

## Peer Review File

Article information: <https://dx.doi.org/10.21037/jtd-22-1289>

### Reviewer A

The authors have detailed the number and outcomes from lung cancer surgery at their institution from 2018 to 2021. Their goal was to evaluate the effect of the pandemic on outcomes from lung cancer surgery.

#### Major points

Comment 1: The

Reply 1: We request the Reviewer A to check if this is a typographical error.

Comment 2: The authors say in lines 16-18 of page 4 that “retrospective studies have shown that the operative mortality rates in patients undergoing elective surgery at the beginning of COVID-19 pandemic were higher than during the prepandemic period.” In fact many studies have shown that mortality rates did not increase. The authors should provide references to support their claim. The authors provided 3 references (8—10) in the sentence directly afterward. But one of those references, reference 8, showed that there was no difference in operative mortality.

Reply 2: Thank you for your valuable suggestion. As you mentioned, our study also showed the postoperative morbidity and mortality non-inferiority. Using reference 8 and another reference which showed the non-inferiority in postoperative complication, the description from lines 1, page 4 to line 3, page 5 were modified.

Comment 3: What were the specific months in which the groups were divided? For example, was January 2020 considered prepandemic or pandemic? It appears that all of 2020 and 2021 was considered pandemic. But the authors say in page 11 that “the first wave of the pandemic occurred in April of the same year.” It may make more sense to make April 2020 as the first month of the pandemic period.

Reply 3: Thank you for your important suggestion. I agree with your thoughts regarding the start of the pandemic. However, this study is basically a year-over-year comparison and the COVID-19 cases in Japan had already developed in January 2020. To account for the importance in consistency among all figures, we decided to retain the current style of comparison.

Comment 4: Related to comment 3, what was the social situation in the city of their institution in 2020? In the northern United States, for example, most lockdowns went into effect in March 2020. Most institutions stopped doing elective surgery for non-cancer cases for a short period in April or May 2020. Having this information for this

institution in the discussion would be helpful.

Reply 4: Thank you for your comment. We added detailed descriptions concerning the lockdown in other countries and regarding the circumstance in our hospital in lines 3–5, page 14.

Comment 5: Why do the authors think that the rate of minimally invasive surgery decreased (increase??) during the pandemic period? This should be addressed in the discussion if possible.

Reply 5: We think the reason is that minimally invasive surgery could be safely performed even during the COVID-19 pandemic. However, the number of minimally invasive surgeries started gradually increasing from 2019 itself. We think this is probably an institutional reason, and not an effect of the pandemic. We further explained this in the Discussion section (from line 14, page 15 to line 6, page 16).

Comment 6: In Figure 2 it says that the tumors being compared are just Stage I tumors. But in the violin plots listed it seems that many of the tumors are greater than 40 mm. That would make the tumors at least a Stage II. It may be that the authors included all tumors and not just Stage I tumors, but it needs to be clarified.

Reply 6: The 8th TNM stage was applied in this study. The cases whose tumor size was more than 40 mm were  $\leq 30$  mm in invasive size. We checked all the cases in Figure 2 and can confirm that they were pathological Stage I tumors.

Minor points

Comment 7: In Table 1 it would be better for the authors to list the percent or ratio of patients instead of just the absolute numbers. As an example, it would be better to say for hypertension that the 2018-2019 groups had 28.9% (128/443).

Reply 7: We appreciate your suggestion. Accordingly, we have added the percent ratio for all variables in Table 1.

Comment 8: In lines 8–10 on page 9 it says that “in the prepandemic group, the proportion of patients who received video-assisted thoracic surgery and robot-assisted thoracic surgery approaches increased significantly compared with the pandemic group.” Instead of “increased” it should be “was higher.”

Reply 8: Thank you for your comment. As you recommended, we changed the description in line 11, page 9.

**Reviewer B**

I would first like to congratulate the authors for a very complete and well structured work. There are nevertheless some aspects that could be improved:

Comment 1: ABSTRACT: In the Background, instead giving some random information about COVID-19, it should be more specific, structuring it into one sentence about the current state of the information, one sentence about which is the existing gap of information and one last sentence about how this work will fill that gap.

Reply 1: We modified the Background section in lines 11–14, page 2 as per the structure you recommended.

Comment 2: INTRODUCTION:

It doesn't fit with the conclusion. Your conclusion is that lung cancer surgery was safely perform during COVID-19 pandemic, but according to the introduction, that is not the objective of the paper, so you should rewrite the introduction to include it.

Reply 2: Thank you for your suggestion. As mentioned, our study showed the non-inferiority about postoperative morbidity and mortality. Therefore, we modified the Introduction section from lines 18, page 4 to line 3, page 5 using another reference which showed non-inferiority in postoperative complication.

