Author’s response to reviews

Title: The prognostic significance of the postoperative prognostic nutritional index in patients with colorectal cancer

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Author’s response to reviews: see over
Reviewer: Dr. Jesse Joshua Smith

Major compulsory revisions:

We added the patients who underwent operations in 2005 to this study. First, we evaluated the prognostic significance of the preoperative/postoperative PNI of these patients in the exploratory study. Second, we validated the results which were obtained from the exploratory study using the data of patients who underwent operations between 2006 and 2011. Both the preoperative PNI and the postoperative PNI were significantly associated with patient survival. Moreover, the combination of the preoperative PNI and postoperative PNI was an independent prognostic factor for poor survival.

Minor essential revisions:

a. Although the postoperative PNI was found in all cases, the preoperative PNI was unknown in some patients.

b. We confirmed the accuracy of the results by performing both exploratory and validation studies.

c. We discontinued comparing the preoperative PNI with the postoperative PNI. We also evaluated the significance of the combination of preoperative and postoperative PNI in a multivariate analysis. We confirmed the prognostic significance of the preoperative/postoperative PNI and the combination of the preoperative and postoperative PNI by performing both exploratory and validation studies.
d. We changed ‘clinically’ to ‘clinical’.

e. We added a reference to explain the correlation between the lymphopenia and recurrence.

f. We corrected the labels of the figures.
Reviewer: Dr. Alexander Parikh

Major Compulsory Revisions

1. We added the information about the period from the operation to the first visit after discharge.

2. We added the factors such as tumor depth, adjuvant chemotherapy and the amount of blood lost, which were reported to correlate with patient survival, as the covariates in a multivariate analysis.

3. We changed ‘mean PNI’ to ‘median PNI’. We tested the normality of the data. PNI distribution was found to be normal.

4. In current study, some patients with stage II CRC, who had no risk factors for recurrence were enrolled. These patients rarely relapsed in spite of a lack of adjuvant chemotherapy. This is because no significant relationship was observed between the administration of adjuvant chemotherapy and the survival. We added adjuvant chemotherapy as a covariate in the multivariate analysis.

5. In the validation study, we added the amount of blood loss as a covariate in the multivariate analysis. However, the result was same and the combination of preoperative and postoperative PNI was an independent prognostic factor for poor survival.

6. We evaluated the significance of the combination of preoperative and postoperative PNI in multivariate analysis. The combination of preoperative and postoperative PNI was an
independent prognostic factor for poor survival.

7. We hypothesized that the large postoperative invasiveness worsened the immunonutritional status of the host and that the postoperative PNI correlated with patient survival. We added factors such as the length of hospitalization, days before the initiation of dietary intake and adjuvant chemotherapy, which were considered to correlate with the postoperative immunonutritional status of the host. These factors were associated with the postoperative PNI. From these results, the delay of a postoperative recovery may be associated with a low postoperative PNI.