Peer Review File

Article information: https://dx.doi.org/10.21037/tcr-21-1128

Reviewer A

Comment 1: The materials analyzed come from another country data base, just purely focus on data statistical analysis, no any clinical oriented explanation. A lot of bias in this paper.

Reply 1: We have done the clinical oriented explanation. All of the discussion are based on the data statistical analysis without any bias.

Changes in the text: see page 10, line 201-210.

Comment 2: Why only old peoples included. In clinical view point, cancer staging, organ metastasis, patient performance status, treatment modality and qualities are important factors for patient survival. This paper not included these factors.

Reply 2: We have explained the reason for the included of old people in the introduction. Because more than 73% of esophageal cancer patients were over 65 years of age according to the website of Cancer-Research-UK. Another reason is that age is also a factor that can affect the prognosis of cancer, so we limit it. Similarly, the stage of cancer has been limited to IVB, which can help us exclude factors other than treatment modality. We only study the factor treatment modality. As for the patient performance status and treatment qualities, the SEER database doesn't have the information like these, so we can't analyse it.

Changes in the text: page 3, line 54-55.

Comment 3: The conclusion is not consisted with the data analyzed.

Reply 3: Our conclusion has analyzed the results.

Comment 4: This paper just focus on data analyzed, no clinical implication included. The conclusions did not provide any important clinical information.

Reply 4: We have done the clinical oriented explanation. The clinical significance is that "multimodal therapy in treating patients with DM in stage IVB remains poorly defined. In our study, for the patients treated with chemotherapy, radiotherapy and surgery cannot be considered beneficial for the prognosis: chemotherapy can be deemed to be the primary mode of treatment."

Changes in the text: see page 10, line 207-210.

Reviewer B

Comment 1: Regarding the abstract

The authors concluded that treatment is an independent prognostic factor affecting prognosis. Chemotherapy has a vital role in prognosis. However, no substantiation

was given in the results in the abstract. The authors should revise the abstract accordingly.
Reply 1: We have revised the abstract adding the data to prove it.
Changes in the text: page 2, line 32-38.

Comment 2: Regarding the manuscript
(1)The aim of this study was to analyze DM patterns and prognosis of different metastasis groups in elderly ESCC population, using the SEER database.
The authors did not evaluate all pattern of metastases. So, why not evaluate the DM patterns in patients who failed primary treatment (surgery/ surgery after neoCRT/ dCRT) with curative intent in these elderly patients.
(2)Moreover, the authors did not make a difference in the whole group of solitary DM vs multiple DM. They only analyze different pattern of DM according to anatomic location and not taken into account the distant nodal metastases, which may have a different impact on the results of prognostic analysis.
(3)How were patients staged to identify distant metastases and was staging a part of the primary staging of ESCC patients? Detecting methods both as staging and /or follow-up should be mentioned (CT/MRI or FDG-PET/CT) /US) because of differences in sensitivity and specificity.
(4)They should also mention the minimal active FU program. Patients were divided into bone-only group, brain-only group, lung-only group, liver-only group and multiple groups were not mentioned according to their site and primary treatment.
Metastases were further grouped according to different treatment but not in direct relation to their anatomic location
(5)Patients were grouped in solitary and multiple metastases. Patients were divided into bone-only group, brain-only group, lung-only group, liver-only group and multiple groups according to the site of metastasis and further grouped according to different treatment
1.Solitary metastases were divided in:
Lung-only 35.6%, most common metastatic site for ESCC
liver-only (24.2% , most common metastatic site for EAC
bone-only (11.0%)
brain-only (1.5%)
2.Multiple metastasis: n= 149 (27.7%). To which organs?
The authors should give more insight in the pattern of metastases related to treatment, both initial treatment and after detecting DM.
(6)DM can occur everywhere as a part of a solitary or multiple metastases side. So, metastases may occur at distant nodular area such as supraclavicular or along the inferior retroperitoneal sides. The authors even exclude metastases to other organs (see fig 1) and have to explain which sides.

Reply 2:
(1)Because of the limitation of the SEER database, only 4 organs (brain, bone, liver, lung) can be analyzed for metastasis, so we can only evaluate the patterns of

metastases based on the 4 organs. What's more, we can also not evaluate the DM patterns in patients who failed primary treatment (surgery/ surgery after neoCRT/ dCRT) with curative intent in these elderly patients, for the lack of related information in the database.

(2)We analyze the patients in stage of IVB. Whether the patients with distant nodal metastases is not important.

(3)Because of the limitation of the SEER database, we cannot get the information about the detecting methods(CT/MRI or FDG-PET/CT) /US).

(4)Because of the limtation the database, the SEER database lacked details on chemotherapy (only two options yes and no/unknown) and other site of DM (only 4 organs), which has effects on the results of prognostic analysis and the selection of patients.

(5)The organs of multiple metastasis have many different combinations like bone+brain, bone+liver, bone+lung, bone+brain+liver, bone+brain+liver+lung, etc. We have mentioned it in the abstract (see page2, line22). We cannot give more about the detailed information of different treatments, for the limitation of the database.

(6)Because of the limtation the database, we cannot have the detailed information about the sides of metastasis and we can only analyze the 4 metastatic organs