

## Peer Review File

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### Reviewer A

Chen et al, in their manuscript, “Analysis of risk factors and management of unexpected intraoperative bleeding during video-assisted thoracic surgery for non-small cell lung cancer: a case-control study,” provide insight on the nature and management of intraoperative vascular injury during thoracoscopic lung resection. My comments/questions below:

1. I am confused about what cases are included in this study. The inclusion criteria mentions pneumonectomy, lobectomy, segmentectomy, and wedge resection. However no further detail is provided about whether or not the type of resection was associated with the risk of bleeding. The investigators should include the % of resections in each group. They should also state whether or not extent of resection was associated with unexpected intraoperative bleeding.

Reply 1: Thank you for your advice. We have modified our text as advised. The cases with wedge resection have been excluded. In addition, this is one of limitations of this paper. For many included cases, a special situation was often found, in which lobectomy or segmentectomy was combined with segmental or wedge resection of other lobes. Therefore, it was difficult to distinguish the effects of different surgical resection types on bleeding.

Changes in the text: Page 5, line 11-12.

2. Why were cases for which incomplete lymph node dissection not included? I do not see a good reason to exclude these cases – please enlighten me.

Reply 2: Thank you for your advice. In this study, there were 10 cases with bronchial artery injury in the intraoperative bleeding group, and these cases were often related to complete systematic lymph node dissection. For cases with incomplete lymph node dissection, bronchial artery injury was generally not easy to occur.

Changes in the text: Page 10, line 23-24.

3. “Incomplete clinical data” is listed as an exclusion criterion, but no patients were excluded for this reason – consider eliminating this as an exclusion criterion.

Reply 3: Thank you for your advice. We have modified our text as advised.

Changes in the text: Page 21, Figure 1.

4. “Of” should be “or” (line 13, page 4).

Reply 4: Thank you for your advice. We have modified our text as advised.

Changes in the text: Page 4, line 21.

5. More information should be provided in the methods section regarding how the

surgery is performed. Of interest to the reader given the small number of staple failures is what type of stapler was used. In addition, how were the bleeding events and reason for bleeding adjudicated? Were operative notes reviewed? Were they reviewed by the operating surgeon, impartial party, or both?

Reply 5: Thank you for your advice. We have modified our text as advised. By reviewing the surgical record or video, whether the patient had intraoperative bleeding was judged by two authors (Hongxu Liu and Wei Chen).

Changes in the text: Page 5, line 27-33; and Page 6, line 1-9.

6. The % of patients who experienced a bleeding event should be reported clearly and early in the results section.

Reply 6: Thank you for your advice. We have modified our text as advised.

Changes in the text: Page 6, line 29.

7. I do not understand the reason for propensity-matching in this study. The main purpose of the study, if I understand correctly, was to determine how the groups that experienced bleeding and that did not experience bleeding differed. You are studying the outcome, not the intervention. If you are studying an intervention, propensity matching makes sense (because groups that have different interventions may differ in patient characteristics, and you are trying to control for that). If you are studying an outcome, it does not make much sense.

Reply 7: Thank you for your advice. We have modified our text as advised. Propensity-matching has been deleted.

8. T “categories” should be referred to as T “stage (line 18 page 6 but also elsewhere in text).

Reply 8: Thank you for your advice. We have modified our text as advised.

Changes in the text: Page 7, line 12; Page 15, line 2; and Page 23, Table 2.

9. Would change “cases” to “patients” (line 28, page 7).

Reply 9: Thank you for your advice. We have modified our text as advised.

Changes in the text: Page 8, line 32.

10. The statement that the “pulmonary artery injury occurred relatively easily during left upper lobectomy” in the referenced study seems incorrect. Please review and revise (line 2, page 9).

Reply 10: Thank you for your advice. In the referenced study, on the one hand, the proportion of LUL (43.8%) in PA injury group was highest. On the other hand, for LUL, the rate of PA injury was 3.33%, which was higher than other surgical procedures (1.50% for RUL, 2.78% for RML, 0.76% for RLL).

11. It is a bit harsh to say that the “careless” use of instruments was responsible for injury (line 17, page 9). Again, see point #5 above. How was it decided that “careless” use of the instrument was responsible for the injury. Also “improper” (line 16, page 9)

use is a strange thing to say. Surely, the surgeons who were doing the surgery did not dictate that they were using the instruments improperly or carelessly. This is a weakness/opportunity of the manuscript. An objective, scientific examination of the cases in which bleeding occurred is called for. Did bleeding occur because the vessels were too large for the devices? How EXACTLY did the injuries occur? This is what a reader wants to know, in order to learn something by reading the manuscript.

