**Peer Review File**

Article information: http://dx.doi.org/10.21037/tcr-22-582

**Reviewer A:**

*Please include more details about the pathomechanism of radiation-induced pneumonitis*
*Some minor grammar and spelling issues need to be resolved*

Reply 1: Thanks to the reviewer's suggestion, we have added the relevant mechanism of RP to the Discussion section. At the same time, we have carefully corrected English grammar and spelling issues throughout the manuscript.

Changes in the text: (see Page 12, line 251-255), (see Page 6, line 110-111,119), (see Page 7, line 126-127), (see Page 8, line 162-163), (see Page 8-9, line 168-170), (see Page 9, line 178-179).

**Reviewer B:**

*Methods*
*1) Page 5. Ln 95*
*-In this study, many patients were treated with 3D-CRT or IMRT. Typical radiation filed positioning is wanted to describe. Such as, AP/PA fields with two oblique fields regarding to the 3D-CRT. Such as, volumetric modulated arc therapy or fixed-field IMRT regarding to the IMRT.*

Reply 2: Many thanks for the valuable comments of the reviewer. We have modified our text as advised.

Changes in the text: (see Page 5, line 96-97)

*2) Page 5. Ln 100-*
*-According to Chinese Guidelines for Radiotherapy of Esophageal Carcinoma (Heyi, G. Chinese Guidelines for Radiotherapy of Esophageal Carcinoma (2020 Edition). Prec Radiat Oncol. 2021;5:54-72), elective lymph node irradiation is recommended for definitive RT. The authors CTV concept is explained as GTV plus 5-8mm margin and adjacent lymphatic vessels. It is unclear for me whether elective lymph node irradiation was done or involved-field irradiation was selected. If wide elective node irradiation was omitted, this should be explained clearly for reader to understand*

*your concept.*

Reply 2: Thanks to the suggestions of the reviewer. we have made corresponding changes in the revised manuscript.

Changes in the text: (see Page 5-6, line 98,103-104)

*3) Page 6. Ln 104*
*-The cumulative dose of radiotherapy was ranged 40-60 Gy (maybe 2 Gy per fraction?). Strategy of cumulative radiation dose at author's institution should be explained.*

Reply 2: Thanks to the reviewer's suggestion. Strategy of cumulative radiation dose has been described in the revised manuscript.

Changes in the text: (see Page 6, line 106-107)

*4) Page 7. Ln 135*
*-The authors describe that diagnosis of RP using several radiological changes in the CT radiation filed. Compared with 3D-CRT, definition of "radiation filed" seems ambiguous in IMRT technique. Definition of radiation filed would be recommended to be explained such as irradiated area more than 20 Gy. However, sometimes radiological changes spread outside of irradiation filed in patients with severe RP. Under this condition, definition of "in the CT radiation field" may not be suitable for RP. If there are patients with RP that spread outside of irradiation field in this study, definition of "in the CT radiation field" is recommended to be modify (e.g. around the irradiated lung).*

Reply 2: Many thanks. we have modified our text as advised.

Changes in the text: (see Page 7, line 138)

*Results*
*5)*
*-Generally, several statistical methods have not been explained in Methods section.*

Reply 2: Thanks to the suggestions of the reviewer. the statistical methods used in this study have been detailed in the Methods section of the revised manuscript.

Changes in the text: (see Page 7-8, line143-153)

*6)*

*-Smoking status is categorized in Yes or No. Currently, smoking status is more complexly categorized or assessed using absolute values. I recommend that smoking status as variable should be categorized into scientifically. For example, ">pack-year vs not", "Current smoker vs former or never smoker", "Current smoker vs Ex or never smoker". Website of Ministry of Health, Centers for Disease Control and Prevention will help you.*

Reply 2: Many thanks for the kind suggestions of the reviewer. Further classification of smoking status can predict the occurrence of RP to a certain extent. In this study, we focused on the prediction of RP with or without smoking history. We'll investigate smoking status for further classification according to the kind suggestions of the reviewer.

