

Peer Review File

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Reviewer A

In this manuscript the authors develop a predictive cox model for overall survival and disease specific survival using the SEER/Medicare database. They internally validate the nomogram on a validation cohort. This study offers helpful insight into a rare cancer that would be otherwise challenging to study.

Comment 1: The authors should provide a CONSORT diagram to illustrate their inclusion/exclusion criteria.

Reply 1: We have added a CONSORT diagram to illustrate the inclusion/exclusion criteria as Figure 1 in the revised version.

Changes in the text: We added “The selection process is shown in Figure 1.” (see Page 9, line 119).

Comment 2: This manuscript contains several grammatical errors and could benefit from additional editorial support.

Reply 2: We have had the manuscript edited to rule out grammatical errors. Changes in the text have been highlighted in red with yellow background.

Changes in the text: Modified text has been highlighted (see the revised manuscript).

Comment 3: In my mind the strengths of this manuscript are in describing treatment trends and developing a prognostic model. The comparative effectiveness analysis is of less interest given known issues with residual confounding. If treatment modalities are compared, the authors should also account for patient comorbidity (e.g. charlson comorbidity index) in the multivariable analysis.

Reply 3: It is better to take data about comorbidities into consideration, but related data was not available from the SEER database. Thank you for your advice, we would involve data about comorbidities in our future retrospective analysis.

Changes in the text: none.

Comment 4: There appears to be a typo in Figure 4 in the final line. The MVA HR for radiotherapy is outside the listed 95% CI.

Reply 4: You may mean Table 4. There was a typo, the 95%CI: 0.49(0.26-0.3) have been corrected to 0.49(0.26-0.93).

Changes in the text: We have modified 0.49(0.26-0.3) to 0.49(0.26-0.93). (see Table 4, the final line).

Reviewer B

Comment: Objective errors in the methods, applications, or interpretations were identified in this manuscript that prevent further consideration. Nomogram papers on the SEER database were developed

every month. These studies are based on large databases looking for significant p values, are not able to take into consideration the several factors necessary for chronic disease, and I therefore do not believe that they are scientifically sound.

Reply:

1. Since cervical esophageal cancer is a relatively rare disease, it is difficult to carry out randomized controlled trial or to collect a large number of retrospective CEC samples from single treatment center which is necessary to draw applicable conclusion. Thus, we believe it is a good choice to take advantage of the SEER database when analyzing uncommon diseases although there are truly disadvantages by using the database. The limitations of this study, such as lack of data about comorbidities, have been discussed and listed in the limitation part of the manuscript.

2. Compared with single prognosis factor, nomogram has its superiority in predicting prognosis by incorporating multiple valuable factors. Although many nomogram papers have been published based on the SEER database, there is none specific for CEC. To the best of our knowledge, this is the first nomogram for patients with non-metastatic CEC. The model is likely practical to help identify high-risk patient populations because of its relatively high accuracy. We believe that our model could be a simple and easy tool for both the doctors and patients to estimate the survival.

3. We thank you for your advices, and we would try to collect more detailed information in our next retrospective analysis of CEC cases treated at our center.

Changes in the text: none.