Author’s response to reviews

Title: Application value of nomogram and prognostic factors of gastric cancer patients who underwent D2 radical lymphadenectomy

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Version: 1 Date: 05 Aug 2019

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Response to reviewers

Ibrahim Uygun (Reviewer 1): Dear Authors,
Comments: This is a clinical research study that is describing a new nomogram and prognostic factors of gastric cancer patients. The manuscript is well designed and written, and well referenced.

Finally, this clinical research study in large series patients do add much new insight into the already existing literature on the same subject and do provide new knowledge to the readership. So, the manuscript should be published in BMC Gastroenterology.

No other comment.

Best regards.

Reply: Thanks!

Abdullah Yeniova (Reviewer 2): Manuscript titled "Application value of nomogram and prognostic factors of gastric cancer patients who underwent D2 radical lymphadenectomy" was reviewed according to the journal "BMC Gastroenterology" policy. It contributed to the literature regarding the
prognostic scoring systems for gastric cancer survival. It can be published with minor revision. The criticism regarding to manuscript policy can be found below.

Comments 1: Most important criticism is about the term "nomogram". Authors should explain the term "nomogram" definitively. Because most of the readers will be clinician and I think information about nomogram is insufficient. For example authors should explain how they score the index? Information should understandable for readers who did not know advanced statistics.

Reply: Thanks! The definition of the term “nomograph” has been added in the introduction section. And calculation method of c-index has been added in the “Statistical analysis” section.

Comments 2: Background section of abstract is insufficient. Abstract is the most important part of the manuscript so authors should include a sentence highlighted the aim of the study and why they do this study?

Reply: Thanks! The aim of this study has been added in the abstract section.

Comments 3: Tumor markers should be written as CA 15-3 and CA 19-9.

Reply: Thank you! The tumor makers have been written in the right form.

Comments 4: I think the sentence "more and more studies" (page 4 and line 39-41) is exaggerative because there are only there studies in references regarding this issue.

Reply: Thank you! This sentence has been replaced by other words.

Comments 5: Demographic data of patients should be given in "Result" section not in the Methods" section (page 5 line 27-32).

Reply: Thanks! The Demographic data of patients have been moved to the “Result” section.

Comments 6: Predictive factors like tumor stage, tumor location, tumor size, pathological type, vascular invasion, nerve invasion, Borrmann classification, the number of lymph node metastases are well known predictive factors but there is little data about the factors like hemoglobin [Hb], platelet count, neutrophil count, lymphocyte count, neutrophil-lymphocyte ratio, serum albumin, body mass index, celiac artery variations. Authors should explain why they include these factors and give reference.

Reply:  Thanks! The factors such as Hb[1], platelet count[2], neutrophil-lymphocyte ratio[3], and serum albumin[4] have been demonstrated that could act as prognostic factors in patients with malignant tumors. Body mass index (BMI) has been also reported could affect the prognosis of cancer patients[5-6].

Amy Tyberg, MD (Reviewer 3): This is a nicely written retrospective study looking at prognostic factors of gastric cancer survival after surgical resection, as well as evaluating a new nomogram to predict post-surgical survival.

A few comments:

Comments 1: The authors state that patients who underwent neoadjuvant chemoradiotherapy were excluded. However, there are some patients with stage III tumors included in the study which generally would qualify for neoadjuvant therapy. Why were these patients not given neoadjuvant therapy?
Reply: Thank you! Although neoadjuvant therapy was effective for the advanced gastric cancer, some patients with stage III tumors had refused this therapy because of personal factors. Some patients were intolerance to the chemotheraphy, and some patients refused treatment for financial reasons.

Comments 2: I am surprised that tumor histology was not a prognostic factor. Signet cell tumors are considered more aggressive and higher risk tumors. How do you explain in this study that the histology was not significant? Were these tumors all earlier stage than other tumor histologies?
Reply: Thanks! Tumor pathological type was not correlated to the prognosis of patients with gastric cancer after D2 radical resection in this study. The reason may be the small sample size of the present study. Most patients enrolled in this study were adenocarcinoma (87.6%). Only a fraction of patients were signet cell tumors, mucous carcinomas and undifferentiated tumors (12.7%). The small number of patients with signet cell tumors or undifferentiated tumors may result in our findings. To fully understand this matter, further studies are needed.

Comments 3: Was any subgroup analysis done on survival? Aka could BMI be more associated with surgical risk/mortality rather than disease recurrence mortality? It might be useful to have a nomogram looking at disease-free survival rather than overall survival.
Reply: Thanks for your suggestion! The subgroup analysis hasn’t done in this study. DFS is a surrogate endpoint of OS, which is usually used in the studies of patients who had underwent radical surgery. Although DFS can provide direct evidence of clinical benefit, it is only the surrogate endpoint of OS in the absence of OS data. In this study, we aimed to establish a new nomogram to predict the long-term survival of gastric cancer patients who had underwent D2 radical lymphadenectomy. We had enough data of OS, so we did not need to use DFS as the endpoint of this study.

Comments 4: Negative margins was not listed as a data point - was this looked at?
Reply: Sorry, the negative margins were not made.
Comments 5: The authors state that having a nomogram could be helpful in formulating individualized treatment decision-making for patients - how do they anticipate this would change clinical practice? Changing surveillance intervals? Neoadjuvant therapy for higher risk patients?
Reply: Thank you! The c-index of the nomogram established in this study was 0.76, the predictive capability of the nomogram was better than that of the TNM staging system of AJCC. The nomogram may help doctors predict the prognosis and survival of the patients. And for the patients with poor prognosis predicted by the nomogram, more treatments will be needed before or after the operation, such as neoadjuvant therapy and adjuvant chemotherapy. But the practical value of the nomogram should be tested in more studies.