Reply 11: Thank you for your advice. In fact, except for stapler-related bleeding, we can find that most bleeding cases were caused by accidents and could be avoided to some extent in clinical practice by recalling and watching surgical videos. In the cases with tight lymph nodes around blood vessels, due to insufficient judgment, in the process of separating blood vessels and lymph nodes through ultrasonic scalpel, electric hook or surgical instruments, accidental damage to blood vessels will inevitably occur. This is something that every surgeon doesn't want to mention and can't avoid.

Changes in the text: Page 11, line2-9.

12. I would love to have the investigators categorize the reasons for injury into “stapler,” “energy”, “dissection,” or other. It is unclear if the harmonic scalpel and hook injured the artery when energy was being applied or when dissection was being done. Reconsider the way that you are classifying and describing how these vascular injuries occurred.

Reply 12: Thank you for your advice. We have modified our text as advised.

Changes in the text: Page 24, Table 4.

13. There is significant research out there that would contradict the assertion by the investigators that patients who experience significant intraoperative bleeding have similar/identical outcomes to those who don't. Namely, that these patients can experience longer hospital stays, more complications, and potentially even worse long-term outcomes (especially if you look at transfusion vs no transfusion, which is linked with intraoperative vascular injury). I suggest that they find these studies and include/address them as counterpoint to their stated beliefs.

Reply 13: Thank you for your advice. After deletion of propensity-matching, it can be seen from the study that intraoperative bleeding means longer hospital stay and the incidence of complications.

14. I would like to hear more about the “disposable banding-retractor” (page 11). Are we talking about tourniquets? Metal clamps? Something else? I have not heard this term before.

Reply 14: Thank you for your advice. “Disposable banding-retractor” is a kind of tourniquet. In order to avoid misunderstanding, "disposable belt retractor" has been changed to "tourniquet".

Changes in the text: Page 13, line 14-22.

15. What is “planned prolongation of incision” (line 32, page 11). Please reword.

Reply 15: Thank you for your advice. “Planned prolongation of incision” has been explained.

Changes in the text: Page 13, line 27-29.

16. “Personal” (page 21, table 4) should be reworded.

Reply 16: According to point #12 above, personal reason has been deleted.

17. I am surprised that the rate of simultaneous application of various methods was not higher (Table 4). Many surgeons will use hemostatic agents in addition to one of the abovementioned agents. Again, any specific tips/details on how to use suture to close intraoperative vascular injuries, particularly thoracoscopically, will be helpful to the reader.

Reply 17: In our center, the hemostasis could be achieved by one method, especially for suture. So hemostatic agents were rarely used as supplement hemostasis. For the suture, our method is consistent with the current mainstream method. Because it is not the main purpose of this study, it should not be explained in detail.

18. How did the coping strategy to deal with bleeding differ depending on site of bleeding (eg. vein, artery, bronchial, azygos)?

Reply 18: Thank you for your advice. This is the limitation of this study. Except pulmonary artery injury, there were relatively few cases of other vascular injuries, so the differences of coping strategies according to different vascular injuries were difficult to further be obtained. This will be the next research goal.

Changes in the text: Page 14, line 25-29.

19. I am confused about the word “Trunk” in Table 5. There is a truncus artery. Is that what they mean by upper lobe artery trunk? What does “pulmonary trunk” mean? Does it mean “left main pulmonary artery”? How is “lower lobe artery trunk” different from “basilar arterial trunk”? Does “basilar” mean distal to the origin of the superior segmental artery branch and “lower lobe artery trunk” mean proximal to it? Please clarify. An illustration/diagram instead of table might be helpful.

Reply 19: Thank you for your advice. The content of this part has been adjusted.

Changes in the text: Page 26, Table 5.

## **Reviewer B**

This article is very interesting.

Although there are many data they are presented with confusion and the discussion is too long and I become bored while reading the discussion.

I posed several questions and made some comments, and intraoperative bleeding is a very serious complication and the authors need to be very clear.

I therefore suggested to divide the discussion in small chapter to make things simple.

page 6 line 7-6 uniportal

COMMENT: between the 67 patients with bleeding, authors should give the number of patients operated with uniportal and multiportal approach.

Reply: Thank you for your advice. We have modified our text as advised. Only one patient completed the operation under multiportal VATS.

Changes in the text: Page 6, line 31-33; and Page 7, line 1.

page 7 line 8 misuse of harmonic scalpel.

COMMENT: What does it mean? the authors need to be more precise.

Reply: Thank you for your advice. Has been further illustrated.

Changes in the text: Page 8, line 9-11.

page 7 line 8, 9

COMMENT: what does it mean improper operation of surgical instrumentation? Please clarify

Reply: Thank you for your advice. Has been further illustrated.

Changes in the text: Page 8, line 12-14.

page 7 line 7

COMMENT: It is important to know what are the stapler problems.

Reply: Thank you for your advice. Has been further illustrated.

Changes in the text: Page 8, line 8-9.

table 5.

pulmonary trunk 4.

COMMENT I presume that this type of injury has been the most difficult to treat. How these patients have been treated?

