

## Peer review file

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### Reviewer A

**Comment 1:** *Unfortunately, the definition of both the exposure (artery size) and the outcome (bleeding) are arbitrary for this small retrospective study. You have defined both as dichotomous variables (size either greater or less than 2mm) and blood less than or greater to 50cc) and both are really continuous variables and therefore should be analyzed as such. Furthermore, a blood loss of 50cc is still quite small and hard to imagine that this is really a reasonable definition for intraoperative bleeding.*

**Reply 1:** Since the diameter of the bronchial artery is usually 2 mm or less (1), 2 mm was used as the cutoff value. In our study, the median amount of bleeding was 27 ml; therefore, 50 ml was used as the cutoff value. In response to the reviewer's comments, we added a univariate analysis with a cutoff value of 200 ml for the intraoperative blood loss. In addition, Figure 3A and B were added to show the correlation between the bronchial artery diameter and bleeding volume, and between the bronchial artery and operation time.

(1) Bruzzi JF, Multi-detector row CT of hemoptysis. *Radiographics*. 2006;26:3-22.

#### **Changes in the text:**

Patients were divided into the following two groups based on bronchial artery diameters:  $\leq 2$  mm and  $> 2$  mm groups, since the diameter of the bronchial artery is usually 2 mm or less (10). (Page 8 - 9, lines 142 - 144)

Unadjusted analysis of intraoperative blood loss was also performed between  $\leq 200$  ml and  $> 200$  ml groups; however, the results were similar (Table 1). (Page 12, lines 213 - 214)

### Reviewer B

**Comment 1: ABSTRACT:** *Would recommend the change:*

*The present study investigated whether highly vascularized bronchial arteries affect the intraoperative blood loss and the operative time of video-assisted thoracic (VATS)*

*lobectomy for patients with non-small cell lung cancer.*

*Would also recommend saying “unadjusted” instead of “univariate”.*

*Would recommend “multivariable” instead of “multivariate”*

**Reply 1:** We agree with these comments. We have revised accordingly.

**Changes in the text:**

The present study investigated whether highly vascularized bronchial arteries affect the intraoperative blood loss and the operative time of video-assisted thoracic surgery (VATS) lobectomy for patients with non-small cell lung cancer. (Page 3, lines 42 - 44)

Among the 175 patients enrolled, risk factors for intraoperative blood loss >50 ml were being male (p = 0.005), a history of smoking (p = 0.01), percent forced expiratory volume in 1 second (FEV1.0%) <70% (p = 0.012), squamous cell carcinoma (p = 0.049), and a bronchial artery diameter >2.0 mm (p < 0.001) in the unadjusted analysis, and a bronchial artery diameter >2.0 mm (p < 0.001) in the multivariable analysis. Risk factors for an operative time >200 minutes were being male (p < 0.001), a history of smoking (p = 0.007), FEV1.0% <70% (p = 0.011), squamous cell carcinoma (p = 0.046), a bronchial artery diameter >2.0 mm (p < 0.001), and experience of surgeon <10 years (p = 0.011) in the unadjusted analysis, and being male (p = 0.047), a bronchial artery diameter >2.0 mm (p = 0.024), and experience of surgeon <10 years (p = 0.047) in the multivariable analysis. (Page 3 - 4, lines 52 - 61)

**Comment 2: INTRODUCTION:**

*Line 67: would strongly suggest adding an additional newer citation about VATS:*

*Yang et al. A National Analysis of Short-term Outcomes and Long-term Survival Following Thoracoscopic Versus Open Lobectomy for Clinical Stage II Non-Small-Cell Lung Cancer. Ann Surg. 2021 Mar 1;273(3):595-605.*

**Reply 2:** We agree with this comment. We have revised accordingly.

**Changes in the text:**

In recent year, the feasibility of VATS lobectomy for stage II (cN1) non-small cell lung cancer (NSCLC) has also been demonstrated (4). (Page 5, lines 73 - 75)

4. Yang CJ, Kumar A, Deng JZ, et al. A National Analysis of Short-term Outcomes and Long-term Survival Following Thoracoscopic Versus Open Lobectomy for Clinical Stage II Non-Small-Cell Lung Cancer. Ann Surg. 2021;273:595-605. (Reference 4)

**Comment 3: Methods/Results:**

*It is very interesting that the authors were able to measure surgeon experience data. Very few studies have this information. If possible, can the authors incorporate surgeon*

*experience in their modeling?*

*Can the authors also add FEV1 and DLCO to their modeling?*

*If this is not possible, then I would recommend for future studies to incorporate surgeon experience and pulmonary function tests in the modeling.*

**Reply 2:** We appreciate the Reviewer's insightful comments. We have added these factors into our analysis. Unfortunately, DLCO / VA was not added to the results because we could not lead interesting data.

