Reviewer A

Comment 1: The objective of this work is to demonstrate the influence of upper gastrointestinal cancer surgery on postoperative complications. This work has some limitations, notably the unicentric character. It only reflects the surgical practice of a single team; the results will be difficult to extrapolate. We would like to have more information on the qualities of the logistic model. By example: The discriminative ability of the model was expressed by the area under the receiver operating characteristic curve (AUC ROC). The reliability of the model was assessed with the Hosmer–Lemeshow goodness-of-fit test. There are other methods to show the good calibration of the model between observed and predicted probabilities.

Reply 1: Thank you for this helpful comment. Certainly, as you pointed out, this is a retrospective study at a single facility, and we believe that this study might not be applicable to patients in other institutions. Also, when predicting a two-variable event with a two-variable outcome, it is difficult to draw an ROC curve. In this study, we described the Hosmer–Lemeshow test results which was also used to evaluate multicollinearity. So, we revised the manuscript as follows,

Changes in the text:
A backward stepwise selection method was used to build logistic regression models. We checked the multicollinearity of these factors in logistic regression models by Hosmer–Lemeshow test. (Page 4, Line 20)

Reviewer B

Comment 1: Thank you for the opportunity to review the manuscript, "Impact of previous upper gastrointestinal cancer surgery on complications after lobectomy for lung cancer." This retrospective analysis examined the association between previous upper gastrointestinal cancer surgery and postoperative pulmonary complications after thoracoscopic lobectomy. The authors thoroughly explored the association between previous upper gastrointestinal cancer surgery and postoperative pulmonary complications after thoracoscopic lobectomy. However, there are several points where additional detail or clarity is required.

Generally speaking, the event rate for the complications is rather low. In order to make

inferences about association or causality, one needs to adjust for various factors in a regression model, or some type of propensity score matching. For a regression, about 10-15 events per variable are needed in order to have reliability. In this small cohort, very few had a UGIS (various types) while few reached endpoints. Thus, I would venture to say that no clinical decision can be made based on the present study. Perhaps use of a multi-institutional database may enhance the statistical power of this analysis.

Reply 1: Thank you for your helpful advice. Certainly, as you pointed out, this is a retrospective study at a single facility, and we believe that this result is not everything. This is a small cohort study with a small number of events. Therefore, we think that no clinical decision can be made based on our study. However, as a preliminary step of multi-institutional research, I believe that it is meaningful, to some extent, that these results are released to the world. Thus, we added this sentence in our Limitations statement:

Changes in the text: This study had several limitations. First, this retrospective case-control study was conducted at a single institution; thus, more data accumulation is needed to validate our findings. Considering that this was a small cohort study and the number of events was also small, the use of a multi-institutional large database may enhance the statistical power of this analysis. (Page 7, Line 18)

Comments 2 and 3: I offer the following comments for the authors' consideration.
Introduction
1. The portion of the claim found primarily on page 3, line 8 that reports "that was diagnosed during subsequent follow-up" is lacking reference. It is unclear if references 4-6 are intended to support that portion of the claim.
2. In page 3, line 19 author mentions there are few studies on the short-term outcomes of surgery for lung cancer arising after UGIC surgery. However, these studies are not cited. It would be helpful to the reader to include these references in the text.

Reply 2 and 3: Thank you for your advice. As you pointed out, there was a slightly unclear part in the Introduction. Thus, we revised our introduction as follows:

Changes in the text:
The incidence risk of primary lung cancer is higher in patients with a cancer history (3), especially in patients with smoking-related malignancies and in patients with a history of esophageal, gastric, or head and neck cancer, and subsequent primary lung cancer is diagnosed during follow-up for other cancers (4-6). (Page 3, Line 8)

Although some studies have evaluated long-term prognosis of patients who have undergone lung cancer surgery, there are only a few studies on the short-term outcomes of surgery for lung cancer arising after UGIC surgery (1). (Page 3, Line 18)

Comment 4: Methods

1. Page 3, lines 24 and 29, its unclear how this information was obtained. Please specify if an institutional database, EHR, or some other method was used.

