

Peer Review File

Article Information: <https://dx.doi.org/10.21037/jtd-21-1895>

Reviewer A: In a retrospective study Dr. Jian and colleague compared the surgical results of video-assisted and robotic-assisted combined anatomic pulmonary subsegmentectomy. They found that there were more N1, N2 lymph nodes and stations dissected in the robotic-assisted group than in video-assisted group. In addition, higher cost was observed in robotic-assisted group compared to video-assisted group. Finally, the author concluded that the both approaches are safe and feasible for the patients with early-stage NSCLC. The robotic approach might contribute to the potential improvement of N1 and N2 lymph node retrieval.

I'm very pleased to have read this manuscript on a relevant clinical topic in our professional field. I also congratulate the authors on the successful surgery. Indeed, combined subsegmentectomy has been increasingly adopted in the recent years and may achieve the equal oncological efficiency for T1 NSCLC and GGO compared with lobectomy.

1. Looking at the Table 1, the majority of patients involved in the present study had a nearly normal pulmonary function (FEV1% over 80%). However, more than 10% of the patients suffered from pneumonia after the combined subsegmentectomy (Table 3). This complication rate was much higher than that following VATS lobectomy in the literature. I'd suggest the author to comment on this issue.

Response: Thank you so much for this important point. Postoperative pneumonia (POP) is one of the most common complications in patients with lung cancer (LC) undergoing therapeutic surgical resection. We have checked some studies and found that the reported incidence of POP following LC surgery was quite different and various, ranging from 2.2 to 31.7%[1,2,3,4,5,6,7]. The diagnosis criteria of POP (WS 382-2012) applied in our study were as follows:

- (1) Two chest X-ray exams at least and it should meet at least one of the following criteria, including new or progressive and persistent lung infiltrations, shadows, consolidation, and cavity formation;
- (2) Fever (body temperature $>38^{\circ}\text{C}$) and no other clear cause, peripheral blood $\text{WBC}>12\times 10^9/\text{L}$ or $<4\times 10^9/\text{L}$ and aged ≥ 70 years old without other clear cause, and mental changes. At least one of these conditions is met.
- (3) The emergence of new phlegm or the change of the characteristics of sputum, or respiratory secretions increase, sputum suction or need number increase, the emergence of new cough, difficulty breathing or breathing rate faster, or the original cough, difficulty breathing or shortness of breath, the lungs or bronchial breath sounds, gas exchange situation worse, Increased oxygen demand or mechanical ventilation support. At least two of these conditions are met.

According to this criteria, the complication rate of POP in our study was much higher than that following VATS lobectomy in some literatures.

- [1] Sandri A, Papagiannopoulos K, Milton R, et al. Major morbidity after video-assisted thoracic surgery lung resections: a comparison between the European Society of Thoracic Surgeons definition and the Thoracic Morbidity and Mortality system[J]. J Thorac Dis, 2015, 7(7): 1174-1180.
- [2] Schussler O, Alifano M, Dermine H, et al. Postoperative pneumonia after major lung resection[J]. Am J Respir Crit Care Med, 2006, 173(10): 1161-1169.
- [3] Lee JY, Jin SM, Lee CH, et al. Risk factors of postoperative pneumonia after lung cancer surgery[J]. J Korean Med Sci, 2011, 26(8): 979-984.
- [4] Kaneda H, Nakano T, Taniguchi Y, et al. Impact of previous gastrectomy on postoperative pneumonia after pulmonary resection in lung cancer patients[J]. Interact Cardiovasc Thorac Surg, 2012, 14(6): 750-753.
- [5] Doddoli C, Thomas P, Thirion X, et al. Postoperative complications in relation with induction therapy for lung cancer[J]. Eur J Cardiothorac Surg, 2001, 20(2): 385-390.
- [6] Dominguez-Ventura A, Allen MS, Cassivi SD, et al. Lung cancer in octogenarians: factors affecting morbidity and mortality after pulmonary resection[J]. Ann Thorac Surg, 2006, 82(4): 1175-1179.
- [7] White M, Martin-Loeches I, Lawless MW, et al. Hospital-acquired pneumonia after lung resection surgery is associated with characteristic cytokine gene expression[J]. Chest, 2011, 139(3): 626-632.

