Peer Review File

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Reviewer A

Comment 1: Line 129-131: Lymph nodes management is unclear. Lymphadenectomy is a key point in the surgical management of NSCLC. Lymph nodes upstaging should appear, and this point needs to be developed in the text.

Reply 1: When we perform segmentectomies for small-sized, GGO dominant tumors such as those included in this study, only hilar lymph node sampling are performed. When we perform segmentectomies for frail cases that are intolerable for lobectomies, systemic lymph node dissection is still not performed, only sampling is performed. There were no cases that upstaged in lymph nodes in this study. A description on this has been added.

Changes in the text: In cases of primary lung cancer, there were cases with visceral pleural invasion or tumor diameter that reached pathological stage 1B or above, but none of the cases were upstaged due to lymph node metastasis.(Page9, Line154-156)

Comment 2: Line 306-307: Author concludes that there is no difference in learning curve between simple and complex segmentectomy. It's surprising, hypothesis and explanation of these results should be argued in the text.

Reply 2: Basically, what is done in a simple or complex segmentectomy is the same and makes no difference, in our experience. We previously reported no significant differences in perioperative results including blood loss, operation time, drainage, hospitalization and morbidity between simple and complex segmentectomy group (J Thorac Dis. 2021 May;13(5):3001-3009).

Comment 3: Table 2: please write numbers on each groups: (Complex segmentectomy n=), and percentage values for each may be helpful to the understanding

Reply 3: We added the data in Table 2 as pointed out.

Changes in the text: Page 22, Table 2

Reviewer B

Comment 1: However, the application of CUSUM analysis in this study is problematic. CUSUM is designed for statistical process control where the outcome measure is predetermined. When CUSUM is applied to a series where the mean of the entire series becomes the target outcome, the CUSUM analysis becomes self-referential and subject to overinterpretation, if not erroneous interpretation. By definition, operative times that are decreasing linearly will yield a bell-shaped CUSUM curve. Simply attributing learning phases to the upslope, plateau, and downslope of such a curve is meaningless. Unfortunately, this type of error seems to be perpetuated in the surgical learning curve literature in general, and thoracic surgery learning curve literature specifically. The

paper by Dimitrovska et al. cited by the authors is a case in point where learning phases are erroneously attributed to sections of the CUSUM curve. In fact we recently commented on the Dimitrovska paper: Rakovich G, Woodall WH, Steiner S. Comment on the CUSUM surgical learning curve analysis in Dimitrovska et al. (2022). Interact Cardiovasc Thorac Surg 2022 Jul 9;35(2):ivac184. doi: 10.1093/icvts/ivac184. There is an additional point here: in theory, any CUSUM curve calculated as outlined in the methods section starts and ends with « 0 », by definition. This is not the case in the curves reported here, and I suspect there was an error in calculation somewhere. In addition, since the plot of the raw operative times is essentially linear and horizontal, there does not actually seem to be any real progress in operative times happening in this study, which seems puzzling. I strongly encourage the authors to consult the following papers on the application of CUSUM analysis to surgical learning curves in general as well as a discussion of the CUSUM curve and its limitations when applied to segmentectomy specifically :

• Woodall WH, Rakovich G, Steiner SH. An overview and critique of the use of cumulative sum methods with surgical learning curve data. Stat Med 2021 Mar 15;40(6):1400-1413. doi: 10.1002/sim.8847

• Rakovich G, Belahmira G, Woodall WH, Berdugo J. Learning curve for completely thoracoscopic anatomic sublobar resection. Minerva Surg 2022 Apr;77(2):101-108. doi: 10.23736/S2724-5691.21.08895-X

Reply 1: As pointed out, CUSUM technique has the potential to be self-referential and subject to overinterpretation. However, the CUSUM make possible rapid and powerful assessments of changes, or in the slopes of trends, in data collected at regular intervals of time. Although there is a fundamental question as to whether operative time alone can be used as a measure of surgical proficiency, it is a good visual indication of the reduction in operative time over time, either in an individual or in a single team. The method of dividing the learning curve created by CUSUM into three Phases based on its slope has been the most commonly used method (“The robotic surgery learning curve of a surgeon experienced in video-assisted thoracoscopic surgery compared with his own video-assisted thoracoscopic surgery learning curve for anatomical lung resections.” European Journal of Cardio-Thoracic Surgery 61 (2022) 289–296), which we have also adopted. The process is very clearly described as follows: in the 1st phase, the operating time is slowly reduced, in the 2nd phase the technique is going to be stable, and in the 3rd phase it is further mastered and shortened. Limitations and problems with CUSUM have been added to the Discussion section.

Changes in the text: Finally, the limitations of using CUSUM analysis as a surgical learning curve have been pointed out (28), and further study is needed on better methods, including the fundamental question of whether it is correct to measure surgical proficiency in terms of operating time. (Page 24, Line 240-242)

Comment 2: The authors describe the surgical experience of the two surgeons involved in the study. It is mentioned that surgeon H.I. performed 17 uniportal segmentectomies. Was this prior to the beginning of the study period? If so, then these 17 cases would be a part of his learning curve, and yet they would not have been included in this analysis.

Please clarify. Also, did the surgeons perform uniportal segmentectomies exclusively during the study period?
Reply 2: Those 17 cases are included in this study. During this study period, a variety of surgical procedures were performed, including uniportal lobectomies, wedge resections and thoracotomy.