Reply: Thank you for your advice. The treatment algorithm of our institution for intraoperative bleeding is summarized in Figure 2. Our methods are consistent with the current mainstream method. Because it is not the main purpose of this study, it should not be explained in detail.

Between the reason for intraoperative bleeding why the experience of the operating surgeon was not included?

Who was the operating surgeon? Was a resident?

Reply: Thank you for your advice. This is the limitation of this study.

Changes in the text: Page 14, line 16-17.

Were the bleeding classified according to the amount of blood lost?

Reply: Thank you for your advice. In our study, the identification of intraoperative vascular injury only included the injury of major blood vessels and their branches in the thoracic cavity; the injury of small blood vessels that were difficult to distinguish with the naked eye, such as wound oozing caused by the release of pleural adhesions and dissection of lymph nodes, was not considered as intraoperative bleeding.

No data on preoperative neoadjuvant or immunotherapy. It is necessary to have these data to know if they can be related to.

Reply: Thank you for your advice. This is the limitation of this study.

Changes in the text: Page 14, line 17-19.

Discussion is too long and I must admit that although the article is interesting I was bored.

It is probably better divided in small chapter such as

surgeon experience

stapler misfire

human error

repair of the main PA

Use of haemostatic sealent

Indication for thoracotomy

Reply: Thank you for your advice. We have modified our text as advised.

Changes in the text: Page 9, line 18; Page 10, line 5; Page 10, line 29; Page 11, line 29; Page 12, line 29; and Page 14, line 11.

Uniportal video-assisted thoracic surgery treatment of intra- operative complications.  
J Vis Surg 2018;4:23

### **Reviewer C**

The original article (title: Analysis of risk factors and management of unexpected intraoperative bleeding during video-assisted thoracic surgery for non-small cell lung cancer: a case-control study) was introduced. This article is very well written and is considered worthy of publication.

However, the very important Institutional Review Board (IRB, approval number) approval process is omitted. Therefore, it is recommended to resubmit after IRB approval.

Reply: Thank you for your advice. We have modified our text as advised.

Changes in the text: Page 4, line 11-12.

### **Reviewer D**

Review of the paper entitled: "Analysis of risk factors and management of unexpected intraoperative bleeding during video-assisted thoracic surgery for non-small cell lung cancer: a case-control study" by Wei Chen et al Department of Thoracic Surgery, Cancer Hospital of Dalian University of Technology, Liaoning Cancer Hospital & Institute, Shenyang, China. The authors reported the post-operative outcomes of

patients with intra operative bleeding (IBG, n=67) comparing them with a large counterpart (1025). The authors demonstrated several and well-known risk factors of intra operative bleeding and conversion from vats to thoracotomy and also showed that post-operative outcomes were comparable between the two groups. In my opinion the paper is good, but it does not lead any new information or findings to the reader because in literature several and multi-institutional papers have been published on this topic (only for example: Bongiolatti S. Risk factors and impact of conversion from VATS to open lobectomy: analysis from a national database. *Surg Endosc.* 2019 Dec;33(12):3953-3962. doi: 10.1007/s00464-019-06682-5. Epub 2019 Jan 31. Erratum in: *Surg Endosc.* 2019 Jun 4;: PMID: 30706153.; Bertolaccini L, Conversion due to vascular injury during video-assisted thoracic surgery lobectomy: A multicentre retrospective analysis from the Italian video-assisted thoracic surgery group registry. *Eur J Surg Oncol.* 2019 May;45(5):857-862. doi: 10.1016/j.ejso.2018.12.023. Epub 2019 Jan 8. PMID: 30661924.).

I suggest some modifications of the study, in particular:

- wedge resection should be excluded because the risk of bleeding is absolutely lower than lobectomy or segmentectomy

**Reply: Thank you for your advice. The cases with wedge resection have been excluded.**

**Changes in the text: Page 5, line 11-12.**

- the method used to construct the propensity match analysis must be clarified, maybe by a statistician and also the software SPSS v 22 does not run any propensity match analysis

- the PSM could be performed in a ratio 1:2 or 1:3 or 1:4 because the RG is very big.

**Reply: According to another reviewer's opinion, the propensity match analysis has been deleted.**

## **Reviewer E**

The article by Wei Chen et al. does not provide any information that goes beyond current knowledge. As such it does not add any novel information to the field. There are some methodological issues that need to be addressed.

1) The power of non-significant results needs to be calculated. This is particularly important as operation time and bleeding increase the risk of acute lung injury. The power of this study to detect such complication is most likely to low.

**Reply: Thank you for your advice. This is a limitation of our study. Because this study is retrospective, patients with acute lung injury cannot be identified.**

2) It remains unclear how precisely the amount of blood loss was established. How was quantification of blood loss achieved in this retrospective study?

**Reply: Thank you for your advice. Because this study is retrospective, the quantification of blood loss is based on the surgical records.**