Author’s response to reviews

Title: Preoperative systemic inflammation score (SIS) is superior to neutrophil to lymphocyte ratio (NLR) as a predicting indicator in patients with esophageal squamous cell carcinoma

Authors:
Xiaobin Fu (danielfu1990@126.com)
Tingting Li (twostops@126.com)
Yaqing Dai (yaqingdai@126.com)
Jiancheng Li (jianchengli_jack@126.com)

Version: 1 Date: 12 Jun 2019

Author’s response to reviews:

Dear Editors and Reviewers:

On behalf of my co-authors, we thank you very much for giving us the constructive comments and suggestions on our manuscript entitled “Preoperative systemic inflammation score (SIS) is superior to neutrophil to lymphocyte ratio (NLR) as a predicting indicator in patients with esophageal squamous cell carcinoma” (ID: BCAN-D-19-01362). These comments are all valuable and helpful for revising and improving our paper. The concerns raised by the editor and reviewers are listed below, followed by a point to point response to them. Revised portions are marked with red color in the paper. We hope the revised manuscript would meet your expectations.

Responds to the reviewer’s comments:

Reviewer 1:

Major comment 1: The authors stated this cohort patients underwent esophagectomy with 3-FL lymphadenectomy, but did not mention the surgical procedure, e.g., open thoracotomy or thoracoscopic surgery.

Response: Thank you for your comprehensive consideration. We have supplemented the surgical procedure in the revised manuscript (Patients and methods section, paragraph 2, page 6).
Major comment 2: It is well known that the preoperative therapy should affect the preoperative blood cell count and nutritional status. The authors should state regarding the preoperative treatment in the materials and methods section.

Response: Thank you for your suggestion. We have supplemented the preoperative treatments in the revised manuscript (Patients and methods section, paragraph 3, page 6-7).

Minor concern 1: Table 2: Tumor length Yes and No.

Response: We apologize for our negligence in writing the tumor length Yes and No in Table 2. The correct tumor length was ≤5cm and >5cm in our study. We have made the corrections in the revised manuscript (Table 2)

We are very grateful to the reviewer for improving this manuscript.

Reviewer 2:

Comment 1: There are many mistakes (P-value in univariate analysis). Please confirm.

Response: We apologize for our mistake. We have confirmed the P-value in the univariate analysis. We have made the correction in the revised manuscript (Result section, paragraph 1, page 12).

Comment 2: In Table 2, NLR was not correlated with well-known prognostic factors, such as the N stage and Stage (P=0.266 and P=0.109, respectively). However, NLR is one of representative blood markers for predicting tumor progression in patients with various malignancies, including ESCC. How do the authors discuss about these results?

Response: Thank you for your comprehensive consideration. Except for TNM stage, tumor location, tumor cell grade, and tumor burden were also significantly affecting the ESCC patients’ OS. These factors influenced the outcomes of ESCC patients but not significantly association with T stage, N stage, and clinical stage in many studies. Moreover, the tumor location and tumor cell grade were staging factors in the 8th edition TNM stage issued by AJCC that significantly affected patients’ OS. The factors mentioned above may influenced patients’ OS in different ways and had not correlation among them.

Comment 3: In Table 2, the statistical relationship between SIS and N stage should be indicate as P-value.

Response: We are very sorry for our mistake in the table 2 in our manuscript. We have made the correction in the revised manuscript (Table 2) according to the Reviewer’s comments.
Comment 4: In Table 2, SIS was not correlated with T stage, N stage and stage (P=0.102, P=0.161, and P=0.117, respectively). However, SIS, T stage, and N stage are independent prognostic indicators in multivariate analysis (Table 3). How do the authors discuss about these results?

Response: Thank you for your comprehensive consideration. In a similar study by Hao Duan (Prognostic role of neutrophil-lymphocyte ratio in operable esophageal squamous cell carcinoma) demonstrated that NLR was not correlated with N stage and stage, but NLR, N stage and stage were independent factors in that study. Moreover, as we mentioned above, staging factors including the tumor location and tumor cell grade issued in the 8th edition TNM stage significantly affected ESCC patients’ OS. However, the factors were not significantly correlation with TNM stage. SIS may influence the outcomes of ESCC in the different way.

Comments 5: Serum CEA and SCC are useful blood markers for the clinical management of patients with ESCC. How about the relationship between these serum markers and NLR or SIS?

Response: Thank you for your comprehensive consideration. As you mentioned above, CEA and SCC are important blood markers for ESCC. However, due to the limitations of the retrospective study, these data were not included in our study. CEA and SCC will be considered in our future research studies.

Comment 6: In the present study, AUC was indicated for setting the optimal cutoff value. AUC for NLR, LMR, and Alb was 0.566, 0.576, and 0.578. These results suggest low accuracy. How do the authors discuss about these results?

Response: As you mentioned above, AUC for NLR, LMR, Alb was not satisfied. In our study, we combined the Alb and LMR to defined SIS to increase the accuracy in predicting the ESCC patients’ overall survival. Moreover, the C-index increased slightly in the model with SIS, which suggesting that the adding the SIS to the multivariate model increasing the predictive accuracy of the OS in the ESCC patients in our study. SIS may be treated as a novel factor in ESCC patients.

Comment 7: ROC curve should be indicated as Figure.

Response: Thank you for your comprehensive consideration. We have supplemented the ROC curve in the revised manuscript (Figure 1).

Comment 8: P-value for NLR should be indicated in multivariate analysis (Table 3).

Response: Thank you for your comprehensive consideration. In our study, NLR was not independent factor in the multivariate analysis and that was the reason why we did not indicate the P-value in the table 3.
We are very grateful to the reviewer for improving this manuscript.

We tried our best to improve the manuscript and made some changes in the manuscript. These changes will not influence the content and framework of the paper. And here we did not list the changes but marked in red in revised paper.

We appreciate for Editors/Reviewers’ warm work earnestly, and hope that the correction will meet with approval. Once again, thank you very much for your comments and suggestions.

Sincerely,

Jiancheng Li, MD, PhD

Department of Radiation Oncology Fujian Medical University Cancer Hospital, Fujian Cancer Hospital, Fuzhou, China 420 Fuma Rd, Jinan District, Fuzhou 350014, China Tel Number: +86-13906900190 Email address: jianchengli_jack@126.com