2. Page 5, line 107 and 115: what does "sub-segmental pneumonectomy" mean?

Response: Thank you for pointing this out. We have delete “sub-segmental pneumonectomy” to make the statement to be more clear and precise. (Changes in the text: Page4 Line92)

3. There are some inappropriate wording and typing errors, e.g. page 8, line 188 ("one single practiced surgeon"), and page 11, line 281

4. I suggest that an English speaker reviews the manuscript before re-submission.

Response: Thank you for pointing this out. A native English speaker has reviewed the manuscript and we have made some modifications on these inappropriate wording and typing errors.(Changes in the text: Page7 Line183; Page10 Line278)

Reviewer B: The reviewer is honored to review an article about RATS vs. uniport VATS combined anatomical subsegmental lung resection. The number of cases was small, which cannot be helped because of the rare type of lung resections. In this meaning, scientific meaning of this article seems limited, but many thoracic surgeons would practically benefit from the publication of this series of surgical procedures. The weakest point of this paper is, unfortunately, there are many typos and grammatical errors in this manuscript. In this current form, this paper does not convey the true meaning of what the authors want to address. Please check the manuscript extensively

again by asking an English editor who is familiar with medicine and surgery. The letters of the captions in the surgical video (video1) were relatively small and looked vague, which should be revised for the better understanding by the potential readers. Moreover, there are several points to be clarified, as follows:

1. Regarding the discussion about the direct and indirect costs in the discussion section, the authors commented “The Chinese's National Medical Insurance System takes care of the cost comes from 334 these two types of surgery in perioperative time”. Does this mean the operative costs including robotic staplers and arms in addition to clips were covered by the insurance? If so, the potential readers would want to know the minute contents of the 4000 dollars.

Response: Thank you so much for this important point. We have confirmed that the Chinese's National Medical Insurance System will cover the clips in the operation, but not include staplers and arms. The indirect costs referred to the sum of all additional costs for the hospital that was comprised of overhead cost and amortization of surgical equipment, including of the purchase and maintenance of minimally invasive platforms. The indirect cost associated with the amortization of surgical equipment was unified within each approach, which was around \$300 for video-assisted surgery and \$4300 for robotic surgery. The standard charges for the amortization of the surgical equipment were decided by the Shanghai Municipal Government. We, as a public hospital, strictly followed the unified charging standard instead of independent pricing. We have provided a more detailed explanation of the indirect costs in the manuscript.(Changes in the text: Page6~7 Line164~169)

2. These surgical procedures seemed relatively difficult. The authors should provide some comments on who was the primary operators in these procedures. Multiple operators or single professional operator for each procedure type?

Response: Thank you for this suggestion. We have added some comments on who was the primary operators in these procedures. (Changes in the text: Page7 Line183~185)

All operations were performed by one general thoracic surgeon (H. L.), and clinical assessments were conducted according to National Comprehensive Cancer Network Guidelines.

3. In video 1, the authors provided nice 3D-CT structures of vessels and bronchi. How often do they make these 3D-CT figures? Does it change and/or help the surgical procedures?

Response: Thank you so much for this important point. It's very common to make these 3D-CT figures in our department, because it does help the surgical procedures. For example, 3D-CT figures can bring a better view and understanding of the location of pulmonary nodule. The surgeons are able to figure out the structural relation between pulmonary nodule and its surrounding tissues or blood vessels. Even more, some

studies have reported that the application of 3D-print technology in lung surgery [1,2].

[1] Li C, Zheng B, Yu Q, et al. Augmented Reality and Three-Dimensional Printing Technologies for Guiding Complex Thoracoscopic Surgery - ScienceDirect[J]. The Annals of Thoracic Surgery, 2020.

[2] Chen Y, Zhang J, Chen Q, et al. Three-dimensional printing technology for localised thoracoscopic segmental resection for lung cancer : a quasi-randomised clinical trial. 2020.

Reviewer C: The authors reported that the safety and efficacy of different treatment approaches for lung cancer cases at a single retrospective center. They performed combined anatomic subsegmentectomy (CATS) for 62 cases of lung cancer with a tumor size of less than 2 cm and a GGO component of more than 50% (and cN0M0), and divided the approaches into 30 cases of multiport VATS (VATS) and 32 cases of robot-assisted thoracic surgery (RATS) to examine their clinical factors.

