

## Peer review file

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### Reviewer A

**Comment 1:** *The aim of the study is not clear. Although authors want to assess the prevention methods, this aim is neither describes in the methodology nor in the results.*

**Reply 1:** Thank you for your important indication. Our purpose of this study was to investigate the risk factors and etiology of middle lobe bronchus kinking following right upper lobectomy. As pointed out, we have not assessed but discussed the prevention methods from the results.

**Changes in the text:** We have changed the description. (See page 3, line 49, in the Abstract section Page 6, line 201, in the Introduction section).

**Comment 2:** *Definition of middle lobe kinking is established with a bronchoscopy (n=13) without confirmation with a CT scan (n=5, 38%). However, the results and the conclusion are based on CT scan data, of which 3 patients over 11 had a CT scan within 6 weeks after surgery. The timing of the CT can cause significant bias as mentioned in your discussion. Probably that these patients should be excluded from the study. Furthermore, without objectified atelectasis, what is the impact of the discovery of a kinking on bronchoscopy, an operator-dependant examination? Unfortunately, there is no clear and consensual definition of a middle lobe bronchus kinking.*

**Reply 2:** Thank you for your indication. As you pointed out, the finding of bronchoscopy was subjective, which could be a bias of this study. Moreover, the most problematic result of middle lobe bronchus kinking is atelectasis of the right middle lobe. Therefore, we have added the objective finding “complete atelectasis” to the definition of middle lobe bronchus kinking as following; i) complete atelectasis of right middle lobe with slit-like obstruction of the middle lobe bronchus found in the postoperative bronchoscopy, ii) no findings to suggest of lobar torsion.

The timing of the CT could be also a bias. Therefore, we have changed to analyze the displacement of residual lobes on CT performed only at 6 months after surgery.

**Changes in the text:**

We have changed the description as following;

Middle lobe bronchus kinking was defined as cases that satisfied the following criteria: i) complete atelectasis of RML (Fig. 1A, 1B) with slit-like obstruction of the middle lobe bronchus (Fig 1B) found in the postoperative bronchoscopy, and ii) no findings suggestive

of lobar torsion. (See Page 8, line 265–267, in the Methods section)

The patients included in this analysis were only those who underwent CT with slices thinner than 2mm at 6 months after right upper lobectomy during follow-up in our hospital. (See Page 8, line 276-277, in the Methods section)

**Comment 3:** *Moreover, how many patients had middle lobe atelectasis in the non-kink group on CT scan?*

**Reply 3:** Thank you for your comment. 5 patients had complete middle lobe atelectasis in the kinking group, while 9 patients had middle lobe atelectasis in the no kink group.

**Changes in the text:** none

**Comment 4:** *Is there a correlation between the displacements (RML, RLL) and the middle lobe kinking?*

**Reply 4:** Thank you for your question. We have analyzed relationship between the displacements (RML, RLL) and the incidence of middle lobe bronchus kinking under the new definition as above. The displacement of RML in the kink group was significantly longer than no kink group ( $P=0.019$ ), while that of RLL was not significantly different compared to that of no kink group ( $P=0.127$ ).

**Changes in the text:** We have added the results and Table 4 as follows;

In the patients who underwent CT at 6 months after surgery, the degree of the cranial displacement of right middle lobe was associated to the incidence of middle lobe bronchus kinking ( $P=0.025$ ). (See page 3, line 59-60, in the Abstract section)

The cranial displacements of the middle and lower lobes were compared between the kink and the no kink groups. The correlations between the displacement of residual lung lobes and the extracted factors in the risk factor analysis were also evaluated. (See page 8-9, line 283-438, in the Methods section)

Table 4 shows the comparison between the degree of cranial displacement of residual RML and RLL in both groups. The displacement of RML in the kink group was significantly more distant than in the no kink group ( $P=0.019$ ), while that of RLL was not significantly longer than no kink group ( $P=0.127$ ). (See page 11, line 632-635, in the Results section)

**Comment 5:** *Please detail the following points:*

*- indication for bronchoscopy (X symptoms, Y XRay atelectasis, other?). 46% of patients had a bronchoscopy (a relatively high percentage). I think it is important to understand why did you perform bronchoscopy in this context.*

*- outcome of patients with middle lobe bronchus kinking - treatment?*

**Reply 5:** Thank you for your question. The details of indication for bronchoscopy were as follows, atelectasis or sputum plugging; 22, bronchial stump confirmation; 39, hemoptysis; 3, others; 7. We routinely performed bronchoscopy for the patients who underwent nodal dissection 2a-2 to check the postoperative ischemic bronchitis.

The all 5 patients with middle lobe bronchus kinking were treated with aeration to the right middle lobe using bronchoscope under fluoroscopy. RML aeration was maintained following the treatment only in 1 patient. In 3 patients, although the aeration was not maintained after the treatment, RML atelectasis was spontaneously improved on CT 6 months later. In one patient, RML atelectasis was not improved on CT even after 6 months.