Comment 3: Integrating two surgeons into a single learning curve is problematic, especially when those two surgeons have different levels of expertise at the outset. I would argue that this makes the data particularly difficult to interpret. It then falls onto the authors to explain why they proceeded in this way and how one should interpret the data. As it stands their data is neither applicable to a team nor to an individual surgeon.
Reply 3: The two surgeons (H.I. and N.M) had almost the same years of experience and there was no significant gap in their knowledge and skills. However, H.I. experienced uniportal VATS surgery first, while N.M. started later. The role of the assistant is also important in the uniportal surgery we perform. The assistant needs to be familiar with operating the camera so as not to disturb the operating space of the surgeon, to show the operative field well and to deploy the lungs. As cooperation between the surgeon and assistant is important, a learning curve has been created to show the process of the surgeon and assistant taking turns and becoming proficient as a team.

Comment 4: Learning is multidimensional, and operative time is only one indicator of the learning process. Are there any other data in this series that would help to describe the development of expertise or to corroborate what the operative times may be telling us?
Reply 4: As you point out, in addition to operation time, for example, blood loss and postoperative complications may be indicators of surgical proficiency. However, both blood loss and postoperative complications were very low in the present study subjects and difficult to use as indicators.

Comment 5: The authors state that (at least in some patients) their choice between wedge resection and segmentectomy was the possibility of getting adequate margins. Is this, then, the rationale for segmentectomy, or rather the fact that segmentectomy, unlike wedge, is an anatomic resection that addresses potential routes of lymphatic spread?
Reply 5: The advantages of segmentectomy compared with wedge resection are that it provides a margin to the hilar side and allows sampling of hilar lymph nodes. As lymphatic flow is mainly towards the hilar side, providing a hilar margin including the dominant bronchus might prevent local recurrence.

Comment 6: The authors should explain how they classify simple vs complex segmentectomies, as several classifications exist.
Reply 6: We described about it (Page 6, Line 82-84; Simple segmentectomy involved resection of the superior segment of the lower lobe (S6), basilar segment on each side, left upper division, and left lingual segment (14). All other procedures were classified

as complex segmentectomy.)

Comment 7: What is meant by preoperative simulation? If relevant, what was the imaging platform that was used?
Reply 7: Contrast-enhanced, high-resolution CT (thickness ≤1 mm) was performed for all enrolled patients prior to surgery. These data were transferred to a workstation 'Ziostation2' (Ziosoft, Inc., Tokyo, Japan) and three-dimensional CT angiography and bronchography were created automatically. The tumor location and dominated bronchus and vessels were identified.

Comment 8: « Intentional » vs « unintentional » segmentectomy is probably not the best choice of words, as the authors probably mean to say that the choice for segmentectomy was either based on oncologic considerations or a compromise dictated by physiologic impairment of the patient.
Reply 8: We consider that it is important to decide preoperatively whether the segmentectomy is oncologically indicated and aggressive to preserve lung function, or oncologically unacceptable but unavoidable and passive. We define the former as intentional and the latter as unintentional.

Comment 9: What is meant by « uniportal surgery requires detachment »?
Reply 9: As you pointed out, the word was inappropriate and has been corrected.
Changes in the text: unique technique (Page4, Line 47)

Comment 10: It would have been relevant to include pathologic stage and margins, as nodal upstaging and margin status are clinically relevant and are potential quality indicators.
Reply 10: In the present study, we did not examine the data about surgical margin. There were no cases that upstaged in lymph nodes in this study. A description on this has been added. And we added the pathologic stage in Table 1 as pointed out.

Changes in the text: In cases of primary lung cancer, there were cases with visceral pleural invasion or tumor diameter that reached pathological stage 1B or above, but none of the cases were upstaged due to lymph node metastasis.(Page9, Line154-156)
Page 21, Table 1

Reviewer C
Comment 1: You should mention the pathological stage in case of lung cancer. No data on lymph node dissection
Reply 1: When we perform segmentectomies for small-sized, GGO dominant tumors such as those included in this study, only hilar lymph node sampling are performed. When we perform segmentectomies for frail cases that are intolerable for lobectomies, systemic lymph node dissection is still not performed, only sampling is performed. There were no cases that upstaged in lymph nodes in this study. A description on this

has been added.
We added the pathologic stage in Table 2 as pointed out.
Changes in the text: In cases of primary lung cancer, there were cases with visceral pleural invasion or tumor diameter that reached pathological stage 1B or above, but none of the cases were upstaged due to lymph node metastasis.(Page9, Line154-156)
Page 21, Table 1

Comment 2: Do you consider that the time is the appropriate factor for determining the learning curve? Or should we better include the post-operative complications rate?
Reply 2: As you point out, in addition to operation time, for example, blood loss and postoperative complications may be indicators of surgical proficiency. However, both blood loss and postoperative complications were very low in the present study subjects and difficult to use as indicators.

Comment 3: My main concern is that you mention that you reach the learning curve after 50 cases. But in your experience, you have done only few difficult segmentectomies (S10 or S9). Can you honestly admit that you reach the learning curve of these difficult segmentectomies after few cases... In my experience, I have >40 cases of these segments and I am still struggling!
Reply 3: As you point out, the number of cases of complex segmentectomies of the basal segment is low. However, adequate peripheral detachment of the pulmonary vein enables accurate identification of arteries and bronchi and allows segmentectomies in the basal segment as well as other segmentectomies. We believe that segmentectomies of all areas can be performed in the same way.

Comment 4: The number of included patients in too low for 2 surgeons.
Reply 4: You are correct in pointing out. We would like to accumulate more cases on these two surgeons in the future for further study.