Article information: https://dx.doi.org/10.21037/ccts-22-12

Reviewer A

Comment 1 : (1) Lung cancer: The treatment of NSCLC is clearly different from that of SCLC, and

the authors could specify the type of lung cancer rather than just "lung cancer" when discussing the impact of surgery on older patients with lung cancer.

Response 1: We agree with the reviewer's suggestion and have specified the type of lung cancer as "non-small cell lung cancer" in the text.

Changes in the text: We have specified the term throughout the manuscript.

Comment 2: (2) Surgery: The title only mentions surgery but the Abstract and Introduction also include radiotherapy and treatment strategies. Why did the treatment strategy discussed in this article not include chemotherapy (Introduction, Methods, and Main Body)?

Response 2: As the reviewer states, we discussed mainly surgery for older patients aged 80 or above in detail. Additionally, with respect to local cancer treatment, radiation therapy is considered as an alternative to surgery, when the latter is not possible. Therefore, we discuss surgery as well as radiation therapy; however, chemotherapy, as a systemic treatment, is considered to be completely different from surgery and local radiation therapy. Thus, we had excluded the description of a chemotherapy strategy for older patients with lung cancer in this review article.

Changes in the text: We have added the content in Page 2 lines 26-29.

Comment 3: (3) Older patients (lines 101-102): "Accordingly, studies of lung cancer surgery in older patients targeted older generations, considering individuals aged \geq 80 years as a good set point". The authors did not explain clearly why they focused primarily on older patients aged \geq 80 years. The previous mentions are aged \geq 75 years or aged \geq 70 years. Furthermore, given the heterogeneity of patients aged \geq 65 years, it is clear that older is not adequately defined by chronological age but requires a more comprehensive assessment of a person's biological age. It is suggested that the authors could emphasize this point.

Response 3: We understand and have considered the reviewer's suggestion. Although there were reports that included lung cancer patients aged 70 or older, the outcomes of these patients did not differ much from that of the entire cohort; thus, it did not describe the true characteristics of older lung cancer patients. To investigate and explore clinically accurate features of older lung cancer patients undergoing surgery and discuss the outcomes unique to these patients, surgeons raised the age cutoff value in the definition of older patients to 80 or above. Accordingly, studies of lung cancer surgery in older patients emphasized on older generations, considering individuals aged \geq 80 years as an accurate starting point. Thereafter, surgeons considered that older patients with lung cancer aged \geq 80 years had comparatively higher surgical risks than other patients who fell under the category of "old" patient.

Changes in the text: We have added the abovementioned content in Page 6 lines 108-116.

Comment 4: The introduction does not describe the existing issues clearly:

(1) The reasons for the emphasis on lung cancer surgery;

Response 4: According to past publications, the results of selected overall outcomes of surgery for older lung cancer patients, despite being poorer than those of younger generations, were still acceptable (3-5). Surgical resection is the most effective therapeutic intervention; however, it is associated with a relatively high risk of morbidity and mortality, especially for older patients, which is a major concern for surgeons. Changes in the text: We added the content in Page 4 lines 61-67.

Comment 5: (2) Why is the treatment strategy for older lung cancer patients more complex;

Response 5: To address the reviewer's concern, we have described additional information in the introduction session:

Furthermore, there are no definitive criteria for surgical indication, an appropriate procedure of limited resection or radical lobectomy, and postoperative follow-ups in our daily clinical practice, which contribute to another complex issue not faced by the younger generations.

Changes in the text: We added the content in Page 4 lines 68-70.

Comment 6: (3) What are the knowledge gaps in lung cancer surgery for elderly patients and what has changed in recent years;

Response 6: We have mentioned the suggested content in the introduction session:

Recent publications demonstrated that the postoperative complication rate and long-term survival of older patients who underwent lung cancer surgery were reasonable; therefore, active surgical treatment is considered desirable. However, objective optimal surgical indications and procedures and outpatient follow-ups based on appropriate risk management, especially for borderline patients with multiple comorbidities, are unclear. Thus, this presents a major knowledge gap in lung cancer surgery for older patients.

