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Reviewer A

Comment 1 :

The authors have analyzed 1260 patients with lung cancer who underwent surgery by using single institutional retrospective survival data. They concluded that survival of stage I lung cancer patients 80 years old or more was almost equivalent to that of younger populations with reasonable postoperative complications. Relatively large study cohort is considered be the strength of this study, however, there exist some problems in this study. The objective of this study described in abstract section is not fully investigated and conclusion does not respond to the objective of this study. Multivariate survival analysis by three age categories (Y group, M group and O group) would be necessary to evaluate the survival impact of age categories. Similarly, multivariate logistic regression analysis for postoperative morbidity and mortality by three age categories (Y group, M group and O group) would be also necessary. Table 4-6 merely show the results of stratified analyses by age categories. Unfortunately, the obtained results from this study are considered be not fully reliable and add few knowledges to readers.

Reply 1 ; We understand the reviewer's suggestion. We analyzed the risk factors for postoperative complications of grade \geq II among Y, M, and O groups, respectively. The results of significant risk factors for postoperative complications varied depending on the groups; higher age and squamous cell carcinoma for Y group, male sex, lower vital capacity, and FEV1/FVC for M group, and lower Charlson comorbidity index for O group.

However, the significant risk index among O group revealed lower CCI compared to a previous study. It was considered that patients with higher CCI were likely to be indicated for the safer procedure of wedge resection, in contrast, patients with lower CCI seemed to be more likely to undergo the more radical surgery of lobectomy. As a result, the latter tended to have more complications than patients with higher CCIs in this cohort. In other words, a sublobar resection procedure might reduce postoperative complications for high-risk patients with higher CCIs, and a radical lobectomy procedure for patients with lower CCIs might have a higher likelihood of postoperative complications, which should be carefully monitored, postoperatively.

Changes in the text: We added the associated content to the Results and Discussion on Page 9 lines 156—159, Page 11 line 205 to Page 12 line 213, and the new Table 5.

Comment 2:

The last sentence in “Abstract” would be better to be shown in “Discussion” section.

Reply 2: We understand the reviewer's suggestion. We moved the sentence to the Discussion section.

Changes in the text: We moved the content to Page 15 line 266—269.

Comment 3:

Table 1. The p-values derived by Kruskal-Wallis test show if there exist the differences among three groups, not in two groups. Mann-Whitney-U test with Bonferroni corrections of significant p-value level

(0.05 divided by 3) would be appropriate for testing differences of continuous variables between two groups in three categories.

Reply 3: We understand the reviewer's suggestion. We checked the analysis and revised the associated content, accordingly.

Changes in the text can be found on Page 6 line 103—113 and Tables 1 and 2.

Comment 4:

3, Table 1 and 2. Fisher's exact test or Chi squared test would be adopted for comparisons of categorical variables such as sex, pack-year category, CEA level and so on.

Reply 4: We understand the reviewer's suggestion and have revised, accordingly.

Change in the text: We revised the content on Page 6 lines 104—105 and Tables 1 and 2.

Reviewer B

Comment 1:

Why the patients divided as three groups; <60 years, 60-79 years, and 80≤ years? The reviewer thinks that dividing as 2 groups; <80 years and 80≤ years is suitable, if the main purpose of this study is to show the surgical risk and survival rates of octogenarian patients.

Reply 1: We understand the reviewer's suggestion, which we followed. However, in this study, we intended to compare surgical results of octogenarians vs middle-aged cohorts, as well as those of octogenarian vs younger cohorts aged ≤60. There were several studies that compared surgical results of octogenarian lung cancer patients with those of septuagenarians, of which result was likely to almost same as two groups. In contrast, little is known about the differences in surgical results between octogenarians and younger patients, thus far. As a result, overall survival was inferior among octogenarians, due to shorter life expectancy, however, oncological survival was similar in both groups, demonstrating that surgical treatment for octogenarians was justified and acceptable, while being cautious of perioperative higher morbidity, even when compared to younger patients. This evidence indicates that it is worth performing procedures for older patients, while maintaining caution for perioperative management.

