Peer Review File

Article information: https://dx.doi.org/10.21037/tau-23-187

Reviewer A

Clear cell renal cell carcinoma (ccRCC) is a highly heterogeneous tumor and is the most common subtype of renal cell carcinoma (RCC). Surgery is used to cure most early ccRCC, but the 5-year overall survival (OS) of ccRCC patients is far from satisfactory. In the manuscript "Construction and validation of a prognostic model for predicting clear cell renal cell carcinoma based on complement-related genes", authors developed and validated a survival prognostic model based on 5 complement-related genes for ccRCC, and elucidated the relationship with tumor immune status and developed a new predictive tool for clinical purposes.
Couple questions are required to be answered before it will be accepted.
(1) Why to focus on complement-related genes in the paper? Please state in the introduction.
Reply 1: Thank you for reminding me. We have modified our text as advised (See page 4, line 109).

(2) The complement-related genes were the crucial topic in the paper. What were the roles of complement in ccRCC? Please state in the introduction.
Reply2: Thank you for reminding me. Since complement factors were rarely studied in ccRCC, we explored the relationship between complement factors and prognosis of patients with ccRCC. In the introduction, we have modified our text as advised and focus on the role of complement in pan-cancer (See page 4, line 111-129).

(3) It was advised to add related reference (DOI: 10.21037/tcr-21-37) about the prognostic model for ccRCC.
Reply 3: Thank you for reminding me. A paper entitled 《Development and validation of the prognostic value of the immune-related genes in clear cell renal cell carcinoma》 has been quoted in this paper . The content might be more appropriate.

(4) It was better to validate the prognostic model, or validate the representative complement-related genes.
Reply 4: Thank you for reminding me. Due to the limitations of existing conditions, we will improve in the future study.

(5) Please make a brief introduction about A2M, APOBEC3G, COL4A2, DOCK4, and NOTCH4 in the discussion.
Reply 5: Thank you for reminding me. We have modified our text as advised (See page 13, line 425-426).

(6) What were the correlations between immune infiltration and complement in ccRCC? Please state in the discussion.
Reply 6: Thank you for reminding me. We have modified our text as advised (See page 13, line 420-422).

(7) Compared to other constructed prognostic model, what were the advantages of constructed prognostic model in the research? Please supplement in the discussion.
Reply 7: Thank you for reminding me. We have modified our text as advised (See page 13, line 438-439).

Reviewer B

First of all, the prediction model was based on risk score and cancer stage to achieve an acceptable level of predictive accuracy, so the authors need to revise the title and elsewhere of this study.
Reply 1: Thank you for your feedback. We are submitting a revised manuscript to address these concerns.

Second, the abstract needs some revisions. The background did not describe why the complement-related genes could facilitate the prediction of prognosis in ccRCC and what the clinical significance of this research focus is. The methods need to describe the clinical factors and prognosis outcomes in the databases, how the clinical factors and complement-related genes were identified, and the indicators for assessing the predictive accuracy such as C-index. The results need to describe the predictors in the prediction model and report the predictive accuracy parameters in both the training and validation samples. The conclusion needs to have comments for the clinical implications of the findings.
Reply 2: Thank you for reminding me. We have modified our text as advised (See page 2, line 57-59; line64-65; page 3, line 71).

Third, in the introduction of the main text, the authors need to have a brief overview of clinical and biological factors associated with the prognosis in ccRCC, analyze the

limitations and knowledge gaps of prior studies, and explain why the complement-related genes could facilitate the prediction of prognosis in ccRCC. Because the model was based on the combination of clinical factors and complement-related genes, the authors need to review why the combination of clinical and biological factors could improve the predictive accuracy.

Reply 3: Thank you for reminding me. We have modified our text as advised (See page 4, line 129-132).

Fourth, in the methodology of the main text, please describe the clinical factors and prognosis outcomes in the databases. Please also describe the identification of clinical factors used in the prediction model. The authors may consider to add more clinical factors to improve the predictive accuracy. In statistics, please report the threshold C-index value for a good predictive model and ensure $P<0.05$ is two-sided.

Reply 4: Thank you for reminding me. We have modified our text as advised (See page 6-7, line 204-205; page 8, line 248-249).

Reviewer C

1. You've mentioned "studies", while only one reference was cited in this sentence. Please check. (You could either choose to revise it to "study" or to give **more than one reference** in this sentence. In the latter case, please keep the citations consecutively in text.)

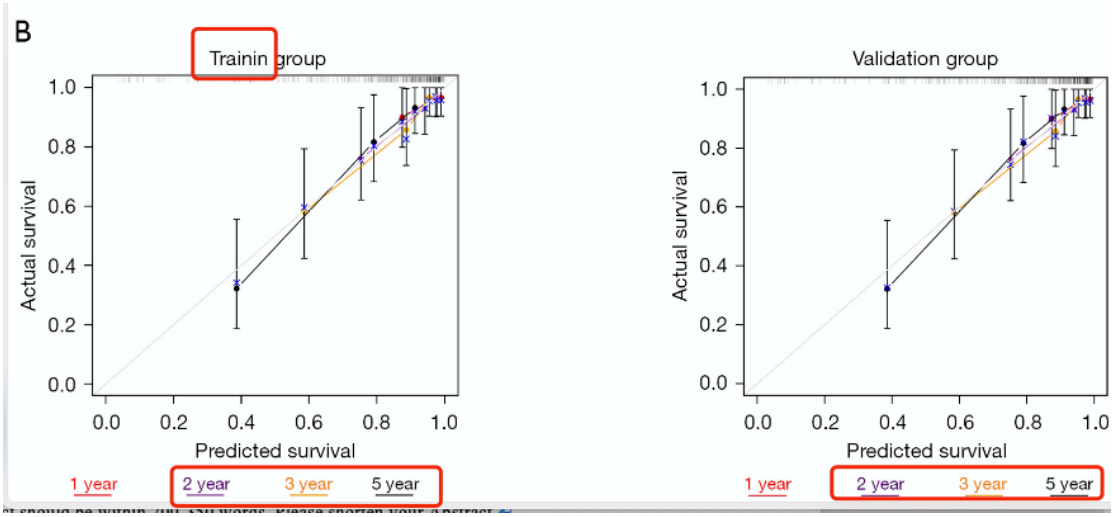
228 According to previous studies, analyses of immune cell infiltration in tumor tissues are
229 important for understanding the pathogenesis of a disease and predicting patient
230 prognosis (20).

Reply 5: Thank you for reminding me. We have modified our text as advised (See page 7, line 227).

2. Figure 4:

a. Please revise it to "Training".

b. Please revise them to "2/3/5 years".



Reply 1: Thank you for reminding me. We have modified our Figure 4 as advised, please see the attached version.