There was no difference in operative time, blood loss, postoperative hospital stay, or drainage duration between the two groups, and RATS required one more lymph node dissection and one more dissected lymph node station. However, total and indirect costs were more than \$4,000 higher in the RATS arm. This is a report that can be used as a reference for respiratory surgeons, as it shows the results of two clinically viable treatment options for lung cancer.

However, I have some concerns that should be addressed regarding the report contents.

(Major comments)

1. Subsegmentectomy for lung cancer is a limited resection; please provide a clear rationale for this procedure in the “Introduction”. In the “Introduction”, please provide a clear rationale for this procedure, clarify the target of the subsegmentectomy, and discuss whether it improves prognosis and preserves function.

Response: Thank you so much for this suggestion. We have fully revised our manuscript and made some modifications on the introduction part to make it more concise and readable. (Changes in the text: Page4 Line83~88)

2. Subsegmentectomy is a limited pulmonary surgery for lung cancer. There is a concern that subsegmentectomy may increase local recurrence due to insufficient resection margin compared to standard surgery. Please indicate the resection margin in the Table.

Response: Thank you so much for this important point. We have further analyzed the resection margin of each group and added them into the Table4. (Changes in the text: Page9 Line240; Page21 Line596)

3. This paper is a report discussing the different approaches. please detail the forceps used in RATS. Please add any procedural innovations.

Response: Thank you for this suggestion. Since we have specifically reported the technical aspects of robotic approach to combined anatomic subsegmentectomy [1], the procedural innovations of RATS were not discussed further in the manuscript. For more information to the readers, we have added some details about the forceps and procedural innovations of RATS. (Changes in the text: Page7 Line172~176; Page8 Line180~189)

[1] Li C, Han Y, Han D, et al. Robotic approach to combined anatomic pulmonary subsegmentectomy: Technical aspects and early results. *Ann Thorac Surg* 2019;107(5):1480-1486.

4. The key to successful segmentectomy is good delineation and resection of the inter-segmental plane. Describe the method for delineation of the inter-segmental plane. Also describe the method of resected bronchial handling in the Table. For example, compare the methods of ligation, stapler or suture closure.

Response: Thank you so much for this important point. We totally agree that the key to successful segmentectomy is good delineation and resection of the inter-segmental plane. Since there are limited cases in our study, it can be meaningless and difficult to compare the methods of ligation, stapler or suture closure in all these surgeries. In fact, these three methods were commonly used together in these surgeries, but not solely used. Still, we hold the same view that this question should be further studied. We have signed up a clinical trial (NCT03192904) to compare the methods of ligation, stapler or suture closure, and the results [1] have been published on *Ann Thorac Surg* for your reference. (Changes in the text: Page7~8 Line176-185)

[1] Xc A, Jin A R, Jie X A, et al. Methods for Dissecting Intersegmental Planes in Segmentectomy: A Randomized Controlled Trial - ScienceDirect[J]. *The Annals of Thoracic Surgery*, 2020, 110(1):258-264.

5. For Figure 1, conversions are seen in 7 of 69 cases (10%). Since this is a problem related to the choice of procedure, please describe the reasons for the 7 conversion cases.

Response: Thank you so much for this important point. 7 conversion cases belong to intraoperative exclusion, which means intraoperative change of surgical plan. In our department, it's common for these patients to take a 3D-CT before surgery, and even more, some patients may have a hook-wire localization. According to preoperative reconstruction of 3D-image and hook-wire localization, subsegmentectomy plus wedge resection sometimes can ensure the safe margin for the patient. Under this circumstance, the CAS procedure will be waived if the patient's consent is obtained. Also, we have added these information in the manuscript. (Changes in the text: Page6 Line142~143)

6. Indicate the lymph node sites that were dissected in RATS and CAS-VATS. Each

lobe of the lung should be divided into its own approach and listed in the Supplement table.