Change in the text: We added the recommended content to Page 9 line 164 -Page 10 line 185.

Comment 2.

The authors told about the surgical risk and survival rates among octogenarian patients with lung cancer in present study. The authors have previously reported some studies which have similar title (ref. 9, 10, 25). It is a little bit difficult to understand the difference between the author's previous reports (ref. 9, 10, 25) and the current study. Please, clarify this issue.

Reply 2: We understand the reviewer's suggestion. Previously, we reported surgical results for lung cancer patients that were limited to octogenarians and did not distinguish between older and younger patient groups. Although an indication of surgery for octogenarians was relatively biased, based on each surgeon's assessment, the simple comparison with surgical outcomes for younger patients might enable us to identify a surgical impact on older patients, especially octogenarians, and help with decision-making for surgical indication moving forward. Specifically, our results indicated that the overall survival of older patients was relatively poor, however, oncological outcomes were equivalent to those of younger patients with acceptable morbidity, suggesting that surgical treatment for older patients, especially those aged ≥80 was considered a valuable

procedure to control cancer progression.

Therefore, we stressed the difference in surgical outcomes between older and younger patients.

Change in the text: We added the associated content on Page 9 line 164 -Page 10 line 185.

Reviewer C

Comment 1:

I think this is a reasonable study with a moderate number of patients. Clearly there is selection bias in offering surgery for the > 80yo age group which contributes to overall survival. The oldest group had limited surgery (which would need to be better defined as sublobar (wedge or segment) and received less adjuvant therapy (2%). In addition, radical surgery will also need to be better defined (ie lobectomy, pneumonectomy). It would probably be worth adding categories to the tables of wedge resection, segmentectomy, lobectomy stratified by age group.

Reply 1: We understand the reviewer's suggestion. As mentioned, we think the say way that there was a selection bias in O group. We changed the phrase "limited resection" to "sublobar resection" and described the procedure precisely

Change in the text: We added the recommended content in Page 15 lines 264—266 of limitation part and Page Tables 1-5.

Comment 2:

Showing KM survival for all comers in Figure 1 is ok, but the authors should caution the reader that these are across all stages of lung cancer. The better KM survival graph would be what is presented in Figure 2.

Reply 2: We understand the reviewer's comment. We apologize for potentially misleading readers regarding the survival analysis.

We added content including all stages of lung cancer to Figure 1 and emphasized the limited analysis in Figure 2.

Change in the text: We added the recommended content to Page 7 lines 131—132, and Page 8 lines 138—139.

Comment 3:

Charlson comorbid index is one measure of frailty. Did the authors collect any other measures of frailty beside sarcopenia?

Reply 3: We understand the reviewer's question. We are very sorry that we cannot provide any other score regarding frailty. However, in this study, we attempted to assess sarcopenia by using body mass index, a simple variable representing preoperative weight loss and the potential influence of cachexia on surgical results among patients stratified by age. Our results confirmed that lower body mass index was a strong factor for long-term survival among octogenarians, demonstrating that nutritional condition is of great value for preoperative lung cancer patients, especially for older patients, in addition to the Charlson comorbidity index.

Change in the text: We added the associated content to Page 13 line 241 - Page 14 line 246.

Comment 4:

I would suggest combining Table 4,5,6 and just showing multivariate analysis for each age group.

Reply 4: We understand the reviewer's suggestion. We changed Tables 4, 5, and 6 accordingly.

Change in the text: We created a new Table 4

Reviewer D

Comment 1:

One of the main purposes of this study is to compare the perioperative surgical results among the three groups. But there are only three characters related to this purpose: postoperative complications, postoperative hospital mortality and hospital stay. Can the authors add more characters reflecting surgical results?