*7) Page 8. Ln 158*
*-Detail of chemotherapy regimen and intent should be explained. Intent of chemotherapy that performed prior to radiotherapy is possible to be palliative intent not as induction.*

Reply 2: Thank you for the suggestions of the reviewer. We study the effect of chemotherapy on RP, which includes radical chemotherapy, adjuvant chemotherapy and palliative chemotherapy. We will further investigate the association of different chemotherapy regimens with RP in follow-up studies based on the reviewer's suggestion.
Changes in the text: (see Page 8, line165)

*8) Page 8. Ln 164*
*-In Table 1, four continuous variables (age, MLD, PTV dose, and V20) are listed. These variables are divided into two categories (age;65 years, MLD;13 Gy, PTV;54 Gy, and V20;25Gy). The authors should explain how to determine the thresholds in Methods section (even if it is not important for your conclusion).*

Reply 2: Age is grouped according to the median, and the grouping of dosimetric parameters is based on the practice of our center.

*9) Page 8. Ln 163*
*-Grade 3 or more RP occur in 8 patients in this cohort. In most clinical trial, severe adverse effects are defined in Grade 3 or more. It is only my interest, I wonder whether your nomogram can predict Grade 3 or more RP clearly.*

Reply 2: Many thanks for the valuable comments of the reviewer. Our nomogram can only predict the occurrence of RP (grade ≥2) for limited sample size. Predicting the occurrence of different levels of RP requires further research.

*Discussion*
*10)*
*In discussion section, the authors describe the epidemiology and principle of RP in first and second paragraph. Continuously, they describe literature review that developing risk factor of RP in thoracic RT using serum biomarkers, radiological findings, and dosimetric feature. This section is well-written and reader can understand about the recent management of RP. However, there seems to be a lack of discussion of limitation in this study. I think this study include several limitations.*
*1 This study includes retrospective feature.*
*2 The number of patients is relatively small compared with the similar article in the past. This limits a statistical power.*
*3 The patient's cohort have heterogeneity feature especially in treatment procedure. For example, around 25% patients received RT alone. In addition, prescribed RT dose is ranged from 40 to 60 Gy. The author should consider this nomogram is based on such heterogeneity data.*
*4 The median RT dose to PTV is 46 Gy. This is relatively low compared with radiation dose used in definitive RT for ESCC (50-60 Gy). The clinician may hesitate to use this low-dose based nomogram model.*

Reply 2: Many thanks for the suggestions of the reviewers, we have added the limitations of this study in the discussion section.

Changes in the text: (see Page 16, line 334-339)

*11) Page 12. Ln 239*
*-In the present study, the authors describe 60% patients developed RP within 6-10 weeks. The reader may be interested in timing of development RP in remaining the 40% patients.*

Reply 2: Thanks for the suggestions of reviewers. We have described in detail the time when patients developed RP in the results section. According to the time of occurrence of RP, among the 30 patients with RP (grade≥ 2), there were 4 cases in 4 weeks of radiotherapy, 18 cases occurred between weeks 6 and 10, 4 cases in 12

weeks, 3 cases in 16 weeks and 1 case in 18 weeks.

Changes in the text: (see Page 9, line170-172)

*12) Page 13. Ln 263*
*-As the author mentioned, glucocorticoids have potential of decreasing CRP levels. Considering this point, it is not negligible that most patient might be received glucocorticoids as antiemetic prophylaxis for chemotherapy-induced nausea in this patient cohort. I think it is not necessary to include whether glucocorticoids administering the as a covariate, it is desirable to mention in discussion section.*

Reply 2: In fact, although glucocorticoids are commonly used in the prevention and treatment of chemotherapy-induced nausea and vomiting. The glucocorticoids at this time are usually small doses and short courses of treatment, which will not suppress the immune status of the body for a long time. In the treatment of RP, the use of glucocorticoids is usually a long-term administration of large doses, which will inhibit the immune function of the body. Therefore, this study considered that glucocorticoids may lead to the decrease of CRP, so the level of CRP was not monitored while using glucocorticoids.

