

Peer Review File

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Reviewer A

Comment 1: I thought that this title was slightly confusing, it is recommended for the authors to alter the title to make it easier for the readers to understand all contents of this manuscript.

Reply 1: We changed the title to make it more descriptive.

Changes in the text: See page1, line4-5

Comment 2: It was interesting that there are cases who show ground glass opacity in three-dimensional analysis when the nodules show the pure solid component in two-dimensional CT. However, even if the thoracic surgeons recognized that information, I wondered whether the thoracic surgeons would change the surgical procedures to limited resections in the cases who had a slight ground glass opacity by the analysis using the three-dimensional CT. What do the authors think about this?

Reply 2: In our analysis this time, we did not investigate the effect of the surgical procedure on the prognosis, and we recognize that this is one of the future research topics. However, the relationship between the prognosis of segmentectomy and lobectomy in 3D pure solid may differ from the results of JCOG0802 and CALGB140503. Therefore, depending on the results of future research, we believe that all thoracic surgeons should determine the surgical procedure after recognizing the presence or absence of GGO by 3D analysis.

Changes in the text: None

Comment 3: In this study, three procedures, lobectomy, segmentectomy, and wedge resection were included. I couldn't understand the selection criteria of procedures for lung cancer in the authors' institution. Therefore, it is recommended for the authors to add selection criteria of procedures for lung cancer.

Reply 3: At our facility, we basically choose lobectomy for 2D pure solid early lung cancer. Segmental resection may be performed as aggressive reduction surgery based on SUVmax, tumor growth rate, tumor marker values, etc., or as passive reduction surgery considering pulmonary function and complications. Regarding partial resection, all cases are carried out as passive reduction surgery. We added.

Changes in the text: See page13, line191-195

Comment 4: OS and RFS were analyzed in all cases who underwent lobectomy, segmentectomy, and wedge resection. I think that it is necessary for the authors to assess the OS and RFS in each procedure.

Reply 4: We also prepared the surgical procedures performed between the two groups in the propensity score match. This time, instead of comparing prognosis between surgical procedures, we are investigating whether the presence or absence of GGO by 3D analysis contributes to pathological findings and prognosis. We are considering future research on prognostic comparison between surgical procedures for this research subject.

Changes in the text: None

Comment 5: Although I understood the preferable outcomes of the cases with ground glass opacity in the three-dimensional CT, it was unclear how these results would affect the decision making of the procedures for Stage 1A-lung cancer.

Reply 5: From the results of this analysis, it was found that the presence or absence of GGO in 3D analysis is a prognostic stratification factor for 2D pure solid early lung cancer. In the future, we will reconsider the research on the influence on the decision of the surgical procedures.

Changes in the text: None

Reviewer B

Comment 1: The title is “Relationship between the detection of ground glass opacity by a three-dimensional analysis and the pathological findings and prognosis in two-dimensional pure solid early lung cancer”

As in the result section reported, the tumor size tended to be larger in the 3D solid group, resulting in less IA1 and more IA3 at the clinical stage. This could potentially contribute to the outcome of the study showing poorer OS and RFS in 3D solid group.

Could you do univariate and multivariate analysis of the OS and RFS, adjusting for tumor size and clinical stage?

Reply 1: I think you are right. We will perform univariate and multivariate analyzes of OS and RFS again with data after propensity score matching adjusted for tumor size and clinical stage, and submit it as a supplemental table.

Changes in the text: See page15, line235-237

Comment 2: The propensity score analysis (PSA) showed the 3D GGO was associated with a significantly better prognosis. The effectiveness of PSA in eliminating the selection bias is not perfect. (A recent study suggested that propensity score matching may accomplish the opposite of its intended goal—increasing imbalance, inefficiency, model dependence, and bias. *Journal of the Society for Social Work and Research*, Volume 11, Number 3. 463-481. doi: 10.1086/711393)

I suggest adding to the limitations of the study that as it is an observational study, we could not eliminate the potential effect of the higher clinical stage in 3D solid group on the poorer outcome in this group. Further prospective clinical trial is recommended to overcome this limitation.

Reply 2: As you pointed out, I added a note about the limitations of bias elimination by propensity score matching.

Changes in the text: See page19, line305-308

Reviewer C

Comment 1: Are there any discrepancy between tumor (consolidation) size measured in 2D view and 3D view causing clinical staging migration such as IA3 -->IA2?

Reply 1: GGOs detected by 3D analysis are located outside solid components that can be recognized in 2D. Therefore, although there may be a difference in the maximum diameter of the tumor, there was almost no difference in the maximum diameter of the solid component. Therefore, there were no cases with different clinical stages in 2D and 3D.

Changes in the text: None

Comment 2: Significant differences in pathology (high SqCC portion in 3D solid group) may be responsible for survival difference. Too big difference of squamous cell cancer factor in OS and PFS is difficult to understand and unbelievable. (HR 2.772 in OS, 0.98 in PFS).

Please analyze again.

Reply 2: As you pointed out, the difference in HR for squamous cell carcinoma OS and RFS in the cox proportional hazards model analysis is very noticeable. I ran the analysis again and got the same result. Many of the Sq cases have emphysema, and it is thought that there are a certain number of cases who died from other respiratory diseases such as pneumonia without recurrence, but this is only speculation.

Changes in the text: None

Comment 3: The figure of 3D analysis in figure 1 is not striking. Please show new figure with actual C/T volume ratio.

Reply 3: As you pointed out, I added the actual C/T volume ratio of the cases presented in Figure 1.

Changes in the text: See Figure 1

Reviewer D

Comment: The work carried out is considered interesting and worthy of further study. The manuscript is believed to be worthy of publication.

Reply: Thank you for your wonderful comment.

Reviewer E

Comment 1: The flow-chart shown in Figure 1 should be shown in the "results".

Reply 1: We have already presented the flow chart of Figure 1 at the beginning of "Results". We have removed the presentation of Figure 1 in the "Methods".

Changes in the text: See page13, line187 and page9, line 129-130

Comment 2: Indication and exclusion criteria should be specified in "Methods" and the paper should be rewritten according to the STROB check list.

Reply 2: We have already mentioned the inclusion and exclusion criteria at the beginning of the "Methods".

Changes in the text: None (see page9, line123-129)

Comment 3: Since the main and secondary endpoints are ambiguous, it is necessary to rewrite them so that they can be understood at a glance in "Methods".

Reply 3: Added as you pointed out.

Changes in the text: See page11, line165-166

Comment 4: You should write more about the follow-up method of the case.

Reply 4: Added as you pointed out.

Changes in the text: See page12, line179-181

Comment 5: The variables used for matching in Propensity score match should be specifically indicated.

Reply 5: Added as you pointed out.

Changes in the text: See page11, line175-176

Comment 6: It is recommended to summarize key results with reference to study objective as 1st paragraph.

Reply 6: Added as you pointed out.

Changes in the text: See page16, line240-242

Reviewer F

Comment: The authors are commended for a well performed study. Can be accepted for publication.

Reply: Thank you for your wonderful comment.