Peer Review File
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Reviewer A

Comment:
The authors chose a very interesting topic on which to perform a study however the sample size is too small to lead to any meaningful clinical conclusions. In addition, I fear that the scant results which inform your conclusion that wedge resections may be associated with less morbidity than segmentectomy will incorrectly influence surgeons to perform more wedge resections than segmentectomies which does not align with published data. The important use of frozen sections in performing sublobar resections also needs to be highlighted to avoid re-resections that can introduce additional and avoidable risk to the patient.

Reply：

Thank you for your valuable feedback and constructive comments on our manuscript.
Regarding the sample size, we recognize that a larger sample size would have provided more statistical power and enhanced the generalizability of our findings. However, achieving a larger sample size in our study was challenging due to the limited patient population undergoing completion lobectomy and the single-center nature of our study. While we acknowledge the limitation of our small sample size, we have taken steps to mitigate its impact on the study outcomes and conclusions. For example, we conducted robust statistical analyses and provided a thorough discussion of the limitations associated with the sample size.
We understand your concern that our limited results may incorrectly influence surgeons to perform more wedge resections than segmentectomies. We want to emphasize that we intended to present our findings as preliminary evidence, highlighting the need for further research in this area. In the revised manuscript, we have now made it clear that our results should not inform immediate changes in clinical practice, but rather provoke more investigation into the topic.
Additionally, we appreciate your point about the important use of frozen sections in performing sublobar resections. We have made revisions to the manuscript to highlight the significance of frozen sections in guiding accurate surgical decision-making and minimizing the risk of re-resections.
Changes in the text: We have modified our text in the Discussion section (see Page 15, Line 297-318).

Reviewer B

Comment:
Great and thought provoking article. Unfortunately has only about 25 patients of the 236 patient charts reviewed, but they still found a significant statistical difference and i believe it has value and adds to the current literature.

I would recommend to describe in the methods or text of the article, the technique/approach used for operation, VATS, uniportal, robotic or type of thoracotomy. Also I would describe conversion to open during the second operation as this is also an important factor to review for complex re operations.

Reply:

Thank you for your valuable feedback and constructive comments on our manuscript, and we appreciate your acknowledgment of our research!

As you are concerned, several problems need to be addressed. According to your nice suggestions, we have made corrections to our previous manuscript in the Methods-Treatment section. The surgical procedures have been added to the text.

Changes in the text: We have modified our text in the Methods-Treatment section (see Page 7, Line 129-136).

Reviewer C

Comment 1:

While it is worthy of praise for authors to perform large number of repeated pulmonary resections, it would be obvious to conclude that an initial strategy of wedge resection is associated with fewer postoperative complications and a lower risk of needing bronchoplasty and angioplasty. Authors should compare the other factors such as the resected location of the initial surgery. In addition, despite of the type of initial surgery, whether mediastinal lymphadenectomy was performed or not during initial surgery may influence the difficulty of the second operation.

Reply 1: Thank you for your insightful comments on our manuscript. We appreciate your suggestions for further analysis.

You rightly point out that it would be valuable to compare other factors, such as the resected location of the initial surgery and the impact of mediastinal lymphadenectomy during the initial surgery, in our study. We agree that these factors could potentially influence the outcomes and should be considered in the analysis, and we have compared the wedge resection and segmentectomy groups in Table 5 and Table 6 to explore the influence of surgical location and lymph node dissection. We have revised the manuscript to include a discussion on the importance of considering these factors in future research to provide a more comprehensive understanding of the topic.

Changes in the text: We have modified Table 2(marked in red) and added Table 5 and Table 6. The result (See Page 10-11, Line 203-209) and discussion section (See Page 14, Line 277-288) were also modified.

Comment 2:

In Figure 1, ‘Patients with wedge resection for primary surgery (n=9)’ should be changed to ‘Patients with segmentectomy for primary surgery (n=9)’.

Reply 2:

We were really sorry for our careless mistakes. Thank you for your reminder.

Changes in the text: We have modified Figure 1.

Reviewer D

Comment 1:
Authors should discuss the percentage of the patients who underwent intended sublobar resection.
Reply 1: Thank you for your valuable comments on our manuscript. Of the 25 patients, nine (36%) underwent intentional resections and the other 16 were compromised. We have added this factor in Table 2.
Changes in the text: We have modified Table 2, marked in red.
Comment 2:
Authors should clarify the pathological and clinical stage of the tumor (TNM).
Reply 2: Thank you for your valuable comments on our manuscript. We have clarified TNM staging as clinical or pathological in the table.
Changes in the text: We have modified Table 2 and Table 3, marked in red.
Comment 3:
Figure 1 should be modified. Patients with "segmentectomy" for primary surgery (n=9) is true?
Reply 3: We were really sorry for our careless mistakes. It was true that nine patients underwent segmentectomy for initial surgery, and the other 16 patients underwent wedge resection. Thank you for your reminder!
Changes in the text: We have modified Figure 1.

