TCR TRANSLATIONAL CANCER RESEARCH
ADVANCES CLINICAL MEDICINE TOWARD THE GOAL OF IMPROVING PATIENTS' QUALITY OF LIFE
IMPACT FACTOR 1.241

Peer Review File

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Reviewer A

Comment 1: in introduction, to my knowledge, AJCC may be just one of the staging systems and is not a prognostic model for OCS.
Reply 1: We are thankful that the reviewer pointed out this important issue, and we have changed in the introduction section of text.
Changes in the text: We have modified our introduction section of text as advised (see Page 3, line 48-49).

Comment 2: Will it be able to identify and analyze CSS (cancer-specific survival) in addition to os to further add value to this study?
Reply 2: Thank you for the comment. We have tried to consider the suggested possibility (and originally we already thought of that), however, we have found the number of samples with CSS (cancer-specific survival) records does not currently meet the test efficiency, and we only focused on the OS of OCS patients.
Changes in the text: N/A

Comment 3: Is a regimen of chemotherapy and results of debulking surgery able to know? incorporation of taxanes over the platinum-based chemotherapy further improved the survival and complete and/or optimal cytoreductive surgery is one of the major prognosticators these variables, if possible, should be analyzed otherwise, this may be another limitation of this study.
Reply 3: We are very sorry for this problem. The SEER database is not comprehensive. Although the SEER database captures data on the use of chemotherapy, the explicit agents utilized, number of cycles, and timing were not recorded. Similarly, the results of debulking were also not recorded. Thus, this is another limitation of this study.
Changes in the text: We have modified our discussion section of text (see Page 10, line 198-200).

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Reviewer B

In the submitted manuscript, Liu et al. have shown a prognostic nomogram was constructed based on an independent prognostic factor of ovarian carcinosarcoma. The performance of the new model is better than the AJCC staging system in predicting the survival time of ovarian carcinosarcoma in clinical practice.

Comment 1: Line 88: You used a log-rank test to check intergroup differences between training and validation groups. Do you mean there are no significant differences in survival status between the two groups?
Reply 1: Thank the reviewer for the comment. The reviewer is correct. The log-rank test was used to explore the survival difference between training and validation groups, and the results demonstrated that there were no statistically significant intergroup differences in survival status between 2 groups (p-value=0.6, > 0.05).
Changes in the text: N/A

Comment 2: Line 109: What does “histological grades III/IV” mean? Grade IV? You have to explain what grading scheme do you use for ovarian carcinosarcoma.
Reply 2: We thank the referee for the valuable comments. First, the histological grades refer to the tumor histological grade, and we have modified our methods section of text (see Page 4, line 75, 77). Besides, the tumor histological grade was defined according to the SEER database, and classified as grade I: well-differentiated; grade II: moderately differentiated; and grade III /IV: poorly differentiated, undifferentiated or anaplastic.
Changes in the text: We have modified our methods section of text (see Page 4, line 75-80).

Comment 3: Table 1 and 2: What is the histological stage? Is it different from the AJCC stage? You have to show the reference to explain it.
Reply 3: All patients were staged according to the SEER stage (localized, regional, and distant). Besides, we chose the AJCC stage based on the sixth edition of the Derived AJCC Stage Group.
Changes in the text: We have modified our methods section of text (see Page 4, line 80-82).

Comment 4: Table 2: It is not acceptable that P-values are shown as <0.10 and <0.05. Provide the real p-values.

Reply 4: We are thankful that the reviewer pointed out this important issue, and we have corrected the p-values figures in table 2.

Changes in the text: We have corrected the p-values figures in table 2.

Comment 5: Figure 3: Compare the AUCs of nomogram and AJCC stage and provide the p-values.

Reply 5: Special thanks for the comments. In our study, we used the area under the time-dependent receiver operating characteristics (ROC) curve (AUC) to evaluate the discrimination ability of the nomogram. The AUC was widely used, but its increment is not obvious when comparing 2 present models.

In order to determine whether the new model was advantageous (to compare the differences of nomogram and AJCC stage), we applied 2 relatively new indicators: the net reclassification improvement (NRI) and integrated discrimination improvement (IDI). The NRI is mainly used to compare the predictive powers of new and old models at a set tangent level, while the IDI considers different tangent lines, which can be used to assess the overall improvement of the model. These 2 indicators are easy to calculate and understand in practical clinical applications.

As we shown in the result of the text, the above-2 indicators clearly show that the nomogram has better discriminative ability than AJCC staging. Therefore, in our study, we used NRI and IDI to compare the differences of nomogram and AJCC stage and increase the accuracy and comprehensiveness of the comparisons, and it does not need p-values.

Changes in the text: N/A

Comment 6: Line 141 to 143: Provide the p-values of NRIs.

Reply 6: As described in the previous reply, NRI is mainly used to compare the predictive powers of new and old models at a set tangent level. Since our study is based on prediction model, we load “nricens” package in R software to calculate NRI, which was the first method recommended by the literature (In-depth mining of clinical data: the construction of clinical prediction model with R). No p-value is displayed in the result of this R code, and the assessment metrics mainly rely on the minimum value of NRI.

Interpretation of results:

If the minimum value of NRI > 0, it means positive improvement, which indicates that new marker has better predictive value comparing to original marker;

If NRI <0, it means negative improvement, which indicates that new marker has worse predictive value comparing to original marker;

If NRI =0, it means no improvement.

In our study, the NRIs at 1-, 3-, and 5-year OS were all > 0, which mean that our nomogram had better discriminative ability than AJCC staging.

Besides, available evidence shows that NRI and IDI are 2 metrics that are usually used together in the assessment of prognostic model, IDI has p-value (see Page 4, line 149-150), which can further confirm and more directly show that the better discriminative ability of our nomogram.

Changes in the text: N/A