

Peer Review File

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Reviewer A

- 1) First, the title needs to accurately describe the clinical research design of this study, i.e., a retrospective cohort study.

Reply: Thanks! That's a good idea. I thought the original title would be better in a broad way. At first draft of this paper, it was once adopted. However that will narrow the papers scope. So we deleted it. If you think it's necessary, we can do it.

- 2) Second, the abstract is not adequate and needs further revisions. The background only indicate the knowledge gap but did not describe the clinical significance of this research focus. The methods need to describe the inclusion of subjects, assessment of baseline factors, follow up procedures, and more detailed statistical methods such as Cox regression. The results need to first briefly summarize the clinical characteristics of the study sample, as well as HR and accurate P values for the identified factors. The current conclusion should be tone down due to the lack of control group and the retrospective research design.

Reply: Thanks for good suggestion. Due to the words number limitation in the abstract, only several main factors were selected in brief. But all-above mentioned factors were detailed in the method part. Thank you again!

- 3) Third, a more detailed review for the treatment of CESCC, treatment outcomes, and limitations of prior studies is needed. The authors need to explain why their data could answer the unaddressed questions in prior studies.

Reply: I think the limitations of prior studies were in line 109-114 Pg.4, and more explanation was detailed comparing with our results in the discussion part.

- 4) Fourth, in the methodology of the main text, please describe the clinical research design, sample size estimation of this study, details of follow up, and how to ensure the quality of the outcome assessment. In statistics, details of the Cox regression analysis are needed and please ensure $P < 0.05$ is two-sided.

Reply: OK! The revision was detailed in the statistical analysis.

Changes in text:

Line 253,254 Pg.8.

The baseline characteristics and disease factors were summarized with descriptive statistics in 120 patients.

Line 257,258 Pg.8.

A Cox proportional hazard model was used for multivariate analysis (two-sided test with $P < 0.05$ considered significant).

- 5) Finally, please consider to cite several related papers: 1. Yen JH, Jen CW, Huang TT, Tsai YC, Cheng SHC. Association of supraclavicular node metastasis with survival in node

positive esophageal squamous cell carcinoma patients treated using definitive chemoradiation. *Ther Radiol Oncol* 2020;4:28. 2. Yan K, Wei W, Shen W, Du X, Zhu S, Zhao H, Wang X, Yang J, Zhang X, Deng W. Combining the systemic inflammation response index and prognostic nutritional index to predict the prognosis of locally advanced elderly esophageal squamous cell carcinoma patients undergoing definitive radiotherapy. *J Gastrointest Oncol* 2022;13(1):13-25. doi: 10.21037/jgo-21-784. 3. Li C, Li B, Yang Y, Liu J, Zhang M, Zhang H, Tan L, Shen X, Li Z. Stratified treatment of localized cervical esophageal squamous cell carcinoma induced by neoadjuvant immunotherapy plus chemotherapy (SCENIC). *J Thorac Dis* 2022;14(9):3277-3284. doi: 10.21037/jtd-22-402.

Reply: I think the first and third paper were very important which are cited as Reference17 &18. Thank you for your suggestion.

Changes in text: Line 553-558, Pg.17.

17 Yen JH, Jen CW, Huang TT et al. Association of supraclavicular node metastasis with survival in node positive esophageal squamous cell carcinoma patients treated using definitive chemoradiation. *Ther Radiol Oncol* 2020;4:28

18 Li C, Li B, Yang Y, Liu J, Zhang M et al. Stratified treatment of localized cervical esophageal squamous cell carcinoma induced by neoadjuvant immunotherapy plus chemotherapy (SCENIC). *J Thorac Dis* 2022;14(9):3277-84.

Reviewer B

The paper titled “Long-term clinical outcomes and prognosis after definitive radiotherapy for patients with cervical esophageal squamous cell carcinoma: a single-institution retrospective study” is interesting. Definitive radiotherapy is a reasonable curative treatment option with laryngopharyngeal preservation for CESCC patients. Radical treatments for lymph node metastases may improve the OS and LRFFS times. Monitoring for thyroid function may be warranted during long-term follow-up. However, there are several minor issues that if addressed would significantly improve the manuscript.

1) In addition to radiation-induced hypothyroidism, the incidence rate of cardiovascular diseases is not low. Follow up on cardiovascular symptoms among long-term survivors should be increased.

Reply: Thank you for your suggestion! In our follow-up, no patients died of heart attack. And in the radiation therapy for the cervical esophageal squamous cell carcinoma, the lower margin of the radiation field was above the top boundary of heart, so the hearts of patients were not encompassed in the definitive radiation therapy. So the heart or/and vascular examination were not within the scope of follow-up as usual. Sorry for that.

2) What is the efficacy and toxicity of concurrent chemoradiotherapy in patients with cervical esophageal squamous cell carcinoma? Suggest adding relevant content.

Reply: Acute and late toxicities part was listed in line 301-320 Pg.9&10. Thanks.

3) It is suggested to compare the long-term outcomes between neoadjuvant chemotherapy + surgery and definitive chemoradiotherapy for cervical esophageal squamous cell carcinoma.

Reply: Surgery, which can cause many problems, is not advised in NCCN guideline for cervical esophageal squamous cell carcinoma patients. And now in our MDT for esophageal cancer, the cervical esophageal cancer patients usually didn't receive the surgery, and only several patients did it in the early years. So the patients who did receive the surgery were excluded in this study. Sorry for that.

4) This study is a retrospective analysis, which is likely to cause some deviations in the results. It needs to be further confirmed by multi-center clinical trials.

Reply: OK! Thanks you! In the last paragraph of discussion, "Future prospective multicenter, randomized, open-label studies with larger populations and accurate standards are necessary to confirm our results for CESCC with long-term follow-up." in line 470-473 Pg.14. Thank you again.

5) The introduction part of this paper is not comprehensive enough, and the similar papers have not been cited, such as "Stratified treatment of localized cervical esophageal squamous cell carcinoma induced by neoadjuvant immunotherapy plus chemotherapy (SCENIC), J Thorac Dis, PMID: 36245591". It is recommended to quote the article.

Reply: thank you! It's cited as Reference18.

Changes in text: Line 556-558, Pg.18.

18 Li C, Li B, Yang Y, Liu J, Zhang M et al. Stratified treatment of localized cervical esophageal squamous cell carcinoma induced by neoadjuvant immunotherapy plus chemotherapy (SCENIC). J Thorac Dis 2022;14(9):3277-84.

6) What is the long-term impact of prognostic nutritional index in cervical esophageal squamous cell carcinoma patients undergoing definitive radiotherapy? Suggest adding relevant content.

Reply: Thanks for your advice! Prognostic nutritional index is an important influential factor in the cancer patients especially for the massive trauma treatment such as the surgery. This factor is not usually adopted in the prognostic analysis in the radiation therapy study. Our paper is about a retrospective study. So we didn't collect the relevant data at first. Sorry for that! I think we will try to use this prognostic nutritional index for our all next study. Thank you again!