Peer Review File

Reviewer A

Comment 1: Please add more tools in Material & methods.

Such as Hub gene identification & validation with CytoHubba pug in cytoscape & ToppGene web server in BIODICA, GEPIA2 to create gene expression profiling interactive analysis (GEPIA)/ validation with PCA analysis. The decision depends on the researchers.

Reply 1: Thanks for this kind suggestion.

The goal of our study was to develop a prognostic model in EAC. Based on this, we first screened out the differentially expressed genes in EAC as candidate genes, which were thought to account for the progress of EAC. Then, genes associated with OS were further identified to construct a prognostic model. If we add the proposed content such as hub gene identification and validation, the research focus will not be clear, and the whole article also needs to be rewrote. Generally, the identification of hub genes is to find potential biomarker and therapy target, which is not suitable for the construction of a prognostic model. Therefore, we decide not to add such analysis.

Changes in the text: None.

Comment 2: Please add the new article in discussion part, Transcriptomic analysis of esophageal cancer reveals hub genes and networks involved in cancer progression, address by Chatterjee D et al., 2023. It is very confirmation for existing ABLIM3 gene and overall survival in EAC patients as well. This must be edited as reviewer comments.

Reply 2: Thanks for this nice suggestion. We have added the above-mentioned article in the discussion and rewrote the research progress on the four prognostic genes according to the most recent studies. As for ABLIM3, we only found a Chinese invention patent for using an ABLIM3 gene expression detecting product as a diagnostic tool for esophageal cancer, and it lacks a corresponding published article. This needs reviewer's further verification.

Changes in the text: we have modified our text as advised (see Page 8-9, line 296-300, 304-310, 312-316, 326-328, 330-337).
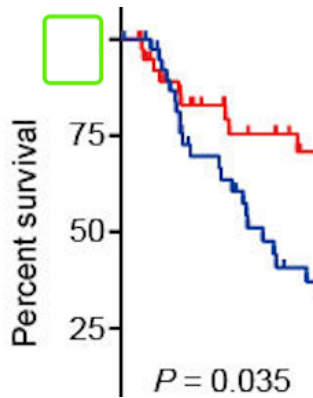
Reviewer B

1. All abbreviations in the Highlight box should be defined. Please provide the full names of OS and EAC in the highlight box.

   Reply: Thanks for this suggestion. We have added the full names of OS and EAC in our revised manuscript. (see Page 1, line 18-19).
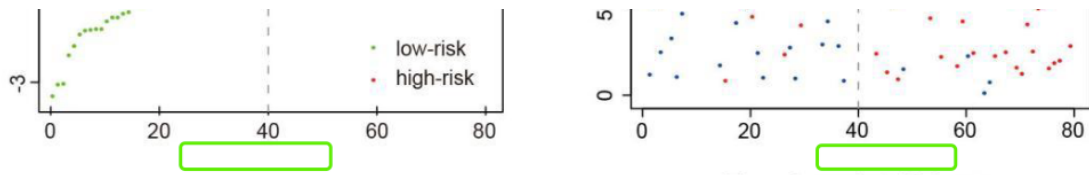
2. Figures and tables
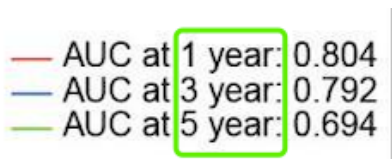   - Figure 1A: Please complete the scale.

   Reply: Thanks for this reminder. We have completed the scale in the new figure .

   - Please add the description of x-axis in Figure 2A-B.

   Reply: Thanks for this reminder. We have added the description of x-axis in the new figure.

   - Figure 2D: Plesae revise "1 year, 3 year, 5 year" to "1-year, 3-year, 5-year".

   Reply: Thanks for this reminder. We have revised the figure as suggested.

- All abbreviations in figures/tables and legends should be explained. ROC, AUC in Figure 2 for example. Please check all abbreviations and provide the full names in the corresponding legends/footnote (including the supplementary tables).

Reply: Thanks for this reminder. We have provied the full names of all abbreviations in the figures/tables and legends (see Page 15, line 522; Page 17, line 525; Page 22, line 541-542, line 546-547).

- The following highlighted data in the abstract and main text is inconsistent with that in Figure 2D. Please check and revise.

66   as an independent factor in overall survival prediction. In the time-dependent ROC analysis,
67   the areas under the curves (AUCs) were 0.804, 0.792 and 0.695 for 1-, 3- and 5-year
68   survival prediction, respectively, suggesting a good performance. Functional enrichment

dependent ROC curve were 0.804, 0.792 and 0.695 for 1-, 3- and 5-year survival prediction, respectively (Fig. 2D). ¶

— AUC at 1 year: 0.804
— AUC at 3 year: 0.792
— AUC at 5 year: 0.694

Reply: Thanks for this reminder. We have corrected the inconsistent data in the new figure.