**Changes in the text:** We have added the description as follows;

Bronchoscopy was performed by a surgeon in the cases with suspected right middle lobe kinking due to abnormal chest roentgenogram findings such as atelectasis, opacification or any other findings. Bronchoscopy was also performed in the cases with diabetes or nodal dissection 2a-2 to check for postoperative ischemic bronchitis in the early postoperative period. (See page 7, line 250-253, in the Methods section)

The treatment and outcome of middle lobe bronchus kinking

All 5 patients with middle lobe bronchus kinking were treated with aeration to RML using bronchoscope under fluoroscopy. Following the treatment, RML aeration was maintained only in 1 patient. In 3 patients, RML atelectasis spontaneously improved on CT 6 months later; and in 1 patient, RML atelectasis did not improve on CT even after 6 months. No complication occurred following RML aeration. (See page 11, line 523-526, in the Results section)

**Comment 6:** *Please inform who performed bronchoscopies (surgeons? pneumologist?)*

**Reply 6:** Thank you for your question. Bronchoscopy was performed by surgeons.

**Changes in the text:** We have added the sentence as following;

Bronchoscopy was performed by a surgeon in the cases with suspected right middle lobe kinking due to abnormal chest roentgenogram findings such as atelectasis, opacification or any other findings. (See page 7, line 250-252, in the Methods section)

**Comment 7:** *This study is interesting and the topic important. However the impact of the results on clinical practice is limited. Unfortunately, there is no cutoff or score for use in clinical practice.*

**Reply 7:** Thank you for your insightful comments. As you pointed out, the cutoff value can help us to predict the risk of right middle bronchus kinking in the clinical settings.

Therefore, we have calculated cutoff values using ROC curve. The optimal cutoff values of RML/right thoracic cavity and RML/RUL were 0.149 (AUC 0.815, specificity 0.800, sensitivity 0.818) and 0.312 (AUC 0.864, specificity 0.600, sensitivity 0.965).

**Changes in the text:** We have changed the description in the discussion as follows; Sensitivity, Specificity, optimal cut off value, and areas under the curves (AUC) were calculated by receiver operating characteristic (ROC) curves. (See page 9, line 442-444, in the Discussion section)

The ROC curves of RML/right thoracic cavity and RML/RUL as risk factors are shown in Figure 3. The Youdan index was selected to calculate the optimal cutoff values in the ROC curve. The optimal cutoff values of RML/right thoracic cavity and RML/RUL were 0.149 (AUC 0.815, specificity 0.800, sensitivity 0.818), and 0.312 (AUC 0.864, specificity 0.600, sensitivity 0.965). (See page 10, line 484-487, in the Results section)

The former was previously reported with various methods as a prevention for RML torsion (18). In fact, the degree of cranial displacement of RML was longer than that of RLL. Therefore, the fixation of RML to RLL may reduce the cranial displacement of RML and prevent middle lobe bronchus kinking.

(See page 15, line 878-882, in the Discussion section)

Figure .3. ROC curves of RML/RUL (Red line) and RML/RTC (Blue line) as a risk factors for middle lobe bronchus kinking. (A) The optimal cutoff values of RML/RUL were 0.312 (AUC 0.864, specificity 0.600, sensitivity 0.965). (B) The optimal cutoff values of RML/RTC were 0.149 (AUC 0.815, specificity 0.800, sensitivity 0.818). ROC: receiver operating characteristics, RTC: right thoracic cavity

(See page 23, line 1290-1293, in the Figure legends section)

**Comment 8:** *lines 37-40: Thank you for being more specific: According to the ref 7, a short bronchus could increase the risk of kinking. The impact of the mobilization of the inferior pulmonary ligament is debated with contradictory studies (ref 16).*

**Reply 8:** Thank you for your comments. In this section, we mentioned the risk factors of lung torsion. The risk factors of lung torsion, not bronchial kinking includes the mobilization of the inferior pulmonary ligament. Therefore, we include the mobilization of the inferior pulmonary ligament but not the distance between carina and middle lobe orifice here.

According to the ref 7, “the distance between carina and middle lobe orifice was the predictor of kinking only in univariate analysis. The reason for this is unclear, but the load on a shorter middle bronchus might be too great, making it kink more readily”. Therefore, it is difficult to discuss the etiology of bronchial kinking from this factor.

**Changes in the text:** We have added the description about the risk factor “the distance from carina and middle lobe orifice” as follows;

The distance between the carina and middle lobe orifice was reported as a risk factor of middle lobe bronchus kinking, but the etiology was unclear (8). (See page 5, line 169-170, in the Introduction section)

**Comment 9:** *lines 47-53. Probably this paragraph should be moved in the discussion with argumentation.*

**Reply 9:** Thank you for your suggestion. We totally agree with you.

**Changes in the text:** We have moved the sentence you pointed out to the discussion part. (See page 12, line 770-777, in the discussion section)

**Comment 10:** *Is the surgical approach (VATS or open) associated with a higher risk?*

**Reply 10:** Thank you for your question. We have added the factor “Surgical approach” in the risk analysis, which had no significant difference between the both groups (P = 0.616)

**Changes in the text:** We have added additional factor about the surgical approach in the risk analysis. (See table 2).