Reply 1: We understand the reviewer's suggestion. We discussed the various preoperative factors affecting postoperative outcomes, especially among older patients. Many variables had already been reported as risk factors for surgical results. If possible, assessment of patient pre- and postoperative status, mental and cognitive condition, and performance status might be desirable to analyze postoperative course more precisely, especially for older patients. Unfortunately, we were not able to add more characteristics in this study, however, we presented that a lower body mass index calculated by height and body weight, was a potentially valuable factor, as well as higher pathological stages, for which data are easily collected worldwide without any special equipment. We described this point as a limitation.

Change in the text: We added the associated content to Page 15 lines 268–270.

Comment 2:

The mean observation time for the old group was only 22.6 months, while the study aimed to compare the 5-year survival rates among the groups. The results are not reliable here since the follow-up time was quite short.

Reply 2: We understand the reviewer's concern. The follow-up time of O group was shorter than the other groups, partly because more recent patients had undergone surgery, and partly because of increased non-cancer related deaths. Additionally, the life-expectancy period was very short in our cohort. Regardless of the short observation time, we consider these to be reasonable results and that a future study with a longer observation time will ultimately confirm the trend we observed.

Change in the text: We added the associated content to Page 10 line 180–185.

Comment 3:

Postoperative complication and postoperative adjuvant therapy are two prognostic factors, why are they not included in the Cox proportional hazard model?

Reply 3: We understand the reviewer's question. We included preoperative variables for the Cox proportional hazard model in this study. As suggested, we added the two variables of postoperative complication and adjuvant therapy to the Cox proportional hazard model in the revised manuscript. The result revealed that postoperative complication and postoperative adjuvant therapy were not a significant risk factor in this cohort.

Change in the text: We added the results in Page 8 lines 145–146, to Table 3 and the new Table 4.

Comment 4:

The “Statistical analyses” part should be rewritten.

Reply 4: We understand the reviewer's comment and agree that the description was insufficient. Therefore, we rewrote the “Statistical analyses” section more precisely to address all statistical analyses.

Change in the text: We rewrote the Statistical analyses section on Page 6 line 103–113.

Comment 5:

In Table 1, the proportion of patients who received adjuvant therapy in the old group was extremely low. Can the authors explain why?

Reply 5: We understood the reviewer's question. In daily clinical practice, we usually discuss an indication for adjuvant chemotherapy on a case-by-case basis. Among the O group aged ≥ 80 , we do not generally perform adjuvant therapy due to age-related organ damage and intolerance of physical and mental conditions for adjuvant platinum-doublet chemotherapy. As a result, the proportion of adjuvant therapy was significantly lower in the older group. This may be one reason for the poor survival among O group.

Change in the text: We added the requested content to Page 10 lines 177–180.

Comment 6:

When categorizing surgical procedures, the authors used “limited resection” and “radical resection”. I think it is not appropriate, please amend it.

Reply 6: We understand the reviewer's suggestion. We considered “limited resection” as wedge resection or segmentectomy, and “radical resection” as lobectomy or pneumonectomy. As the reviewer mentioned, “limited resection” and “radical resection” were not appropriate phrases. Hence, we renamed the procedure correctly as follows; wedge resection, segmentectomy, lobectomy, and pneumonectomy and have included a definition of limited resection, including wedge resection and segmentectomy.

Change in the text: We revised the content on Page 7 lines 123, Page 10 lines 171–172, and Tables 1–5.

Comment 7:

Standard uptake value max is a prognostic factor in middle aged patients, please use the bold font for it in Table 5.

Reply 7: We understand the reviewer's suggestion.

Change in the text: We changed the font of the new Table 4, accordingly.

Comment 8:

The authors mentioned “incomplete resection” in Line 133, does it mean “palliative surgery”?

Reply 8: We understand the reviewer's question. We considered “incomplete resection” as “palliative surgery”.

Change in the text: We changed the phrase, accordingly on Page 7 line 117.

Comment 9:

Line 50 “total complication rate” should be “higher total complication rate”

Reply 9: We understand the reviewer's comment. We changed the phrase, accordingly.

Change in the text: We changed the phrase on Page 2 line 43.