

January 25, 2017

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 32117-review.doc).

**Title:** Clinical utility of the platelet-lymphocyte ratio as a predictor of postoperative complications after radical gastrectomy for clinical T2-4 gastric cancer

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**Name of Journal:** *World Journal of Gastroenterology*

**ESPS Manuscript NO:** 32117

The manuscript has been improved according to the suggestions of reviewers:

1 Format has been updated

2 Revision has been made according to the suggestions of the reviewer

(1) Reviewer 01220166

- This paper was generally well written, and it may be an important issue to consider appropriate management and treatment in patients with gastric cancer. As the results of this study, platelet-lymphocyte ratio was more sensitive than the other systemic inflammatory response markers.

Reply) We thank the Reviewer for favorable comments.

- Could you show the concrete results with regard to these other markers including neutrophil-lymphocyte ratio, GPS and PNI?

Reply) The area under the curve and cutoff values of neutrophil-lymphocyte ratio, GPS and PNI were newly provided in the text (page 10, line 2-3).

(2) Reviewer 02549032

- This is an interesting, single center retrospective study on clinical utility of preoperative predictors of postoperative complications for clinical T2-4 gastric cancer. The authors made a high quality

statistical analysis and found a new statistical, easy, reproducible and overall available index, the PLR ratio, to predict the postoperative complications after radical gastrectomy for clinical T2-4 gastric cancer. The study is suitable for publication.

Reply) Thank you for your encouraging comments.

1. In page 9, in line 16 instead of <> should be <> .<<(Table 3). With respect to the types of complications, the high (should be low) PLR group exhibited an increased prevalence of anastomotic leakage, leakage of pancreatic fluids, intraabdominal abscess and bowel obstruction compared to the high PLR group. However, the differences were not statistically significant (Figure 2).>>>

Reply) We apologize for these typing errors. They have been corrected.

2. In the discussion the authors stated that: << The PLR, a combination of circulating platelet and lymphocyte counts, is a representative index of systemic inflammation>>. Please explain more the low PLR or the high PLR is indication of inflammation or index of compromised immune reaction to cancer?

Reply) Both systemic inflammation and compromised immune reaction to cancer can be represented by low PLR. This content has now been added in the Discussion part (page 11, line 12-13).

3. The extended lymph node resection may be resulted in elimination to the total immune system and predisposed to sensitivity to postoperative inflammatory complications?

Reply) We agree with the Reviewer's opinion that lymph node dissection might influence on immune systems. In this study, we selectively included patients who underwent D2 lymphadenectomy, so that all patients were in the same conditions on this point.

4. A low PLR is related to low Lymphocyte and so to compromised cell-mediated immunity, while on the other hand high PLT is mainly related to thrombosis. So it is not the systemic inflammation only but the combination of impaired cell-mediated immunity and high thrombophilic diathesis and systemic inflammation that increase the risk of postoperative complications?

Reply) We appreciate this thoughtful suggestion. The relevant descriptions have been provided in the revised text (page 12, line 22-page 13, line 1).

5. May be the extended lymph node resection further impairing the cell-mediated immunity and so this aggressive policy may be not the optional in such serious cases?

Reply) As demonstrated by a previous phase III clinical trial (Sasako, et al. N Engl J Med. 2008 Jul 31;359(5):453-62), extended lymphadenectomy including para-aortic and hepatic hilum nodes increased postoperative complications, at least in part, due to impaired cell-mediated immunity. In this study, extent of lymphadenectomy was limited to D2 in all patients.

6. What is the clinical impact of this finding? Should the authors recommend other treatment planning? Eg instead of extensive lymph node resection, the postoperative radio-chemotherapy for radiation induced lymph node resection could be an option?

Reply) We thank the Reviewer for this thoughtful comment. The concept of the present study was to propose a method of identifying patients at risk of postoperative complications, but not to evaluate survival benefit of systemic lymphadenectomy. Our results suggested that surgeons can provide precise informed consent information and identify high-risk patients to tailor perioperative care as an attempt to ultimately improve postoperative short-term outcomes for patients undergoing a gastrectomy using PLR. Additionally, PLR could at least become a potential constituent of integrated scoring systems for surgical risk assessment like the SURPAS and POSSUM systems.

3 Languages and typesetting have been edited by native speakers as shown in the certificate.

Thank you again for publishing our manuscript in the *World Journal of Gastroenterology*.

Sincerely yours,

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