Changes in the text: We added the content in Page 4 line 70-75.

Comment 7: (4) Regarding the novelty of this review compared with similar reviews (lines 104-106), we suggest that the authors move it to the Introduction.

Response 7: We have moved the sentence to the Introduction section; previous review articles also summarized the outcomes of lung cancer surgery in older patients; however, they merely stated the surgical results based on several older studies (6-8).

Changes in the text: We moved the sentence to Page 4 lines 64-65.

Comment 8: Methods

(1) We suggest the authors also add the date of search ("31 October 2022") in the text.

Response 8: Thank you for your kind suggestion. We have added the date of search in the text. Changes in the text: Page 5 line 83.

Comment 9: (2) Does the author have restrictions on the type of literature? Are systematic reviews taken into account?

Response 9: We had restricted the included articles to those on octogenarian lung cancer surgery, and excluded case reports, studies with a sample size under 50, and systematic reviews.

Comment 10: (3) We also suggest the authors add an independent supplement table to present the detailed search strategy of PubMed. The authors could present search terms connected by the Boolean operators in Table X.

Response 10: We have added a supplement table 1 showing the Boolean operators. Changes in the text: We added the new supplement table 1, and comment in Page 5 lines 89-90.

Comment 11: (4) Table X (The search strategy summary) should be cited in the text. In addition, please name Table X as Table 1, and change the numbering of subsequent tables accordingly.

Response 11: According to the reviewer's suggestion, we have made a new Table 1.

Changes in the text: We have added the new table 1 and changed the numbers of the subsequent tables.

Comment 12: (1) Errors in section numbering: "4. Postoperative complications and mortality among older patients with lung cancer" and "4. Conclusions".

Response 12: Thank you for pointing out this error regarding the numbering of the sections. We have rectified our error accordingly.

Changes in the text: We have corrected the section numbering.

Comment 13: (2) As stated in comment 1(3), it is suggested that the authors could add the type of lung cancer and the clinical features (e.g., cardiopulmonary function, comorbidities) in the text as well as in the tables (like table 1).

Response 13: We have included the procedures and co-morbidity, as well as the morbidity and mortality rates. Changes in the text: We have added the content in Page 7 line 130-134.

Comment 14: Conclusions

Lines 324-326: "we can properly select an operable patient and perform an optimal procedure mainly on a case-by-case basis according to the experience of the surgeon". Could the authors specify how to select and develop the optimal treatment strategy (e.g., risk assessment, screening, multidisciplinary management)? Are there some limitations in this regard? Does the author have some experiences or recommendations?

Response 14: As suggested, there were some limitations in achieving a consensus in indication or procedure for lung cancer surgery in older patients among surgeons worldwide. In case of marginal high-risk patients, we may use the database system produced by STS or ESTS to predict postoperative morbidity and mortality to decide a surgical indication and procedure with high accuracy. However, considering the surgical results, similar outcomes were obtained worldwide. While this is interesting, this resulted in the assumption that surgeons selected almost the same indication and procedure even in a marginal patient with multiple comorbidities in a poor performance status.

Changes in the text: We added that content in Page 8 lines 150-157 and Page 17 line 350-351.

Reviewer B

Comment 15: There is no specific number quoted in the introduction part. Eg. "the number of older

patients afflicted by it is increasing" and "surgery for older patients with cancer is associated with a relatively higher risk". I'd like to see more accurate data to show the exact proportion of old patients in Japan and the increased surgical risk for them.

Response 15: We have described the accurate data in the manuscript; In Japan, the number of older lung cancer patients aged 80 or above undergoing surgery has increased up to 1.5 times compared to 10 years ago (from 2273/26092, 8.7% in 2007 to 5779/44140, 13.1% in 2017) (3, 4). According to past publications, the results of selected overall outcomes of surgery for older lung cancer patient aged 80 or above, despite being poorer than those of younger generations, are still acceptable; the postoperative morbidity rate was 20-28%, while mortality rate was 2.3-8% (5, 6).