Reply 4: Thank you for your helpful comment. Certainly, as you said, we were unable to specify the source of clinical patient data and postoperative complications. We conducted research using electronic medical records and patient databases. Therefore, we revised our methods as follows:

Changes in the text:

Postoperative complications that occurred during hospitalization or within 3 months after surgery were extracted. We defined postoperative complications as those included in Clavien–Dindo grade ≥ II complications (13,14). We included the following postoperative pulmonary complications, as in our previous study: pneumonia; pneumonitis such as atelectasis and aspiration pneumonia; bronchopleural fistula; empyema; and respiratory failure including asthma attack, acute exacerbation of idiopathic pulmonary fibrosis, pleural effusion due to pleurisy, pulmonary thromboembolism, and chylothorax (15). All clinical data and the information of complications was obtained from our institutional database. (Page 4, Line 14)

Comment 5: Results

1. Page 4 lines 30 and line 31 the number of patients is included in parenthesis following a percentage, but in prior lines (page 4 lines 24, 27, and 28) a different syntax is used. Authors should be consistent in their presentation of information.

Reply 5: Thank you for your helpful comment. Regarding the first point, I am sorry that the percentage is difficult to understand. However, since the comparison between the two groups is performed using the ratio, I would like to keep the numerical value as it is as much as possible. Therefore, we added a supplement as follows,

Changes in the text:

Figure 2 shows the prevalence of postoperative pulmonary complications. Accounting for some overlap, 7.7% (5 in 65 patients in the UGIC group) of patients with a history of UGIC surgery developed pneumonia and bronchopleural fistula, and 6.1% (4 in 65 patients in the UGIC group) developed empyema (Figure 2). (Page 5, Line 3)

Comments 6 and 7:
2. Page 5, lines 1 and 2, would benefit from rephrasing for clarity, although most patients were older men who were heavy smokers with a lower vital capacity, Table 1 clarifies that this was not a homogenous group contrary to what the text implies.
3. Page 5, line 15 odds ratios for smoking index and tumor size should be included in text, notably these effect sizes are quite small thus it would be helpful to be included for the reader's consideration.

Reply 6 and 7: Thank you for your helpful comment. Regarding the first point, I am sorry that these sentences were difficult to understand. We have also added the odds ratios for the smoking index and tumor size as advised. Thus, we revised the Results as follows,

Changes in the text:
Patient characteristics according to a history of UGIC surgery are shown in Table 1. Patients with a history of UGIC tended to be older, heavier smokers, and had lower lung function in terms of vital capacity. (Page 5, Line 6)

Multivariable analysis revealed that the history of UGIC surgery was an independent factor associated with postoperative pulmonary complications (odds ratio [OR] = 2.92, p = 0.016), as were smoking index (OR = 1.01, p < 0.001) and tumor size (OR =1.03, p = 0.038). (Page 5, Line 18)

Comment 8: 4. Page 5, lines 21-24, there is a conclusion made regarding pulmonary complications in patients with previous lower gastrointestinal cancer surgery, however the sample only included 1 individual who had both previous lower gastrointestinal cancer surgery and pulmonary complications. It is not possible to make generalized conclusions based on an individual, as such this comparison should be omitted from the manuscript. This should be removed from the abstract as well, page 2, line 21.

Reply 8: Thank you for your helpful comment. Indeed, as you said, there is only one pulmonary complication in the LGIC group. Although it is not possible to make a statistically significant difference, as there was only one actual pulmonary complication, we considered it meaningful to describe this in our Results. For this reason, the following statements have been added to the limitation as follows,

Changes in the text:
First, this retrospective case-control study was conducted at a single institution; thus, more

data accumulation is needed to validate our findings. Considering that this is a small cohort study and the number of events is also small, the use of a large multi-institutional database may enhance the statistical power of this analysis. (Page 7, Line 18)

Comments 9 and 10: Discussion
1. Page 6, lines 22 and 24 by convention avoid referencing tables in the discussion section.
2. Page 7, lines 12-15, additional limitations should be mentioned. Notably the sample only included 14 people with previous "other cancer surgery" who had pulmonary complications and 39 across the entire study. It is difficult to generalize findings in such a small group to the population thus limitations of sample size must be mentioned.