Response: Thank you for this suggestion. In our department, the standardized lymph node dissection is performed based on NCCN guidelines and due to this, we did not mention the dissected lymph node sites in our manuscript. It was imperative to first confirm N0 status. Not only N2 lymph nodes but also No. 12 and 13 lymph nodes were sampled for frozen section examination. If results were positive, we converted to lobectomy and systematic lymph node dissection. According to the NCCN guidelines, one or more nodes should be sampled from all mediastinal stations. For right-sided cancers, an adequate mediastinal lymphadenectomy should include stations 2R, 4R, 7, 8, and 9. For left-sided cancers, stations 4L, 5, 6, 7, 8, and 9 should be sampled. Patients should have N1 and N2 node resection and mapping (American Thoracic Society map) with a minimum of 3 N2 stations sampled or a complete lymph node dissection, which means N1 and N2 node resection and mapping should be a routine component of lung cancer resections, and a minimum of three N2 stations sampled or complete lymph node dissection. Also, we have added these information in the manuscript. (Changes in the text: Page8 Line184~187)

(Minor comments)

7. Table 4 What is the breakdown of "Benign"? If it is AAH, please describe it as such.

Response: No, "Benign" does not include "AAH". The breakdown of "Benign" means no evidence of malignancy and there are only normal tissues being found.

8. Describe the model used for the RATS.

Response: As we mentioned in the methods part, the da Vinci S/Si system (Model S/Si) was used in this study (Page7 Line171). We preferred using 4 arms and an auxiliary port for CAS. The 12-mm camera port was on the eighth intercostal space of the midaxillary line. The 15-mm auxiliary port, 8-mm arm 2 port, and 8-mm arm 3 port were all on the eighth intercostal space (anterior axillary line, posterior axillary line, and 2 cm from the spine, respectively). The 8-mm arm port 1 was on the fifth intercostal space of the anterior axillary line.

The current and more advanced da Vinci Xi system gained new features including rotating boom-mounted arms with better dexterity and patient clearance, improved stapling capabilities, integration with fluorescence imaging, improved camera optics, and a redesigned smaller endoscope which can be inserted through any 8 mm robotic port. Compared with the older da Vinci S/Si system used in this trial, these new features of the Xi system could potentially improve maneuverability and dexterity, shorten docking and operating time, and reduce surgical trauma. The more sophisticated robotic system may also reduce the risk of conversion to an open thoracotomy and improve

surgical capabilities especially for challenging cases. However, there are also different opinions. Some surgeons may think the main difference between the most recent system and the older ones is the ability of the console surgeon to perform stapling of the vascular structures. Despite this, many surgeons including one of the authors (A.E.A.) continue to prefer bedside stapling.

9. Indicate the number of editions of the TNM used for case selection.

Response: As we mentioned in the methods part, the 8th editions of the TNM were used for case selection.(Page7 Line158)

Reviewer D: I reviewed the manuscript entitled “Robotic versus thoracoscopic combined anatomic pulmonary subsegmentectomy for early-stage lung cancer: Early results of a cohort study” This report was interesting for me because the number of the patients who underwent sublobar resections has increased with CT check-up; although it has a few limitations.

(Major comments)

1. I thought that this article contains recent trends about minimally invasive approaches and sublobar resections in small-sized early-stage lung cancer. However, I'm doubtful whether the robotic combined anatomic subsegmentectomy is useful because the cost of this approach is more expensive than that of the thoracoscopic approach, even if the robotic approach enables us to dissect more lymph nodes than the thoracoscopic approach. Actually, Zhang Y. et al. reported that in GGO-dominant lung cancer, lymph node metastasis has not been recognized (Ann Thorac Surg. 2020;109:1061-1068). Therefore, I think that it is not important to assess the number of dissected lymph nodes in small-sized GGO-dominant lung cancer. How do the authors feel about this importance of the lymph node dissection?