**Comment 11:** *line 69: the title "risk analysis" should be replaced by "definition of middle lobe..."*

**Reply 11:** Thank you for your suggestion. We think the title should be changed.

**Changes in the text:** we have divided the sentence as following; “The definition of middle lobe bronchus kinking” and “The analysis of risk factors”. (See page 7, line 255, and page 8, line 269, in the Methods section)

**Comment 12:** *Line 188-198: The purpose to decrease the risk of middle lobe kinking seems complicated. Why not discuss suture or other between RML and RLL?*

**Reply 12:** Thank you for your insightful comment. As you pointed out, the fixation of RML as a prevention method should be discussed. There are some methods to fix RML to RLL for prevention of RML torsion (H Uramoto, Ann Thorac Surg. 2010 Dec;90(6):2028-30). Therefore, the fixation can be expected to reduce the mobilization of RML. We have added the description about the fixation between RML and RLL as an option to prevent right middle lobe bronchus kinking.

**Changes in the text:** We have added the description about the fixation as follows; Two methods to prevent middle lobe bronchus kinking can be envisioned; i) fixation of

RML to prevent migration to cranial side and ii) reduction of migration by somehow filling in the residual space. The former was previously reported with various methods as a prevention for RML torsion (18). In fact, the degree of cranial displacement of RML was longer than that of RLL. Therefore, the fixation of RML to RLL may reduce the cranial displacement of RML and prevent middle lobe bronchus kinking. The latter might keep the residual lobes close to their original positions and prevent kinking of the middle lobe bronchus (9). (See page 15, line 878-883, in the Discussion section)

## **Reviewer B**

**Comment 1:** *Were all of the patients operated for lung cancer? If so, what kind the histology of the tumors was diagnosed and what was the clinical stage of the disease? Do you think, that the title of the study should be changed?*

**Reply 1:** Thank you for your question. Most of the patients were operated for lung cancer, but there are some patients who were operated for metastatic lung tumor or benign disease as shown in Table 1. Therefore, we consider the title should not be changed.

**Changes in the text:** none

**Comment 2:** *What type of postoperative analgesia was used? Did you use epidural catheter in your patients?*

**Reply 2:** Thank you for your question. The patients were treated with epidural catheter if they have no contraindications, and oral medication for postoperative analgesia.

**Changes in the text:** None.

**Comment 3:** *Did any complications develop in the early perioperative period?*

**Reply 3:** Thank you for your question. There are some patients who underwent complications in the early postoperative period (Thoracic 17, Cardiac 8, others 2).

**Changes in the text:** We have added the information about complication in Table 1.

**Comment 4:** *Did any of the patients require re-do surgery due to complications in the early postoperative period?*

**Reply 4:** Thank you for your question. There are 3 patients who underwent re-do surgery due to the following reasons; empyema 2, hemoptysis 1. These patients were included in the no kink group.

**Changes in the text:** none

**Comment 5:** *What kind of treatment was used when bronchus kinking was diagnosed?*

**Reply 5:** Thank you for your comment. The all 5 patients of middle lobe bronchus kinking were treated with aeration to RML using bronchoscope under fluoroscopy. RML aeration was maintained following the treatment only in 1 patient. In 3 patients, although the aeration was not maintained after the treatment. RML atelectasis was spontaneously improved on CT 6 months later. In 1 patient, RML atelectasis was not improved on CT even after 6 months.

**Changes in the text:** We have added the sentence about the treatment as follows;

The treatment and outcome of middle bronchus kinking

All 5 patients of middle lobe bronchus kinking were treated with aeration to the RML using bronchoscope under fluoroscopy. Following the treatment, RML aeration was maintained only in 1 patient; in 3 patients, RML atelectasis spontaneously improved on CT 6 months later; and in 1 patient, RML atelectasis did not improve on CT even after 6 months. No complication occurred following RML aeration. (See page 11, line 522-526, in the Results section)

In our hospital, all patients with middle lobe bronchus kinking were treated with aeration to the RML. As a result, RML atelectasis improved in 1 patient during the treatment, 3 patients improved spontaneously within 6 months of follow-up, and 1 patient was not improved even after 6 months follow-up. Although no complication occurred following the aeration in our experience, RML atelectasis improved only 1, which suggests the limited efficacy of aeration, although more studies would be needed to confirm this. Moreover, most of the patients in our study improved spontaneously. Thus, long-term remodeling in the thoracic cavity could improve middle bronchus kinking. (See page 15-16, line 893-994)

**Comment 6:** *How long was the hospital stay in both studied groups?*

**Reply 6:** Thank you for your important question. The postoperative hospital stay of kink group was significantly longer than that of no kink group ( $23.00 \pm 19.20$  vs  $12.16 \pm 23.38$ ,  $P = 0.004$ ).

