Peer Review File

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Response to Reviewer's Comment:

We sincerely thank you for careful reading and are privileged to receive your thoughtful suggestion. And we feel terribly sorry about our omissions. Although there might be some problems that we couldn't solve, we do try our best to modify this study and hope that all corrections are satisfactory. In addition, the followings are answers to your questions:

Comment 1: SEER database may not be suitable for your study. You want to know the exact indication of surgery among octogenarians. As a thoracic surgeon who want to perform a successful operation, we should know information about not only cancer, but also function of the patient. However, SEER does not have such information. It seems reasonable to find a database that satisfies the conditions or to analyze between groups that have no choice but to have similar conditions (patients who have undergone surgery for stage I lung cancer may be similar).

Reply 1: Thanks a lot for this key advice. As you are concerned, comorbidity and cardiac/pulmonary functions are so critical as to decide whether surgery or not. Firstly, as for our design of this study, Zheng C's work(1) and Liang W's study(2) are our major references. The former tried to distinguish optimal esophagectomy candidates in elderly patients based on SEER database, and the latter wanted to identify optimal candidates for primary tumor resection among metastatic non-small cell lung cancer patients. Then we utilized a web-based predicted model to create user-friendly access. Secondly, we choose cancerspecific survival (CSS) as the primary endpoint, which could partly avoid the influence of non-cancer elements including comorbidity and cardiac/pulmonary functions, to a certain extent. In other words, cancer-specific death excluded the death from comorbidity and cardiac/pulmonary functions, which could help us get more solid results. CSS of surgery & beneficial group identified by our predicted model is significantly improved compared with non-surgery group (HR: 0.40, 95% CI: 0.36-0.44) and non-beneficial & surgery group (HR: 0.43, 95% CI: 0.36-0.53). Meanwhile, there is no significant difference in NCSS (noncancer specific survival) between the beneficial & surgery group and nonbeneficial & surgery group (p= 0.258). These results have been added as supplementary figure 3, which suggested that patients in beneficial & surgery group might indeed benefit from surgery not only just benefit from good cardiac/ pulmonary functions. Thirdly, the competing risk model was used in our study(3). Through a subdistribution analysis of competing risks, competing risk model doesn't treat the competing risks of the event of interest as censored observations but directly translates to the survival probability. Although it is so a pity that lack of data on comorbidity and cardiac/pulmonary functions, we have tried a lot to complete our study. It is meaningful and necessary to incorporate them into a more integrated predicted model in future research.

Changes in the text:

We have added the above results to Results (pages 13, lines 270-276; pages 16, lines 340-355); added figures to Supplementary figure 3 and Supplementary table 2.

Comment 2: Authors categorized all surgeries as a same group (that is,

OPERATION), but as you know, wedge and others are different because the former is diagnostic, but the latter is curative. Moreover, wedge can be performed in patients who have poor lung/cardiac function, but pneumonectomy should be just in the patients of good function. Therefore, patients with wedge and with pneumonectomy are different absolutely, especially in octogenarians. As you know, apple and orange are not comparable. How about performing a separate analysis per each surgery?

Reply 2: The reviewer's comments are significant and we can learn a lot. Yes, this problem does exist, patients with different lung/cardiac functions may receive different surgical approaches. With this in mind, we draw Kaplan-Meier curves and found that patients who received wedge resection indeed has poorer OS (p = 0.025) and CSS (p = 0.026) than those with lobectomy in the beneficial & surgery group. Meanwhile, above all of them have improved survival than patients in non-beneficial & surgery group and non-surgery group. Then We performed a subgroup analysis. (Supplementary figure 4 A, B, and C). In detail, patients were divided into different groups according to surgical approach, and the beneficial group always has improved CSS than those in non-beneficial group. We also performed the same analysis on stage I patients because most patients who received sub-lobectomy resection were stage I and observed similar results (Supplementary figure 4 D, E, and F). These suggest that our predicted model could identify specific patients who might benefit from surgery-resection in different surgical approach groups. Return to the objective of our study, we try to identify specific patients who might potentially benefit from surgical resection. Which surgical approach would be performed needs more information including cancer and noncancer factors to make a decision.

Changes in the text:

We have added the above results to the part of Results (pages 13, lines 276-280; pages 16, lines 328-331); added figures to Supplementary figure 4.

Comment 3: Interpretation of the data is also important. octogenarians are in a special situation. Their remained life is shorter than younger one and it may be various as their lifestyle. In some part of treatments, not being harm may be more important than being radical. If this particularity is overlooked, it can be interpreted that surgery is helpful even for stage IV patients. In other words, the reason for longer survival may not be because of the surgery, but because of the good condition that allowed the operation to be performed. How about interpreting the results again by carefully thinking the causal relationship?

Reply 3: We appreciate your kind suggestions sincerely which pointed out the key problem. Some sentences are so deterministic to mislead others. We have amended the manuscript accordingly.

Changes in the text:

We have modified the description as advise (pages 11, lines 220-221; pages 15, lines 308-311, line 314-315; pages 17, lines 360-364).

[References]

- Zheng C, Luo C, Xie K, et al. Distinguishing optimal esophagectomy candidates in elderly patients: A nomogram based on propensity score matching. Eur J Surg Oncol 2022;48(4):909–16.
- Liang H, Liu Z, Huang J, et al. Identifying optimal candidates for primary tumor resection among metastatic non-small cell lung cancer patients : a population-based predictive model. Transl Lung Cancer Res 2021;10(1):279– 91.
- 3. Zhang Z. Survival analysis in the presence of competing risks. Ann Transl Med 2017;5(3).