Response: Thank you so much for this important point. Li et al. [1] reported that RATS, compared with VATS, is associated with more lymph nodes stations examined and a higher number of LNs harvested. This could be attributed to the three-dimensional imaging, high-definition visualization, better maneuverability, and improved dexterity provided by the robot-assisted system, which endows the surgeon with better dissection capabilities for LNs around vessels and bronchi. Although all lymph nodes dissected from both groups of patients in our study were negative for metastasis, there may be a potential tendency to understage patients if adequate lymph node dissection is not performed. The sizes of the dissected lymph nodes are of great importance for precise and accurate pathological staging, as there may be latent neglected positive lymph node metastasis. The latest National Comprehensive Cancer Network guidelines also emphasize the importance of adequate lymph node dissection in sublobar resection. Extended segmental resection not only involves the removal of the affected and adjacent segments but also includes aggressive dissection of LNs surrounding the

bronchi of the affected subsegment, as well as the hilum and mediastinum. However, in this study, the patient's survival benefit from the additional number of LNs and stations dissected from the RATS group may have been negligible. Dezube et al.[2] recently reported a correlation between the number of LNs harvested and long-term survival according to the National Cancer Database, and they found that, for lobectomy, the optimal number of LNs dissected is four, with no survival benefit when additional LN sampling was performed. However, further studies, preferably randomized controlled trials, are required to clarify the clinical relevance between the improved LNs harvest and long-term survival in the RATS group. However, the potential survival benefit derived from an extra number of LNs and station retrieved in the RATS group may be negligible. Further studies, preferably randomized controlled trials, are needed to clarify any clinical relevance between the improved LNs dissection in the RATS group and long-term survival.

[1] Li JT, Liu PY, Huang J et al. Perioperative outcomes of radical lobectomies using roboticassisted thoracoscopic technique vs. Video-assisted thoracoscopic technique: Retrospective study of 1,075 consecutive p-stage i non-small cell lung cancer cases. J Thorac Dis 2019;11(3):882-891.

[2] Dezube AR, Mazzola E, Bravo-Iñiguez CE, et al. Analysis of lymph node sampling minimums in early stage non-small-cell lung cancer. Semin Thorac Cardiovasc Surg 2021;33(3):834-845.

2. I could not understand the definition of combined anatomic subsegmentectomy. The definition of subsegmentectomy is vague. I wonder if the authors' subsegmentectomy is truly a pure subsegmentectomy. If anything, this article might be describing both anatomic subsegmentectomy and segmentectomy combined with adjacent subsegmentectomy. Is it appropriate to assess the outcomes contained between these two procedures?

Response: Thank you for the question. The definition of combined anatomic subsegmentectomy is based on the published articles [1,2]. In these articles, both anatomic subsegmentectomy and segmentectomy combined with adjacent subsegmentectomy were divided into combined anatomic subsegmentectomy.

[1] Yoshimoto K , Nomori H , Mori T , et al. Combined subsegmentectomy: postoperative pulmonary function compared to multiple segmental resection[J]. Journal of Cardiothoracic Surgery, 2011, 6(1):17-17.

[2] Li C, Han Y, Han D, et al. Robotic approach to combined anatomic pulmonary subsegmentectomy: Technical aspects and early results. Ann Thorac Surg 2019;107(5):1480-1486.

3. I think that it is better to emphasize the technical usefulness of a robotic subsegmentectomy in the discussion section.

Response: Thank you for this suggestion. We totally agree with this comment, and we have further discussed the technical usefulness of a robotic combined subsegmentectomy in the discussion section. (Changes in the text: Page11~12 Line288~303)

(Minor comments)

1. If the authors want to emphasize the usefulness of anatomic robotic combined subsegmentectomy, the actual video of not only thoracoscopic combined anatomic subsegmentectomy but also robotic combined anatomic subsegmentectomy should be shared.

Response: Thank you so much for this suggestion. We totally agree with this comment, and we have shared an actual video of robotic combined anatomic subsegmentectomy followed by this manuscript.

2. In line 56, “Larger amounts...” should be revised to “larger amounts...”.

3. In line 79, “sub-lobectomy” should be revised to “sublobectomy”.

4. In line 107 and 115, is the term “sub-segmental pneumonectomy” appropriate? Is it better to describe as “subsegmental lobectomy”?

5. In line 281, the term “shows results.” was not understood. (Copy/paste error?)

Response: Thank you for pointing this out. A native English speaker has reviewed the manuscript and we have made some modifications on these inappropriate wording and typing errors.

6. What was the ratio of ground glass opacity in each tumor on the CT findings? The ratio should be described in Table 1.