**Changes in the text:** We have added the factor “postoperative hospital stay” in the analysis as follows;

Consequently, postoperative hospital stay in the kink group was significantly longer than the no kink group ( $23 \pm 19.20$  vs  $12.16 \pm 23.38$ ,  $P = 0.004$ ). (See page 11, line 526-527, in the Results section, and Table 2)

**Comment 7:** *The headings of the tables should include the total number of patients in both groups for clarity.*

**Reply 7:** Thank you for your indication. We agree with you.

**Changes in the text:** We have included the total number of patients in both group in the headings of the tables. (See page 25, line 1336, page 27, line 1357, page 29, line 1377)

**Comment 8:** *The type of statistical tests which were used should be included in legend of each table*

**Reply 8:** Thank you for your suggestion.

**Changes in the text:** We have included the type of statistical tests in legend of each table. (See page 28, line 1362-1363, page 29, line 1380, page 30, line 1389)

#### **Reviewer C**

**Comment 1:** *I would like you to add a figure of the middle lobe bronchus kinking defined as they met the criteria.*

**Reply1:** Thank you for your suggestion. We totally agree with you.

**Changes in the text:** We have added figures that can show the middle lobe bronchus kinking. (See Figure 1)

**Comment 2:** *(line 61) at xx hospital---> at our hospital*

**Reply 2:** Thank you for your suggestion.

**Changes in the text:** We have changed the sentence as advised. (See page 6, line 209, in the Methods section)

**Comment 3:** *(line 97 & 132) correlation-ships ---> correlationships +50*

**Reply 3:** Thank you for your suggestion. On advice of a native English editor, we decided to not use the words “correlationships” and “correlation-shops”. We have replaced the word to “correlation”.

**Changes in the text:** We have changed the sentence. (See page 8, line 283, in the Methods section, page 11, line 635, in the Results section)

**Comment 4:** *(line 108-111)*

*In total, 209 patients underwent right upper lobectomy in xx hospital from January 2011 to December 2017. A total of 23 patients were excluded for the following reasons: segmentectomy or lobectomy of other lobe (13), bronchoplasty or carinal resection (7),*



*hypoplasia of RML (2), and middle lobar torsion (1). Of those, 186 patients met inclusion criteria and were enrolled in this study*

*---> Among 209 patients who underwent right upper lobectomy, 23 patients were excluded for the following reasons: segmentectomy or lobectomy of other lobe (13), bronchoplasty or carinal resection (7), hypoplasia of RML (2), and middle lobar torsion (1). The remaining 186 patients met the inclusion criteria and were enrolled in this study*

**Reply 4:** Thank you for your suggestion.

**Changes in the text:** We have changed the sentence as advised. (See page 9, line 450-453, in the Results section)

**Comment 5:** *(line 123-125)*

*RUL volumes of the kink and no kink groups were  $860.62 \pm 213.76$  and  $863.01 \pm 238.45$  ( $P = 0.919$ ), respectively. RML volumes of the kink and no kink groups were  $352.31 \pm 113.36$  and  $428.08 \pm 133.11$  ( $P = 0.052$ ), respectively.*

*---> RUL volumes of the kink and no kink groups were  $860.62 \pm 213.76$  ml and  $863.01 \pm 238.45$  ml ( $P = 0.919$ ), respectively. RML volumes of the kink and no kink groups were  $352.31 \pm 113.36$  ml and  $428.08 \pm 133.11$  ml ( $P = 0.052$ ), respectively.*

**Reply 5:** Thank you for your suggestion.

**Changes in the text:** We have changed the sentence as advised. (See page 10, line 481-483)

**Comment 6:** *(Table 1) Table 1 Characteristics ---> Table 1: Clinical characteristics of the patients*

**Reply 6:** Thank you for your suggestion.

**Changes in the text:** We have changed the heading of Table 1 as advised. (See page 25, line 1338)

**Comment 7:** *(Table 1 and 2) Age; BMI ---> Age (Years); BMI (kg/m<sup>2</sup>)*

**Reply:** Thank you for your pointing.

**Changes in the text:** We have changed the sentence as advised. (See Table 1, 2)

**Reviewer D**

**Comment 1:** *I could wish for a more thorough discussion of your results, and maybe*

*put them into better perspective. Computing the volumes of the lobes and afterwards calculate the ratios is not very applicable as a routine, maybe you could write more about your thoughts on how to put your findings into practice?*

**Reply 1:** Thank you for your insightful comments. Although calculating the ratios is not very applicable as a routine practice, it could be beneficial in the case with relatively large RUL or relatively small RML. We have added the cut-off value to apply it easily in the clinical settings. The optimal cutoff values of RML/right thoracic cavity and RML/RUL were 0.149 (AUC 0.815, specificity 0.800, sensitivity 0.818) and 0.312 (AUC 0.864, specificity 0.600, sensitivity 0.965). Therefore, we suggest that, not routinely, but when we notice a big RUL or small RML before right upper lobectomy, the calculation of the volume ratio could help the risk assessment of postoperative middle lobe bronchus kinking.

**Changes in the text:** We have added the sentence as following;

The ROC curves of RML/right thoracic cavity and RML/RUL as risk factors were shown in Figure 3. The Youdan index was selected to calculate the optimal cutoff values in the ROC curve. The optimal cutoff values of RML/right thoracic cavity and RML/RUL were 0.149 (AUC 0.815, specificity 0.800, sensitivity 0.818) and 0.312 (AUC 0.864, specificity 0.600, sensitivity 0.965).