Reviewer E

Comment 1:
I suggest deleting the word "delayed" because I think that it could generate confusion od misunderstanding to the authors. At the first glance, I thought that delayed could refer to some oncological results instead of post-operative outcomes;
Reply 1:
Thank you for your valuable comment. We initially chose this term to emphasize that our second surgery was not a remedial one(which happens not long after the first surgery), but a “delayed” one (which means intervals between operations were longer than that of remedial surgeries). We have considered other choices like “long after” as a substitute, however, we believe that “delayed” can better convey the meaning of “long interval”, thus we prefer not to change. Thank you again for your understanding!
Comment 2:
I suggest to completely review the statistical corner and analysis because the study population is small and then data reporting could be considered more accurate with median and IQR instead of mean and SD also because this study population is not normally distributed (I think due to the small numbers). I suggest a deep review by a statistician;
Reply 2:
Thank you for your constructive comments on our manuscript, we have reviewed the statistical part of the manuscript with the help of a statistics professor at our medical school. We did realize that several variables (such as age) were not normally distributed

either from the sample size or histogram, however, the Shapiro-Wilk test supported the zero hypothesis ($p>0.05$, not rejecting the assumption of a normal distribution) for the same variable. Therefore, the decision of whether it was normally distributed could be quite subjective, so we provided mean and SD as well to provide more comprehensive data. We apologize for the low sample size and statistical descriptions that may have inconvenienced your understanding of the article. Thank you again for your professional review!

Comment 3:

I suggest inserting a detailed list of complications, kind of complications and grade of complications;

Reply 3:

Thank you for your constructive comments on our manuscript, we have added a table to indicate the level of complications (classified as major or minor ones).

Changes in the text: We have modified Table 4, marked in red.

Comment 4:

what about oncological results after completion lobectomy? Could the authors comment on that?

Reply 4:

Thank you for your constructive comments on our manuscript, we have added a graph to indicate the RFS (recurrence-free survival) and OS (overall survival) between wedge resection and segmentectomy group after the completion lobectomy.

Changes in the text: We have added Figure 2 and modified the method (see Page 8, Line 155-161), results (see Page 11, Line 214-221), and discussion section (See Page14-15, Line 294-310).

Comment 5:

Pathological information should be implemented inserting the post-operative diagnosis (adenocarcinoma, squamous cell, other), surgical and pathological margins, pattern of adenocarcinoma, type of lymph node dissection

Reply 5:

Thank you for your constructive comments on our manuscript, and we have inserted the factors you mentioned in the Table.

Changes in the text: We have modified Table 2 and Table 3, marked in red. And results were also modified (see Page 9, Line 178-185).

Comment 6:

I suggest inserting some details of adjuvant therapy because these treatment could have an impact on the results of completion lobectomy;

Reply 6: Thank you for your constructive comments on our manuscript, and we have inserted details of adjuvant therapy in the table.

Changes in the text: We have modified Table 2 and Table 3, marked in red.

Comment 7:

L163 "no perioperative complications were reported (8): this sentence is not completely correct because Takamori et al reported 2 complications on 8 patients (25%), no mortality, nor cancer recurrence. Please modify the text accordingly.

Reply 7: We sincerely thank the reviewer for careful reading, and we apologize for the

careless mistakes. As suggested by the reviewer, we have corrected the text according to the literature.
Changes in the text: We have modified the text (see Line 259).

Reviewer F

Comment 1:
There is a small mistake in the flow diagram (segmentectomy group)
Reply 1:
We were really sorry for our careless mistakes. Thank you for your reminder.
Changes in the text:
We have modified Figure 1.
Comment 2:
I have only one remark: why so much wedge (and not anatomical resection) initially whereas it seems that these first surgeries were performed for compromised sub lobar resection but finally not for such an early stage (because surprisingly high rate of adjuvant treatment)?
Reply 2: Thank you for your valuable and professional comments on our manuscript. We agree that applying adjuvant therapy to patients indicates that the tumors are not so early-staged, because 16 out of 25 patients (64%) underwent compromised sublobar resections, which means lobectomy was preferred for this group of patients, but a "compromised" sublobar resection was done due to the patient's underlying disease or poor lung function. And we believe a postoperative adjuvant therapy (mostly chemotherapy) was necessary in this case. Thus, we think there is no contradiction between them. Thank you again for your professional review!