Comment 3: METHODS:

You have studied the whole pandemic period (2020-2021) as a unit, but since –as you refer-, there has been several waves, maybe it would be necessary besides that general study, to perform a more specific study per wave, comparing the prepandemic period with each wave and its post-wave period. During these 2 years have been periods of almost normal life, so it would be interesting in order to really be able to affirm that surgery can safely be performed, to know the real impact not just of the whole period, but also during the worst parts of the pandemic.

Reply 3: Thank you for your insightful comment. As you pointed out, the effect of the COVID wave gradually diminished in 2021. We focused on the number of lung cancer surgeries for each wave of the pandemic and created Figure S4. Please note that in this Figure, the surgery number itself had an increasing trend. Therefore, the effect of the pandemic seems to decrease, especially in the latter parts of 2021. We explained this content from line 16, page 11 to line 1, page 12.

## **Reviewer C**

Thank you very much for the presentation of real-world data on surgical volume,

patients' demographics and surgical approaches during prepandemic and pandemic periods in a high surgical volume Hospital in Japan!

We appreciate the effort of the Hospital to maintain the surgical practice uninterrupted during these challenging times. We also notice that there was no delay between first patient presentation and surgery in both prepandemic and pandemic periods, which highlights again an effective workflow of the surgical department.

Overall, the article is well written and structured, has a concise conclusion and is based on a large volume cohort.

However, addressing a common topic during the COVID-19 pandemics, it is difficult, in my opinion, to add with the present study approach, novel and original aspects that could be of clinical impact and interest for the readers of the JTD Journal. Taking into account that similar data have already been reported in many previous papers, I think that the present article should address other- possibly unanswered- aspects that might be of interest for the routine workflow of every surgical department.

Based on these considerations, I think that the present study lacks on novelty and should be revised accordingly. Please find attached some comments that underline the need for a major revision of the article. Thank you for your effort!

I recommend a major revision of the article in order to improve the robustness of the results and overall novelty of the paper:

Comment 1: ABSTRACT:

In the Methods section of the abstract, I recommend to add a brief description of the study design according to the STROBE recommendations, as well as a brief presentation of the used tests (Page 2, line 15).

Reply 1: Thank you for your suggestion. We modified the Method section from line 16, page 2 to line 4, page 3 to clarify the design and tests used.

Comment 2: We suggest to add the data (median (IQR)) on morbidity and mortality (page 3, line 10), as well as to elaborate on the nomenclature "invasive size" in stage (page 3, line 8).

Reply 2: According to your valuable suggestion, we added data regarding the hospital stay morbidity and mortality, to lines 10–12, page 3. Further, we mentioned the invasive size nomenclature in lines 8–9, page 3.

Comment 3: How were the patients followed up postoperatively and how were the postoperative COVID-19 patients identified? Here, I see a major limitation of the study in the case that no postoperative follow-up (at least systematic phone calls 30 days or 180 days postoperatively, or systematic outpatient swab testing) was performed. I also assume that the asymptomatic, and undiagnosed COVID-19 patients did not routinely performed any tests post-surgery, therefore the real number of the postoperative COVID-19 patients could be biased in the article (page 3 line 9-12).

Reply 3: The postoperative patient follow-up was performed once in 3 months during the first 2 years and once in 6 months during 2–5 years. However, systematic COVID-19 screening was not conducted postoperatively. Therefore, we added this limitation in the Discussion section (line 8-13, page 16).

Comment 4: Please also improve the language by consulting a native speaker (e.g. page 3, line 14-15).

Reply 4: We have revised our manuscript for better English with the help of a native English speaker.

Comment 5:

#### MATERIALS AND METHODS

(Page 7) Please elaborate on the performed screening postoperatively (systematic phone calls with patients or house doctor 30 days/ 180 days postoperatively, PCR testing, nasopharyngeal swabs by COVID-19 suspicion) in order to derive an unbiased number of the real COVID-19 cases postoperatively (page 7 Line 4-9).

Reply 5: We added the postoperative follow-up protocol in lines 8–11, page 7.

Comment 6: I also suggest to remove redundant data reported in main body of the manuscript and Tables (e.g. Supplem. Table 1) in order to improve the readability.

Reply 6: Table S1 was excluded and we simplified the admission protocol explanation in lines 2–6, page 7.

Comment 7: Please specify why you calculated the ratio of COVID-19 patients in this sophisticated manner. I think that, plotting the median (IQR) incidence for each month is more effective and understandable for the readers of the Journal.

Reply 7: Thank you for your valuable comment. When we analyzed the relationship between the increased ratio of COVID-19 and operation volume in Figure 4, we realized that the half-month cumulative total was more effective in understanding the detailed change compared to the monthly approach. As you mentioned, the method was slightly complicated. Therefore, we added additional explanation in Figure S1.