(See page 10, line 486-489, in the Results section)

Although the routine calculation of these volume ratios might not be practical in the clinical settings, we suggest that calculating these indicators could be useful to predict the occurrence of middle lobe bronchus kinking after right upper lobectomy in the cases with relatively large RUL or relatively small RML. (See page 13-14, line 807-837, in the discussion section)

## **Reviewer E**

**Comment 1:** *We need to know a bit more about what is meant by « lobar torsion », and how the authors distinguished this from « kinking ». Please take the time to describe this precisely. It is a key element of the paper.*

**Reply 1:** Thank you for your important comment. Lobar torsion is accompanied with infarction or congestion due to the obstruction of blood flow to the affected lobe. Lobar torsion is suspected by not only bronchial obstruction but also the findings of tortuous bronchus on bronchoscopy, or by the radiologic findings such as progressive consolidation, abnormal anatomic structures. On the other hand, middle bronchial

kinking is not accompanied with the obstruction of blood flow. Bronchial obstruction without the findings mentioned above suggests bronchial kinking.

**Changes in the text:** We have added the detail of lobar torsion as following;

Lobar torsion is an emergent complication leading to infraction or congestion due to the obstruction of blood flow to the affected lobe. Lobar torsion is indicated by the findings of tortuous bronchus on bronchoscopy or radiologic findings such as tortuous obstruction of pulmonary vessels with progressive consolidation, rather than a finding of simple bronchial obstruction (6). (See page 5, line 160-164, in the Introduction section)

**Comment 2:** *Only patients who underwent postoperative bronchoscopy were included in this study. This is addressed in the limitations (which it is) but should be addressed in the Methods section under inclusion/exclusion criteria. The reader also needs to have some sense of the timeline for these bronchoscopies i.e. would a patient being readmitted for a bronchoscopy 3 weeks post-op also be considered for inclusion? Was there any follow-up?*

**Reply 2:** Thank you for your insightful comment. We have added the objective findings “complete atelectasis of RML” to the definition of middle lobe bronchus kinking as following in methods section; i) complete atelectasis of RML with slit-like obstruction of the middle lobe bronchus found in the postoperative bronchoscopy, and ii) no findings to suggest of lobar torsion. Also, Bronchoscopy was performed in the cases with suspected right middle lobe kinking due to abnormal chest roentgenogram findings such as atelectasis, opacification or any other findings. Bronchoscopy was also performed in the cases with diabetes or nodal dissection 2a-2 to check the postoperative ischemic bronchitis in the early postoperative period. The patients who readmitted for performing bronchoscopy are not included in this study. The follow-up was performed using CT for confirming atelectasis of the right middle lobe.

**Changes in the text:** We have added the sentence as follows in method sections;

Bronchoscopy was performed by a surgeon in the cases with suspected right middle lobe kinking due to abnormal chest roentgenogram findings such as atelectasis, opacification or any other findings. Bronchoscopy was also performed in the cases with diabetes or nodal dissection 2a-2 to check for postoperative ischemic bronchitis in the early postoperative period. (See page 7, line 250-253, in the Methods section)

**Comment 3:** *The indications, timeline and scheduling of the patients having undergone CT-scanning should also be addressed in the methods section. Are these routine, elective CT-scans that are done according to a standardized follow-up protocol or are they done*

*as needed, including because of new onset symptoms?*

**Reply 3:** Thank you for your suggestion. The patients with lung cancer underwent CT according to standard follow-up 6 months after surgery.

**Changes in the text:** We have changed the sentence about the indication of CT as follows;

The patients included in this analysis were only those who underwent CT with slices thinner than 2mm at 6 months after right upper lobectomy during follow-up in our hospital. (See page 8, line 276-277, in the Method section)

For this analysis, 83 patients who underwent CT at 6 months ( $\pm$  15 days) after surgery in our hospital were enrolled (3 in the kink group and 80 in the no kink group). A total of 92 patients were excluded because of significant differences of the timing of CT or follow-up in other hospital. (See page 11, line 632-634, in the Results section)

**Comment 4:** *Any conditions that may have « frozen the mediastinum » such as previous contralateral lung resection, radiotherapy, etc. or, in contradistinction, conditions associated with excess tissue laxity (collagen-vascular, etc.) are also presumably part of the exclusion criteria.*

**Reply 4:** Thank you for your insightful comments. As you pointed out, conditions that may have “frozen the mediastinum” can affect the postoperative displacement. We have excluded the patients who underwent thoracic surgery such as median sternotomy or thoracotomy, or mediastinal radiotherapy. Because there were no patients who had the conditions associated with excess tissue laxity, we did not refer this.