Reviewer G

Comment 1:
The results revealed in this study were easily expected. It is natural that the completion lobectomy following wedge resection is more favorable than that following segmentectomy. I think that the authors should describe more detailed operative findings in completion lobectomy after anatomical segmentectomy because anatomical segmentectomy includes various factors regarding technical aspects compared to wedge resection. For example, the factors include the use of a PGA sheet, extents of lymph node dissection, the use of staplers, and the method of intersegmental division, and so on. Thus, the difficulties of completion lobectomy after anatomical segmentectomy would depend on these technical differences. It is recommended that the authors focus on the technical differences during the first segmentectomy. On the other hand, I don't think that completion lobectomy after wedge resection needs to be discussed with this surgery because it is obvious that the completion lobectomy after wedge resection had no difficulties.
Reply 1:
We feel great thanks for your professional review work on our article. We agreed that

completion lobectomy after wedge resection is easier than that after segmentectomy, this is understandable since wedge resection typically involves the removal of a smaller portion of the lung, and subsequent lobectomy would involve removing an entire lobe, which is a more straightforward procedure. However, we believe that there have been no studies comparing the two surgical procedures in this particular scenario, and we believe that this can still be informative. In addition, we similarly wanted to explore the impact of lymph node dissection on the second operation and therefore compared wedge resection with segmentectomy. Thank you again for your nice suggestion!

Comment 2:

It was unclear why the authors defined the term of delayed completion lobectomy as more than 3 months.

Reply 2: Thank you for your valuable comments! We chose three months as the cutoff because we wanted to exclude remedial surgery since remedial surgery is not as difficult a procedure as reopening after a period (which is approximately five weeks according to literature), which may be related to adhesions that form at the pulmonary hilum after the first surgery. Therefore, we chose a much longer interoperative period to study the feasibility of CL.

Comment 3:

How do the authors decide the surgical approaches (VATS or Thoracotomy) in the completion lobectomy? I think that VATS is usually selected in the patients who undergo the completion lobectomy after wedge resection although this study has many patients who received thoracotomy in the completion lobectomy after wedge resection.

Reply 3: Thank you for your valuable comments! In our experience, VATS is usually the first option for completion lobectomy after wedge resection, when we encounter extensive adhesions or damage to the pulmonary artery, we will consider conversion to thoracotomy. Extensive adhesions are the most common reason of conversion to thoracotomy in our institute.

Comment 4:

It was insufficient to express the detailed technical difficulties described in line 146.

Reply 4:

Thank you for your valuable comments! We have added some information to supplement our points, including the reason why it is difficult to perform CL after segmentectomy and several strategies to secure the pulmonary artery according to your suggestion.

Changes in the text: We have modified the discussion section (see Page 12, Line 232-245).

Comment 5:

Please check Figure 1. Both groups were described as wedge resection.

Reply 5:

We were really sorry for our careless mistakes. Thank you for your reminder.

Changes in the text:

We have modified Figure 1.

Comment 6:

I found some mistakes of the use of spaces. Please check your manuscript before submission.

Reply 6:

We sincerely thank the reviewer for careful reading. As suggested by the reviewer, we have deleted the unnecessary spaces.

Changes in the text: We have modified the text.

Reviewer H

Comment 1:

In total, this is a retrospective study of a small cohort. Analyzing 25 patients in two different groups (segmentectomy vs. wedge resection) is statistically very difficult and I would like to question whether the results have any statistical relevance.

Reply 1: Thank you for your valuable feedback and constructive comments on our manuscript.

Regarding the sample size, we recognize that a larger sample size would have provided more statistical power and enhanced the generalizability of our findings. However, achieving a larger sample size in our study was challenging due to the limited patient population undergoing completion lobectomy and the single-center nature of our study. While we acknowledge the limitation of our small sample size, we have taken steps to mitigate its impact on the study outcomes and conclusions. For example, we conducted robust statistical analyses and provided a thorough discussion of the limitations associated with the sample size.

We understand your concern that our limited results may incorrectly influence surgeons to perform more wedge resections than segmentectomies. We want to emphasize that we intended to present our findings as preliminary evidence, highlighting the need for further research in this area. In the revised manuscript, we have now made it clear that our results should not inform immediate changes in clinical practice, but rather provoke more investigation into the topic.

Comment 2:

If the "operations interval" (Table 1) means that the patients were operated on after a median of 35 months and 25 months, then I wonder why the authors chose the cut-off of their patient inclusion after 3 months? Did some patients already have a recurrence after 3 months?