**Changes in the text:**

Among the 175 patients enrolled, risk factors for intraoperative blood loss >50 ml were being male (p = 0.005), a history of smoking (p = 0.01), percent forced expiratory volume in 1 second (FEV1.0%) <70% (p = 0.012), squamous cell carcinoma (p = 0.049), and a bronchial artery diameter >2.0 mm (p < 0.001) in the unadjusted analysis, and a bronchial artery diameter >2.0 mm (p < 0.001) in the multivariable analysis. Risk factors for an operative time >200 minutes were being male (p < 0.001), a history of smoking (p = 0.007), FEV1.0% <70% (p = 0.011), squamous cell carcinoma (p = 0.046), a bronchial artery diameter >2.0 mm (p < 0.001), and experience of surgeon <10 years (p = 0.011) in the unadjusted analysis, and being male (p = 0.047), a bronchial artery diameter >2.0 mm (p = 0.024), and experience of surgeon <10 years (p = 0.047) in the multivariable analysis. (Page 3 - 4, lines 52 - 61)

Risk factors for intraoperative blood loss >50 ml were being male (p = 0.005), a history of smoking (p = 0.01), percent forced expiratory volume in 1 second (FEV1.0%) <70% (p = 0.012), squamous cell carcinoma (p = 0.049), and a bronchial artery diameter >2.0 mm (p < 0.001) in the unadjusted analysis (Table 1), and a bronchial artery diameter >2.0 mm (p < 0.001) in the multivariable analysis (Table 2). (Page 12, lines 208 - 212)

Risk factors for an operative time >200 minutes were being male (p < 0.001), a history of smoking (p = 0.007), FEV1.0% <70% (p = 0.011), squamous cell carcinoma (p = 0.046), a bronchial artery diameter >2.0 mm (p < 0.001), and experience of surgeon <10 years (p = 0.011) in the unadjusted analysis (Table 1), and being male (p = 0.047), a bronchial artery diameter >2.0 mm (p = 0.024), and experience of surgeon <10 years (p = 0.047) in the multivariable analysis (Table 2). (Page 12, lines 214 - 219)

**Reviewer C**

**Comment 1:** *It would be visually appealing and comprehensive to depict the dependence of bronchial artery diameter and intraoperative bleeding and/or duration of surgery by a graphical chart. For example, a column chart or a scatter plot.*

**Reply 1:** We appreciate the Reviewer's insightful comments. We have added figures showing correlations between intraoperative blood loss, operative time and bronchial artery diameter.

**Changes in the text:**

Graphpad prism 5 software was used to analyze the linear correlations between intraoperative blood loss, operative time, and bronchial artery diameter. (Page 9, lines 159 - 160)

**Correlations between intraoperative blood loss, operative time and bronchial artery diameter**

Figure 3A shows correlation between intraoperative blood loss and bronchial artery diameter ( $r^2=0.155$ ,  $p < 0.0001$ ), and Figure 3B shows correlation between operative time and bronchial artery diameter ( $r^2=0.105$ ,  $p < 0.0001$ ). There were poor correlations between intraoperative blood loss, operative time and bronchial artery diameter. (Page 11 - 12, lines 199 - 204)

Figure 3A. Correlations between intraoperative blood loss and bronchial artery diameter.

Figure 3B. Correlations between operative time and bronchial artery diameter. (Page 23, lines 424 - 428)

**Comment 2:** *It would add additional value if you could answer whether bronchial artery diameter was an independent risk factor. Since you have already performed the multivariate analysis, it will be only a matter of statement.*

**Reply 2:** Thank you for the comments. We have revised accordingly.

**Changes in the text:**

Bronchial artery diameter was the most important risk factor of intraoperative bleeding and prolonged operative time during VATS lobectomy. (Page 4, lines 63 - 64)

A bronchial artery diameter  $>2.0$  mm was identified as the independent risk factor for intraoperative bleeding in the multivariate analysis. (Page 17, lines 301 - 303)

**Reviewer D**

**Comment 1:** *I would suggest using a native English grammar check for this paper*

**Reply 1:** Thank you for the comment. The manuscript was checked by a native speaker again.

**Comment 2:** *Please report the complication grade, overall hospital stay, reoperations, ICU admission, bleeding in ml in more to scale (scatter plot), inpatient mortality, 30-day and 90-day mortality. Also, usage of IR for bleeding.*

**Reply 2:** We appreciate the Reviewer's insightful comments. We collected as much data as possible according to the comments and added a table 4.

**Changes in the text:**

No patient required a blood transfusion due to intraoperative bleeding, reoperation and interventional radiology due to postoperative bleeding. (Page 11, lines 195 - 196)

Operative and postoperative results correlating with bronchial artery dilation

Table 4 shows operative and postoperative results in the groups with bronchial artery diameters  $\leq 2.0$  mm and  $> 2.0$  mm. In the BA dilation group, intraoperative blood loss was significantly greater (median, 100 vs 10 mL; IQR, 29 - 205 vs 3 - 50 ml;  $p < 0.0001$ ), the operative time was significantly longer (median, 220 vs 181 minutes; IQR, 196 - 314 vs 151 - 219 minutes;  $p < 0.0001$ ), postoperative complications were significantly more frequent (38.4% vs 9.8%;  $p < 0.0001$ ), and postoperative hospital stay significantly longer (median, 9 vs 7 minutes; IQR, 8 - 13 vs 6 - 9 minutes;  $p < 0.0001$ ). (Page 13, lines 226 - 233)

**Comment 3:** *Also, the site of bleeding? The issue that I have is number 7 nodal dissection where I often use a clip*

**Reply 3:** Thank you for the comment. Intraoperative bleeding in cases with hypervascularized bronchial arteries has been observed during the following: 1) dissection of inflammatory intrathoracic adhesions, 2) dissection around hilar lymph nodes, 3) bleeding from the hilum or lung parenchyma due to lung congestion, and 4) mediastinal lymph node dissection.

**Changes in the text:** No change (already described in page 15, lines 263 -266)

**Comment 4:** *If there is no difference other than operative time.*

**Reply 4:** Excuse me. I'm not sure what the comment means, but thanks to your comments, we've found that there are also statistical differences in postoperative complications and postoperative hospital stay.

**Changes in the text:** No change