**Changes in the text:** We have changed the sentence as follows;

Among 209 patients who underwent right upper lobectomy, 34 patients were excluded for the following reasons: segmentectomy or lobectomy of other lobe (n=13), past history of thoracic surgery or mediastinal radiotherapy (11), bronchoplasty or carinal resection (7), hypoplasia of RML (2), and middle lobar torsion (1). The remaining 175 patients met the inclusion criteria and were enrolled in this study. (See page 9, line 450-453, in the Results section)

**Comment 5:** *The reader needs to know more about intraoperative management. Many surgeons routinely « fix » the middle lobe to the lower lobe with the specific objective of avoiding torsion. Was this standard practice? If so, what technique was used, and how was it reflected in the results? This question should also be addressed in the discussion and conclusion section. It would seem intuitive that if kinking is caused by excessive displacement of the middle lobe, fixing the middle lobe (and doing it correctly) should*

*address at least part of the problem. This issue needs to be discussed in detail.*

**Reply 5:** Thank you for your insightful comments. The fixation is not routinely performed in our institution. As you pointed out, the fixation of RML as a prevention method should be discussed. There are some methods to fix RML to RLL for prevention of RML torsion (H Uramoto, Ann Thorac Surg. 2010 Dec;90(6):2028-30). Therefore, fixation can be expected to reduce the mobilization of RML. We have added the description about the fixation between RML and RLL as an option to prevent right middle lobe bronchus kinking.

**Changes in the text:** We have added the sentence as follows;

Two methods to prevent middle lobe bronchus kinking can be envisioned; i) fixation of RML to prevent migration to cranial side, ii) reduction of migration by somehow filling in the residual space. The former was previously reported with various method as the prevention for RML torsion (18). In fact, the degree of cranial displacement of RML was longer than that of RLL. Therefore, the fixation of RML to RLL may reduce the cranial displacement of RML and prevent middle lobe bronchus kinking. (See page 15, line 880-884, in the Discussion section)

**Comment 6:** *It is not quite clear to me why the authors correlated lung volumes with postoperative displacement, but not with bronchial kinking per se. Was this their goal? They should provide more of a clear rationale in their introduction/hypothesis and in the Methods section. Although they apparently did not repeat bronchoscopy at 6 months, one would expect any significant kinking to be apparent on these CT scans. The authors should specify whether the RML and RLL volumes being referred to are pre-op or post-op (line 132-134).*

*In the discussion, the authors suggest that a solution to prevent kinking is filling residual space. I very much doubt that the « space-filling » solutions discussed have any practical value. Fixing the middle lobe to the lower lobe is the obvious potential solution that is not addressed anywhere, which is a major overlook.*

*The authors have nicely laid out that the preop volume of the middle lobe is associated with postop kinking. Stapling the horizontal fissure is routine but it probably limits postoperative expansion/volume. Any thoughts/alternatives? Any possible difference in patients with a complete horizontal fissure vs those who require stapling?*

**Reply 6:** Thank you for your comments. As you pointed out, we have analyzed relationship between the displacements (RML, RLL) and the incidence of middle lobe bronchus kinking under the new definition. The displacement of RML in the kink group was significantly further than in the no kink group ( $P=0.019$ ), while that of RLL was not

( $P=0.127$ ).

Also, the fixation is not routinely performed in our institution. As you pointed out, the fixation of RML as a prevention method should be discussed. There are some methods to fix RML to RLL for prevention of RML torsion (H Uramoto, Ann Thorac Surg. 2010 Dec;90(6):2028-30). Therefore, the fixation can be expected to reduce the mobilization of RML. We have added the description about the fixation between RML and RLL as an option to prevent right middle lobe bronchus kinking.

Stapling horizontal fissure could be associated with the postoperative volume of RML. We have added the factor “the stapler use of the horizontal fissure” in the risk analysis, which did not have significant difference ( $P = 0.616$ ). We suspect that the volume loss due to stapling in the horizontal fissure is so small that it could not affect the incidence of middle lobe bronchus kinking.

**Changes in the text:** We have added the results of additional analysis as follows;

In the patients who underwent CT at 6 months after surgery, the degree of the cranial displacement of right middle lobe was associated with the incidence of middle lobe bronchus kinking ( $P=0.025$ ). (See page 3, line 59-60, in the Abstract section)

The cranial displacements of the middle and lower lobes were compared between the kink and the no kink groups. (See page 8, line 282-283, in the Methods section)

Table 4 shows the comparison between the degree of cranial displacement of residual RML and RLL in both groups. The displacement of RML in the kink group was significantly more distant than in the no kink group ( $P=0.019$ ), while that of RLL was not ( $P=0.127$ ). (See page 11, line 534-537, in the Results section)

We have added the sentence about the fixation (See page 15, line 880-884, in the Discussion section)

We have added the factor “stapler use in the horizontal fissure” in the risk analysis. (See Table 2)

**Comment 7:** *The analysis of the displacement is basically a rudimentary « 2D » measurement. Clearly, the next step in 2021 should involve some kind of 3D characterization of postoperative changes in lung configuration. I think this should be addressed in the discussion/conclusion. Also, if bronchial kinking has happened, what then? Should it be addressed? What is the natural history? Does it improve (or worsen) with the long-term remodeling of the ipsilateral pleural cavity? Again, 3D modeling in the future should provide part of the answer.*

**Reply:** Thank you for insightful comments. We totally agree with you. We evaluated the displacement on 2D according to the previous report. However, as you pointed out,

3D modeling can allow us to get more information about the displacement after surgery. It would be useful to conduct future studies to assess the bronchial kinking using the 3D modeling. Moreover, in this study, 3 out of 4 patients were improved in the long term follow up. Long term remodeling could improve the bronchial kinking.