Comment 8: RESULTS:

Please check the tables and the results section of the manuscript where you can avoid redundant data.

Please also add the percentages by procedure

s (n%) as well as the P-values derived from the Mann-Whitney-U Test for the procedures in Table 1.

Reply 8: We decided to exclude Table S2 because it repeated information from

Table 1.

We added percentages and checked P-values in Table 1. The P-values of Smoking, Procedure, Approach, Pathology, and Pathological Stage were evaluated by Fisher's exact test.

Comment 9: Page 8 line 15. Could you provide the number of the active smokers? One interesting aspect could be the smoking behavior.

Reply 9: The smoking status information was provided in Table 1. The smoking tendency did not change between the pre-pandemic and pandemic periods.

Comment 10: Page 9 line 9-11: One interesting aspect is the higher frequency of minimally invasive procedures in the pre-pandemic group. Do the authors have any explanations (for the discussion section). Thank you.

Reply 10: In our opinion, this is because we could safely perform minimally invasive surgery even during the COVID-19 pandemic. However, the number of minimally invasive surgeries had gradually increased from 2019 itself. Therefore, we think this is probably an institutional reason and not an effect of the pandemic. We added this in the Discussion section (line 14, page 15 up to line 6, page 16).

Comment 11: Page 11 line 18 combined with page 9 line 17: Given the similar TFS (time first visit to surgery) in the pre-pandemic and pandemic groups, how could you explain the larger tumors in stage one admitted for cancer resection in the pandemic period.

Reply 11: Thank you for your valuable question. We think one of the reasons for tumor enlargement in the pandemic period was the patients' hesitation to get a medical check-up. Lung cancer diagnosis was probably delayed in this period.

Comment 12: DISCUSSION:

Given the limited novelty of the presented data, I suggest to address in the discussion section the following points which might be of clinical interest for each surgical department.

1) How were the patients followed-up postoperatively upon discharge? A major limitation of the study is the identification of the real number of the (asymptomatic patients) which have not been tested postoperatively due to the lack of symptoms. Do you recommend a follow-up by phone calls for the whole cohort 30 days and 90 days after surgery?

Reply 12: Postoperative patient follow-up was performed once in 3 months during the first 2 years and once in 6 months during 2–5 years. (Therefore, there is no need to do a phone call follow-up.) We added the description about this protocol in lines 7–10, page 7. Additionally, we did not check systematic COVID-19 screening

postoperatively. This may be one of the limitations of this study. Therefore, this limitation was added to the Discussion section (lines 8–13, page 16).

Comment 13: 2) Might this approach improve surgical outcome and reduce the “real-world” postoperative COVID-19 incidence?

Reply 13: We did not check COVID-19 tests for all patients. However, we think our follow-up method was appropriate because postoperative morbidity and mortality were not different between the pre-pandemic and pandemic data.

Comment 14: 3) How could you explain the higher number of the minimally invasive procedures in the pre-pandemic period? (Open approaches are associated with increased length of stay which might be critical during COVID-19 pandemics)

Reply 14:

In our opinion, the reason for the increase in minimally invasive surgery is that we could safely perform the minimally invasive surgery even during COVID-19 pandemic. However, the number of minimally invasive surgery had gradually increased from 2019 itself. Therefore, we speculated that this was probably an institutional reason and not an effect of the pandemic. We described this point from line 14, page 15 to line 6, page 16.

When we open and minimally invasive surgery from 2018–2019 was compared, the length of stay was similar. Therefore, we think the approach did not affect the length of stay.)

Comment 15: 4) Given the similar TFS reported between the two groups, which is in your opinion the explanation for the larger tumor size during pandemic period?

Reply 15:

Thank you for your question. We think one of the reasons for tumor enlargement during the pandemic period was patients’ hesitation to get a medical check-up. Lung cancer diagnosis was probably delayed during the pandemic (lines 3–10, page 14).

Comment 16: 5) Which practical aspects could be routinely recommended in the surgical workflow of each department during COVID -19 pandemic?

Thank you for your work!

Reply 16: We added the recommended surgical workflow comment in lines 9–12, page 15.

**Reviewer D**

Comment 1: The authors should be congratulated for performing this study evaluating their outcomes pre- and post-pandemic. My main comment is that this study does not really show anything new. If the authors could add one more year of data for 2022 and discuss the role of vaccines and paxlovid, that would provide more insight into the analysis.

Reply 1: Thank you for your comments. Following your suggestion, we calculated the correlation between the increased ratio of COVID-19 cases and number of surgical cases. Based on the result, the negative correlation, which was seen in Figure 4, was not observed in 2022 data (Figure S3). One of the reasons for this change is the prevalence of vaccine and other therapies. We added this description from line 16, page 11 to line 1, page 12, and in lines 5–10, page 14.