Author’s response to reviews

Title: Prognoses of different pathological subtypes of colorectal cancer at different stages: A population-based retrospective cohort study

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Response to Editor and Reviewers
BMGE-D-19-00428
Prognoses of different pathological subtypes of colorectal cancer in different stages: A population-based retrospective cohort study.

On behalf of myself and the coauthors, many thanks for your helpful review of our manuscript. In accordance with the suggestions please find below the replies to questions and comments posed. More details are using track changes in the resubmission.

We thank you again for taking time to consider our submission, and are confident that the changes applied through these suggestions significantly improve the standard of the document.

Sincerely yours,
Shaotang Li

Editor:

Response: Thanks for your suggestions. We have provided the items
Takuma Higurashi (Reviewer 1): This population-based retrospective cohort study concluded that the patients of different pathological subtypes were only minimally different at the early stage. However, they were significantly different prognosis and patients with MAC and SRCC have worse OS and CCS, which are mainly in advanced CRC (stages III and IV).
This is well written study and novel information, however, this study has some limitations in the following areas.

<Major>
1. One of the strength of this study is large sample, however, excluded people are too many. The study that contains many excluded may have some biases. The authors should minimize the exclusion.
Response: Thanks for your suggestions. We excluded a small number of patients who did not meet the requirements of screening, 86.5% (384,996/445,198) patients remained in the cohort, as shown in figure 1.

<Minor>

1. The manuscript needs editing by a native English speaker.
Response: Thanks for your suggestions. We have revised our manuscript according to your specifications. And we have revised the manuscript by a native English speaker.

Reviewer 2 (Reviewer 2): PEER REVIEWER ASSESSMENTS:
REQUESTED REVISIONS:

The authors are comparing AC to MAC and SRCC prognoses in data from SEER database (2004-2015). In the results section, the authors are lumping MAC and SRCC in their comparisons to AC. Since the values of MAC vs. AC differences were less dramatic than those of SRCC vs. AC, these two entities need to be presented separately in the results section, as it is in Table 3. Moreover, the authors need to run another comparison of MAC vs. SRCC as well. This reviewer expects that the difference will be significant and will affect the emphasis that the authors are putting on the mucin production alone as the main factor for the difference in prognoses. Moreover, the discussion part on the molecular profiles within each of these 3 histologies is shallow and needs further development if really these histologies are associated with specific molecular profiles.

Response: Thanks for your suggestions. We have revised partly our manuscript according to your specifications. In this study, approximately 90.1% (349,891) of the patients were diagnosed with AC, so we chose MAC and SRCC to compare with AC respectively. Meanwhile, we can see from the figure 2 and figure 3 that there are significant differences in different pathological subtypes (include the comparison between MAC and SRCC). We have added the discussion part on the molecular profiles within each of these 3 histologies.

ADDITIONAL REQUESTS/SUGGESTIONS:

The manuscript writing needs a thorough revision. There are many typos and grammatical errors, some of which affect even the presented science e.g. are distinction should be are distinct, patients with MAC patients should be patients with MAC histology, on page 8 line 56: when compared to AC NOT to MAC, and many more mistakes all over that need fixing).

Response: Thanks for your suggestions. We have revised our manuscript according to your specifications. And we have revised the manuscript by a native English speaker.