for each indicator. How did authors consider this arrangement? Why not set two cut-off values for pre-operation and post-operation separately?

**ANSWER:** We enclosed the description of more detailed information to manuscript.

3. In the last paragraph of section "Blood sample examination", authors said " For DFS analysis, we divided the study group into two subgroups - with score 1 and score 2+3". How did authors determine this division principle? Why not divided into three or four groups?

**ANSWER:** There is a numbering/literal mistake. It should be: 0 and 1+2. We summarized group 1 and 2 to the one statistical analysis because the group 1 consists of small samples.

4. In the first paragraph of section "Correlation between monocyte count, MLR, NLR-PLR status, PLT-NLR status and clinicopathological variables of CRC patients" in RESULTS, authors mentioned "The correlations between monocyte count and MLR and anatomoclinical variables were published previously". Please supplement the corresponding reference.

**ANSWER:** The description of the correlation was added to the manuscript that

is reviewing in the another journal and is a separate part of the research.

5. In the first paragraph of section "Prognostic values of monocyte count, MLR, NLR-PLR status and PLT-NLR status in CRC patients" in RESULTS, authors said "Patients with low monocyte count in preoperative blood samples lived approximately 12.3 months (3-year survival) and 28.3 months (5-year survival) as compared to the high group that amounted to 8.25 months (3-year DFS time) and 20.3 months (5-year DFS time)". The previous "3-year survival" and "5-year survival" meant DFS or OS?

**ANSWER:** We examined only the DFS time. There is a literal error. We made a correction in the manuscript.

6. Authors should review the abbreviations again throughout the manuscript. Some abbreviations did not give the full name when they first appeared. And some spelling mistakes existed, for example, In the first paragraph of section "Correlation between monocyte count, MLR, NLR-PLR status, PLT-NLR status and clinicopathological variables of CRC patients" in RESULTS, what is the "PLR-NLR"?

**ANSWER:** We reviewed the manuscript and enclosed the necessary abbreviations.

**Review no. 00073640:**

1. Please be aware of abbreviations – MLR, PLT-NLR, NLR-PLR – the authors introduced these abbreviations more than once, specially MLR can be found in abstract, introduction, materials, results and even in discussion – please correct

**ANSWER:** We corrected them.

2. Page 6 – materials and method section: Authors stated: "The mean age of the patients was 67.5 years, including 40 patients <60 years-old and 120 patients ≥60 years-old." What did you mean by that? It is very confusing statement.

**ANSWER:** We divided patients to the two groups in such way because we believed that older patients may have other value of haematologic parameters.

3. Page 9: Results section - Correlation between monocyte count : Authors stated: "The correlations between monocyte count and MLR

and anatomoclinical variables were published previously.” Please add reference. Anatomoclinical – is this word correct?

**ANSWER:** The description of the correlation was added to the manuscript that is reviewing in the another journal and is a separate part of the research. It also could be clinicopathological.

4. Page 11: third line from the bottom up – CC patients – did you mean CRC patients? - Please be aware on abbreviation of CRC patients – authors introduce CRC abbreviation but in the manuscript they sometimes use CRC patients and sometimes colorectal cancer patients – specially in discussion section

**ANSWER:** There is a spelling mistake. It should be **CRC**.

5. At the end of the discussion section authors need to include explanation about potential limitations of the study (for instance sample size etc) and conclude appropriately - Figure 1B is missing – please correct - Numbers and letters on all Figures 1 and Figures 2 are too small – please correct

**ANSWER:** We corrected them.

### **Review no. 20200305**

In this article, the authors found that postoperative MLR value in whole blood samples can be used as an independent prognostic factor in patients diagnosed with colorectal cancer. The identification of non-invasive prognosticator in cancer is clinically very important.

Generally, the study has some medical significance. The assays were reasonably designed to some extent, and based on the present design, the results were well presented. However, some essential information are lacking in the manuscript which deduced the quality of the manuscript.

To improve the manuscript, I have following suggestions.

1. In Abstract, the authors did not clearly state the background of the study, and the AIM was not well written.

**ANSWER:** In our opinion, we wrote the aim of the study in easy and untestable

way.

2. As a retrospective study, the authors did not exhibit the inclusion or exclusion criteria of patients.

**ANSWER:** We added the inclusion or exclusion criteria of patients in section Materials and Methods: The inclusion criteria were as follows: (1) Pathologically confirmed colorectal cancer; and (2) Treatment with radical resection, (3) Had not received anti-inflammatory therapy. The exclusion criteria were: (1) Incomplete clinicopathological and follow-up data; (2) Presence of the haematologic disorders.

3. Abnormality of WBC and its subtypes is always closely associated with inflammatory response, whether did some patients have inflammation-related diseases?

**ANSWER:** None of patients had inflammation-related diseases. There is one of the exclusion criteria. In most cases, patients additionally received treatment for hypertension, type II diabetes, osteoarthritis and coronary heart disease.

4. In clinical practice, most therapies can have some influence on the changes of laboratory markers, and different therapy would make different impact on them. In the text, the authors presented the detailed anti-tumor therapy information before operation, however, I found that some patients received different anti-tumor therapy from others, how to evaluate the influence of the therapy on the changes of the MLR?

**ANSWER:** We did not evaluate the correlation between MLR and treatment because we have got detailed data about such treatment eg. What kind of the medicines had patients received. In our opinion, without these data it is not possible to say what treatment influences the change of the parameters studied.

5. Was blood cell count determined just using the same analyzer before and after operation?

**ANSWER:** Yes.

6. The authors stated that comparisons among multiple groups were analyzed using one-way ANOVA, however, a further statistical analysis should be performed such as LSD-t or SNK-q test to compare the difference between each groups.

7. Why a 3-year DFS time was observed ?

**ANSWER:** There is the first period of the multisystem control of the patients.

8. Why not investigated the correlations between the MLR, the most important variable of this study in pre and postoperative whole blood samples and clinicopathological features of patients with CRC ?

**ANSWER:** As we mentioned in the manuscript in the section *Correlation between monocyte count, MLR, NLR-PLR status, PLT-NLR status and clinicopathological variables of CRC patients*, we described such correlation in other publication. Instead of this, we can added the most important findings in this manuscript.

9. The authors discussed too many on significnace of monocyte count, NLR-PLR status and PLT-NLR status in CRC patients, but less on the MLR. Why?

**ANSWER:** MLR factor is a new parameter that is researched in the patients with colorectal cancer. Because of that there is a small number of manuscript in such topic.

10. Please include some discussion on the mechanism responsible for the poor prognosis of CRC exhibiting decreased MLR.

**ANSWER:** Obtained results allowed to only compare our findings with others studies.