Changes in the text: We have added the content in Page 4 lines 59-64.

Comment 16: There is no need to divide the introduction part into three paragraphs. And I recommend the authors to add a heading for the result parts and number the result paragraphs as "3.1, 3.2, 3.3...". Response 16: We have changed the introduction part as suggested and have also added headings in the result part, accordingly.

Changes in the text: We have changed in the introduction section and have added the heading numbers in the results part.

Comment 17: Line 119, Page 6: What's the definition for "fine older patients"? Please note that "in case of" is a fixed phrase, corrections are required here.

Response 17: We understand the reviewer's suggestion.

Changes in the text: We have added the content in Page 7 line 134-137.

Comment 18: Line 135, Page 7: According to this paragraph, the summary concluded by the authors ("short-term outcomes, including postoperative morbidity and mortality of older patients, especially octogenarians, undergoing surgery were likely to be poorer than those of younger patients due to physiological senescence, multiple comorbidities, and frailty") merely relies on Yang's study. This is not convincible.

Response 18: We have changed the paragraph to make it more convincible. Changes in the text: We have added the content in Page 8 line 157-162.

Comment 19: Line 164, Page 8: The comparison between older and younger patients here is vague and difficult to understand. Please clarify it clearly.

Response 19: Thank you for pointing this issue out. We have added the age of the younger patients. Changes in the text: Page 8 lines 157-159.

Comment 20: In paragraph 5, the authors focused on prognostic factors for surgical octogenarian patients, instead of their survival data. I would recommend the authors to change the subtitle.

Response 20: We have changed it accordingly to reflect the reviewer's comment.

Changes in the text: We have added the content in Page 8 lines 165.

Comment 21: Line 198, Page 10: Please add the age information of the study cohort from the American

nationwide database study.

Response : The study cohort was patients aged 80 or above. Changes in the text: Page 11 lines 220-223.

Comment 22: Comment 8: Line 208, Page10: The logic of this sentence is quite confusing, "segmentectomy and wedge resection, compared with lobectomy, were not significant risk factors for OS, ... preoperative comorbidity might have a greater impact on OS than the oncological impact, and sublobar resection might reduce non-cancer mortality, especially in the older cohort". Please split this long sentence into several shorter ones and express one meaning in one sentence.

Response 22: We have split this long sentence to make it more readable.

Changes in the text: We have changed the sentence in Page 11 line 230-233.

Comment 23: Line 242, Page 12: Who is being compared here? The octogenarians with lung cancer but hadn't received any treatment?

Response 23: We apologize for the confusion. The intended meaning of the sentence was that the median OS was that of SBRT vs. surgery.

Changes in the text: We have added the content in Page 14 line 271-275.

Comment 24: Line 246, Page 12: "Karnofsky Performance Status, inoperability, solid nodule, tumor size..." Were these prognostic factors for SBRT and other high-energy therapies? Please clarify this sentence.

Response 24: We have clarified the sentence accordingly.

Changes in the text: We added the content in Page 12 line 268-271.

Comment 25: Line 281, Page 14: "Hence, the following approaches to improve the QOL... considered". The following content didn't mention any definitive solutions to improve QOL. Correction is required here.

Response 25: We have corrected the sentence accordingly.

Changes in the text: We have added the content in Page 15 lines 313-315.

Comment 26: In the conclusion part, in addition to surgery selection, summaries of radiation therapy and QOL are also needed.

Response 26: We have added a sentence regarding radiation therapy and QOL; Changes in the text: We have added the content in Page 17 line 353-359.

Comment 27: The language needs further improvement, both grammar and sentence structure. It will be better to understand the meaning when a sentence is not too long. And please avoid too much repetition and simplify your language. I would recommend the authors to find a native English speaker to help revise the paper.

Response 27: We apologize for the errors in English grammar and sentence structure.

Changes in the text: We have prepared a revised manuscript with a native English speaker to rectify this issue.