*13) Page 14. Ln 290*
*Page 15. Ln 318*
*-As the result of univariate analysis, tumor stage and lung V20 seem the strongest risk factor for RP. What do you think reason why tumor stage and lung V20 are not appeared into independent risk factor?*

Reply 2: We considered tumor stage and lung V20 not to be independent risk factors, because neither tumor stage nor lung V20 were statistically different in multivariate analysis.

Minor points

*14) Page 2. Ln 19*
*-Insert space (from 174 patients).*

Reply 2: Thanks for the reviewer's reminder, we have added a space in the corresponding position.

Changes in the text: (see Page 2, line 19)

*15) Page 2. Ln 30*
*-Spell out RT as radiotherapy.*

Reply 2: Thanks for the reviewer 's suggestions, we have made corresponding modifications.

Changes in the text: (see Page 2, line 30)

*16) Page 4. Ln 68*
*-Abbreviate radiation pneumonitis as RP.*

Reply 2: Thank you. we have made corresponding modifications.

Changes in the text: (see Page 4, line 68)

*17) Page 6. Ln 118*
*-Please explain version of TNM stage.*

Reply 2: Tumor stage was classified using the TNM staging system proposed by the American Joint Committee on Cancer (8th edition).

Changes in the text: (see Page 6, line 121-122)

*18) Page 6. Ln 119*
*-The expression "Total PTV" seems not informative enough. Do you mean "Mean dose to total PTV" or "prescribed dose to total PTV"?*

Reply 2: Thanks to the reviewer's suggestion. We have explained it in the method section and corrected the total PTV as the prescribed dose.

Changes in the text: (see Page 6, line 123)

*19) Page 8. Ln 157*
*-87% is wrong value (73.6%).*

Reply 2: Thanks for the reviewer's reminding. We have modified it.

Changes in the text: (see Page 8, line 163)

*20) Page 8. Ln 159*
*-The median of PTV was 46 Gy. As mentioned in methods section, please explain what DVH parameter is used.*

Reply 2: Thanks for the suggestions of the reviewer, we have made explanations in the corresponding parts.

Changes in the text: (see Page 8, line 165)

*21) Page 5. Ln 94*
*Page 9. Ln 168, Ln 169*
*-"Radiation therapy" should be unify into "radiotherapy".*

Reply 2: Thank you. we have modified our text as advised.

Changes in the text: (see Page 5, line 95) (see Page 9, line 177)

*22) Page 15. Ln 319*
-"Radiation pneumonitis" could be abbreviated as RP.

Reply 2: We have corrected it in the manuscript according to the kind suggestions.

Changes in the text: (see Page 15, line 330)

*Table 1*
*23)*
*-To enhance the results of comparing incidence rate of RP between each clinical feature categories, values of percentage are wanted to be aligned. I mean, for example,*

*RT techniques Sum RP Non-RP*
*3DCRT 32(18.4%) 9(28.1%) 23(71.9%)*
*IMRT 142(81.6%) 21(14.8%) 121(85.2%)*

Reply 2: Thanks for the suggestions of the reviewer, we have made corresponding adjustments to the form.

Changes in the text: (see Page 22, line 462)

*24)*
*-The order of clinical feature should be sorted as clinical implications.*
*In my opinion, age, sex, PS, smoking, stage, position, COPD, reticular pattern ground-glass opacity, linear opacities, bronchiectasis, emphysema, RT techniques, MLD, PTV, V20, chemotherapy.*

Reply 2: Thanks for the suggestions of reviewers, we have made corresponding adjustments to the form.

Changes in the text: (see Page 22, line 462)

*Figure3*
*25)*
*-Units should be added to IL-6_2W (pg/mL) and CRP_6W (mg/L).*

Reply 2: We have tried our best to increase the units of the corresponding indicators in the dynamic nomogram.

Changes in the text: Figure3

*Figure S1*
*26)*
*-Regarding to p-value below Mann-whitney U test, it is described "p<0.1" in Methods section.*

Reply 2: We are sorry that our expression was unclear and caused you to misunderstand. We have used a more precise expression in the Methods section of the revised manuscript.

Changes in the text: (see Page 7-8, line 143-153)