Reply 2: Thank you for your valuable comments! We chose three months as the cutoff because we wanted to exclude remedial surgery since remedial surgery is not as difficult a procedure as reopening after a period (which is approximately five weeks according to literature), which may be related to adhesions that form at the pulmonary hilum after the first surgery. Therefore, we chose a much longer interoperative period to study the feasibility of CL.

Comment 3:

Figure 1: The 3rd column in both boxes contains "patients with wedge resection". The first box should contain patients with segmentectomy.

Reply 3: We were really sorry for our careless mistakes. Thank you for your reminder.

Changes in the text: We have modified Figure 1.

Comment 4:

What were the reasons for a bronchoplasty or an angioplasty in three patients?

Reply 4: Thank you for your valuable comments! One of them underwent bronchoplasty because preoperative bronchoscopy suggested a visible tumor in the trachea; the other two both underwent angioplasty because of severe adhesions and difficult vascular isolation. All of these patients had their first surgery as segmentectomy, which reflected the difficulty of segmentectomy compared to wedge resection.

Comment 5:

Table 3: The recurrence rates of 44% and 50% are really high. Do you have an explanation for this high recurrence rates? Would these patients initially have profit of a primary lobectomy?

Reply 5: Thank you for your valuable comments! We are sorry for our statistical presentation that may have inconvenienced your understanding. The 48% and 50% are percentages of completion lobectomy for which the causes were recurrences, not recurrence rates. In this study, 16 out of 25 patients (64%) underwent a compromised sublobar resection, due to poor pulmonary function or underlying disease, and a lobectomy would be inappropriate in this case. Thank you again for your comments!

Comment 6:

What are the reasons why patients did not receive a primary lobectomy for lung cancer during this period? Neither the results of the JCOG0802 nor the CALGB study were published at the time of the study.

Reply 6: Thank you for your valuable comments! We agree that until the results of these two studies are available, the role of sublobar resection for early-stage lung cancer is still debatable, but there have been some single-center studies demonstrated that in individuals with early-stage NSCLC, sublobar resection is comparable to lobectomy, particularly for smaller tumors (2 cm or less in diameter)[1-4]. For patients with underlying diseases or poor pulmonary function, a “compromised” sublobar resection was also a choice. In addition, all surgical decisions are made in consultation with several experienced surgeons to maximize patient benefits in our institution. Thank you again for your professional review!

Reference:

1 Kodama, K., et al., J Thorac Cardiovasc Surg 1997, 114 (3), 347-53.
2 Koike, T., et al., J Thorac Cardiovasc Surg 2003, 125 (4), 924-8.
3 Okada, M., et al., Ann Thorac Surg 2001, 71 (3), 956-60; discussion 961.
4 Wisnivesky, J. P., et al., Ann Surg 2010, 251 (3), 550-4.

Reviewer I

Comment:

Thank you for the interesting work!

You have demonstrated the technical safety of a complementation lobectomy after segmentectomy or wedge resection.

As you describe, the cohort is very small and conclusions should be drawn with some caution.

You also write that CL after wedge resection was associated with fewer immediate postoperative complications.

Were there differences with regard to the localisation of the wedge resection (peripheral vs. central...)

How did the two groups differ in the postoperative phase in terms of oncological outcome (e.g. progression, recurrence, etc.)?

One should be very careful in drawing general conclusions about the best oncological approach (wedge vs. segmentecomy) based on the possible surgical complications after CL.

Reply:

We feel great thanks for your professional review work on our article. As you are concerned, several problems need to be addressed.

We agree that localization of the tumor could potentially influence wedge resection and subsequent completion lobectomy, however, all of the tumors included in our cohort are peripheral ones, thus it would be difficult for us to explore their potential impacts.

According to your nice suggestions, we have added some data on oncology outcomes in the text including Recurrence-free survival (RFS) and Overall survival(OS) after CL.

In addition, we understand your concern that our limited results may incorrectly influence surgeons to perform more wedge resections than segmentectomies. We want to emphasize that we intended to present our findings as preliminary evidence, highlighting the need for further research in this area. In the revised manuscript, we have now made it clear that our results should not inform immediate changes in clinical practice, but rather provoke more investigation into the topic.

Thank you again for your pertinent comments!

Changes in the text:

We have modified Figure 1 and added Figure 2(RFS and OS after CL).

We have also modified the method (see Page 8, Line 155-161), results (see Page 11, Line 214-221), and discussion section (See Page14-15, Line 294-310) for oncological results and decisions between wedge resection and segmentectomy.