The all 5 patients of middle lobe bronchus kinking were treated with aeration to RML using bronchoscope under fluoroscopy. RML aeration was maintained following the treatment only in 1 patient. In 3 patients, although the aeration was not maintained after the treatment. RML atelectasis was spontaneously improved on CT 6 months later. In 1 patient, RML atelectasis was not improved on CT even after 6 months. We have added the description about these points.

**Changes in the text:** We have added the description about 3D modeling and the outcome of the patients as follows;

All 5 patients with middle lobe bronchus kinking were treated with aeration to the RML using bronchoscope under fluoroscopy. Following the treatment, RML aeration was maintained only in 1 patient; in 3 patients, RML atelectasis spontaneously improved on CT 6 months later; and in 1 patient, RML atelectasis did not improve on CT even after 6 months. No complication occurred following RML aeration. (See page 10, line 525-529, in the Results section)

In our hospital, all patients with middle lobe bronchus kinking were treated with aeration to the RML. As a result, RML atelectasis improved in 1 patient during the treatment, 3 patients improved spontaneously within 6 months of follow-up, and 1 patient was not improved even after 6 months follow-up. Although no complication occurred following the aeration in our experience, RML atelectasis improved only 1 of 5 patients, which suggests the limited efficacy of aeration, although more studies would be needed to confirm this. Moreover, most of the patients in our study improved spontaneously. Thus, long-term remodeling in the thoracic cavity could improve middle bronchus kinking. (See page 15-16, line 895-996, in the Discussion section)

Finally, in this study, we evaluated the displacement of the residual lung lobes only towards the cranial side. Future studies that can evaluate the movement of residual lung lobes with three-dimensional analysis are anticipated, which could allow us to get more detailed information about the displacement of residual lobes. (See page 16, line 1000-1002, in the Discussion section)

**Reviewer F**

**Comment 1:** *Inclusion criteria are not clear. In line 64 exclusion criteria are described, but inclusion criteria are described in line 91 and they don't match with description of results in line 110. First, the authors described to have included patients who underwent CT within 6 months of surgery in line 91, but in results included all patients who don't met exclusion criteria in line 110 (186 patients) and selected a subgroup of patients for the study of the displacement of residual lung lobes in line 131 (124 patients). I suppose the authors are studying 4 different groups, but it is not clear since the inclusion criteria are not well specified.*

*The classification between groups in the study was defined by bronchoscopy (Line 70). It is not possible to know if there were more patients with kinking among all the patients of the study that did not undergo a bronchoscopy. It is a big selection bias when the authors did not performed the same study to 54% of all the patients to make the classification between the two main groups of the study.*

**Reply 1:** Thank you for your indication. We mainly conducted 2 analyses, risk analysis and displacement analysis. The former included all patients who underwent right upper lobectomy. The latter included only the patients that underwent in CT at 6 months after right upper lobectomy in our hospital.

As you pointed out, there could be selection bias in former definition. Therefore, we have changed the definition of middle bronchus kinking as follows; i) complete atelectasis of RML (Fig. 1A) with slit-like obstruction of the middle lobe bronchus (Fig 1B) found in the postoperative bronchoscopy, and ii) no findings to suggest of lobar torsion.

**Changes in the text:** We have changed the sentence about the definition of bronchus kinking and inclusion criteria as follows;

The definition of middle lobe bronchus kinking

Middle lobe bronchus kinking was defined as cases that satisfied the following criteria: i) complete atelectasis of RML (Fig. 1A) with slit-like obstruction of the middle lobe bronchus (Fig 1B) found in the postoperative bronchoscopy, and ii) no findings suggestive of lobar torsion.

*The analysis of risk factors*

All the patients who satisfied the above-mentioned criteria were included in this analysis. The cohort was divided into two groups according to the presence of or absence of middle lobe bronchus kinking (kink group and no kink group, respectively) and the risk factors were analyzed. The treatment and outcome of middle lobe bronchus kinking were also extracted.



The analysis of displacement of residual lung lobes

The patients included in this analysis were only those who underwent CT with slices thinner than 2mm at 6 months after right upper lobectomy during follow-up in our hospital. (See page 7-8, line 255-277)

**Comment 2:** *The authors described a high rate of postoperative bronchoscopy (46%), but they don't address any information about intermediate bronchus kinking that have been studied by other authors (see reference).*

*Arai H, Tajiri M, Masuda H, Sekine A, Okudela K, Komatsu S, Iwasawa T, Masuda M. Intermediate bronchial kinking after right upper lobectomy for lung cancer. Asian Cardiovasc Thorac Ann. 2021 Jan;29(1):19-25. doi: 10.1177/0218492320960325. Epub 2020 Sep 21. PMID: 32955915.*

**Reply 2:** Thank you for your comments. According to the reference, the intermediate bronchial kinking is defined as “with a protrusion arising from the posterior wall” on postoperative axial chest CT, not on bronchoscopy, which means bronchial kinking at intermediate bronchus. In fact, there are 14 patients who matched the definition of intermediate bronchial kinking in 6 months CT in our patients. However, we focused not on kinking of the intermediate bronchus but on middle lobe bronchus kinking in this study. We suspect the etiology of middle lobe bronchus kinking differs from intermediate bronchial kinking. Therefore, we did not refer intermediate bronchial kinking in the manuscript