Reply 9 and 10:
Thank you for your helpful comment. I apologize for referencing tables in the Discussion section, we have removed them as advised. Additionally, as mentioned in the previous reply, I added an additional Limitation as follows:

Changes in the text:
We evaluated preoperative nutritional status using serum albumin and prealbumin levels and found that they were significantly lower in patients with a history of UGIC surgery than in those without a history of UGIC surgery (Table 1). However, although nutritional status may have some influence on the risk of morbidity, serum albumin and prealbumin levels were not risk factors for postoperative pulmonary complications in our study (Table 2). (Page 6, Line 24)

First, this retrospective case-control study was conducted at a single institution; thus, more data accumulation is needed to validate our findings. Considering that this is a small cohort study with a small number of events, the use of a multi-institutional large database may enhance the statistical power of this analysis. (Page 7, Line 18)

Comment 11: Conclusions
1. Page 7, lines 20-21 should provide more detail regarding the implications of this research. The authors state that "efforts should be made to prevent postoperative pulmonary complications," however it would be helpful to clinicians and researchers to provide tangible possible interventions to reduce this burden.

Reply 11:
Certainly, as you said, I thought it would be better to provide an example of reducing

preoperative respiratory complications, so we added respiratory rehabilitation and smoking cessation as possible interventions as follows,

Changes in the text: Thus, efforts including preoperative respiratory rehabilitation and smoking cessation should be made to prevent postoperative pulmonary complications in patients with a history of UGIC surgery. (Page 7, Line 27)

Comment 12: Tables and Figures
1. Notably in Table 2 for smoking index, pack-year, it's possible there was a statistical or transcriptional error because the p-value is listed is <0.001, however the confidence interval includes the null value of 1. Given the significant p-value it's unlikely that the null value would be included in the confidence interval. Consider revisiting this analysis to confirm the proper odds ratio, P-value, and confidence intervals are displayed.

Reply 12: Thank you for your helpful comment. I am sorry that there is an error in Table 2 for the smoking index, pack-year. Thus, we revised Table 2.

Reviewer C

This manuscript reports that the previous surgical history of upper GI cancer is a risk factor for complications after pulmonary lobectomy. Despite the manuscript was well-organized, I think the following should be supplemented and explained in order to give useful information to the readers.

Comment 1: In general, patients who underwent upper GI surgery might have poor nutritional status, and as a result, complications after major surgery were expected to increase. However, in this study, nutritional status was assessed only with albumin levels, which were not risk factors for postoperative complication. Is it possible to evaluate using other variables such as BMI or oral intake?

Reply 1: Thank you for helpful advice. During the data collection in this study, the BMI measurements of the surgical patients were retrieved. However, the continuous variable BMI and the incidence of complications were not significantly correlated. In addition, the complication rate was higher in patents with high BMI than in those with normal BMI. For this reason, we thought it would be unreasonable to incorporate BMI into this study. In addition, preoperative intake was evaluated using prealbumin at our hospital. For this reason, prealbumin was added to this study and evaluated.

Comments 2 and 3: In statistics, the authors divided the patients into two groups: patient with history of UGIG and without a history of UGIG, but the difference in the patient number in each group is too large. In addition, patients in the without a history of UGIC group showed severe heterogeneity, including patients who did not undergo surgery, who underwent lower GI surgery, and who underwent other surgeries.

Patients' characteristics are totally different between the two groups (patient with history of UGIG and without a history of UGIG). In particular, pulmonary complications after lobectomy are greatly affected by age, gender, and smoking history. The patients with history of UGIC surgery already have these risk factors. In order to control these variables, it is thought that statistical methods such as case-control matching should be used.

Reply 2 and 3: Thank you for this helpful comment. Certainly, as you pointed out, the number of patients with a history of UGIC is low at 65 patients (4.7%), and it is questionable whether accurate comparisons with other groups have been made. The use of propensity score matching and control matching was also considered when comparing cases with a UGIC history, but it was thought that the comparison group would include a limited, selected case. When we performed propensity score matching, the history of UGIC was significantly associated with the incidence of pulmonary complications (48 patients vs. 48 patients; 12.0% vs. 0 %, $p = 0.011$); however, when comparing all cases and showing significant differences using multivariable analysis, we thought that there was a possibility that the result would be closer to everyday clinical practice. Therefore, we analyzed both patient groups as a whole, and calculated the significant factors using multivariable analysis.