**Changes in the text:** none

**Comment 3:** *The authors have studied 125 patients that underwent CT within 6 months of surgery, but 184 patients of the initial groups presented malignant tumors. What happened with all the rest of the patients with malignant lesions? Why were they not included?*

**Reply 3:** Thank you for your question. Firstly, the timing of CT could be a bias. Therefore, we have changed to analyze the displacement of residual lobes on CT performed only at 6 months after surgery. Because most of the patients who underwent right upper lobectomy were lung cancer patients in this study, they underwent CT about 6 months after surgery. However, because there were some differences in the timing of CT, some patients were excluded. Moreover, some patients were excluded due to follow-up in other hospital after surgery.

**Changes in the text:** We have changed the sentence about the indication of CT as follows.

The patients included in this analysis were only those who underwent CT with slices thinner than 2mm at 6 months after right upper lobectomy during follow-up in our hospital. (See page 8, line 276-277, in the Methods section)

For this analysis, 83 patients who underwent CT at 6 months ( $\pm 15$  days) after surgery in our hospital were enrolled (3 in the kink group and 80 in the no kink group). A total of 92 patients were excluded because of significant differences of the timing of CT or follow-up in other hospital. (See page 11, line 522-524, in the Results section)

**Comment 4:** *The authors analyzed the relationship between the RML/RUL and RML/Right thoracic cavity ratios and the displacement of cranial side of RML and RLL. This displacement can be caused by movement of the lobe or by lobe's hyperinflation, but it may not be representative of the movement of the bronchus. Why didn't the authors use for reference the upper side of the middle or lower lobe bronchus? Did they calculate the hyperinflation of the remaining lobes as have been previously described by Nonaka?*

*Nonaka M, Kadokura M, Tanio N, Yamamoto S, Kataoka D, Inoue K, Takaba T. Changes in lung lobar volume and bronchial deformity after right upper lobectomy. Surg Today. 1998;28(3):285-8. doi: 10.1007/s005950050122. PMID: 9548310.*

**Reply 4:** Thank you for your insightful comments. As you mentioned, the displacement may not be representative of the bronchus. We have modified the methods described in a previous report that calculated the dead space after right upper lobectomy on chest X-ray (H Matsuoka, Surg Today 2004, 34:498-500).

The study by Nonaka et al. calculated the hyperinflation of residual lobes after right upper lobectomy in rabbit. They removed each lobe and calculated the volume. Therefore, it would be difficult to apply the method to humans.

**Changes in the text:** none

**Comment 5:** *The authors conclude that there was an association between the RML/RUL ratio or the RML/right thoracic cavity ratio and the risk of middle lobe bronchus kinking, but in their statistical analysis they did not compare these ratios in both groups, they have only described the findings in patients that underwent a CT within 6 months of right upper lobectomy. So the conclusions are incorrect.*

**Reply 5:** Thank you for your comment. We have added the analysis of relation of the displacement in both groups. The results showed the displacement of RML in the kink

group was significantly further than no kink group ( $P=0.019$ ), while that of RLL was not ( $P=0.127$ ).

**Changes in the text:**

The cranial displacement of the middle and lower lobes were compared between the kink and the no kink groups. The correlations between the displacement of residual lung lobes and the extracted factors in the risk factor analysis were also evaluated. (See page 8, line 282-438, in the Method section)

Table 4 shows the comparison between the degree of cranial displacement of residual RML and RLL in both groups. The displacement of RML in the kink group was significantly more distant than in the no kink group ( $P = 0.019$ ), while that of RLL was not ( $P = 0.127$ ). (See page 11, line 534-537, in the Results section)

**Comment 6:** *The authors state that the aim of the study is investigate risk factors and assess prevention methods, but there is no part in the study to achieve the objective of assessing prevention methods.*

**Reply 6:** Thank you for your indication. Our purpose of this study was to investigate the risk factors and etiology of middle lobe bronchus kinking following right upper lobectomy. As pointed out, we have not assessed but discussed the prevention methods.

**Changes in the text:** We have removed the sentence “and assess the prevention methods”. (See Page 6, line 201).

**Comment 7:** Lines 47 to 53 should be in the Discussion part where the objective and the results of the study are discussed.

**Reply 7:** Thank you for your suggestion. We totally agree with you.

**Changes in the text:** We have moved the sentence you pointed out to the discussion part. (See page 12, line 772-779, in the Discussion section)

**Comment 8:** *The authors state that there weren't difference in the simple volume of each lung lobe (Line 165), but all the lobes were bigger in no kink group in table 3. Did they compare the total lung volume in both groups?*

**Reply:** Thank you for your question. There were no significant differences in the total lung volume in both groups ( $2264 \pm 514.44$  vs  $2295.35 \pm 541.68$ ,  $P = 0.964$ ).

**Changes in the text:** We have added the volume of right thoracic cavity in the Table3.