Response: Thank you so much for this suggestion. We totally agree that the ratio of ground glass opacity in each tumor is important for the diagnosis of patients and the options for surgery. However, in our hospital, it's quite difficult to access these information and we did not mentioned them in our manuscript. Still, we hold the same view that this question should be further studied. In the future, we will collaborate with the medical imaging department of our hospital to identify the significance of the ratio of ground glass opacity in lung surgery.

7. In Table 2, left S6a+S7+8 segmentectomy was described. It was difficult to understand this procedure. Is this procedure left S6b+S7+8 segmentectomy?

Response: We are regretfully sorry about this typo mistake. We have changed “S6a+S7+8” into “S6b+S7+8” in our manuscript. (Changes in the text: Page19 Line542)

Reviewer E: I would like to thank the editor and the office for providing me a great chance to review such an interesting paper.

This paper was well written and almost acceptable. The outcomes and discussions were

consistent with previous reports. The video shown in this article was also stimulating and enjoyable.

I have one request to make. It would be highly appreciated if the authors would upload a video of RATS CAS. Authors have already demonstrated a VATS CAS video (presumably uniportal VATS). I would like to watch RATS CAS video to see how lymph nodes were harvested. If RATS CAS video were shown, the readers would easily understand why RATS offered better lymph node retrieval.

Response: Thank you so much for this suggestion. We totally agree with this comment, and we have shared an actual video of robotic combined anatomic subsegmentectomy followed by this manuscript.

Reviewer F: This study investigated the oncological safety, the early results in the short term, and the cost-benefit of combined anatomic subsegmentectomy using RATS. The authors have shown that RATS CAS had comparable perioperative results compared to VATS CAS, and that pathological safety was also guaranteed. This study will benefit general thoracic surgeons as more lung segmentectomy is expected to be performed in the future.

I have some concerns and questions to strengthen this paper as follows:

(Major comments)

1. Fig1 shows that there were a total of 7 conversions. The authors should note why CAS was switched to segmentectomy or lobectomy? If the reason is insufficient margins, the research methods will need to be significantly modified.

Response: Thank you so much for this important point. 7 conversion cases belong to intraoperative exclusion, which means intraoperative change of surgical plan. In our department, it's common for these patients to take a 3D-CT before surgery, and even more, some patients may have a hook-wire localization. According to preoperative reconstruction of 3D-image and hook-wire localization, subsegmentectomy plus wedge resection sometimes can ensure the safe margin for the patient. Under this circumstance, the CAS procedure will be waived if the patient's consent is obtained. Also, we have added these information in the manuscript. (Changes in the text: Page6 Line142~143)

2. Some cases resulted in pT1b, but I believe this fact does not support the pathological safety of CAS. The eligibility criteria to receive CAS for early-stage lung cancer in this series was nodule 2cm or smaller in size with 50% or more ground-glass appearance on CT. pT1b means the nodule is 505 or less ground-glass appearance on CT. Therefore, these cases might have been excluded from the study. The authors should describe the views on this result in Discussion.

Response: Thank you for the question. We used 8th editions of the TNM for case selection and pathological evaluation. According to this edition, pulmonary nodules which are larger than 1cm but smaller than 2cm can be divided as pT1b. So that means the sizes of tumor in all groups are qualified and we also checked the CT image before surgery to make sure they were 50% or more ground-glass appearance on CT.

Table 1. Eighth edition of TNM staging of lung cancer: Definition of T, N and M

Primary tumor (T)	
T category	Definition
Tx	Tumor that is proven histopathologically (malignant cells in bronchopulmonary secretions/washings) but cannot be assessed or is not demonstrable radiologically or bronchoscopically.
T0	No evidence of primary tumor.
Tis	Carcinoma in situ: Squamous cell carcinoma in situ. Adenocarcinoma in situ (pure lepidic pattern and ≤3 cm in greatest dimension).
T1	Size: ≤3 cm. Airway location: in or distal to the lobar bronchus. Local invasion: none (surrounded by lung or visceral pleura). Subdivisions: T1mi: Minimally invasive adenocarcinoma (pure lepidic pattern, ≤3 cm in greatest dimension and ≤5 mm invasion)—T1a (size ≤1 cm) ^a —T1b (1 cm < size ≤2 cm)—T1c (2 cm < size ≤3 cm).
T2	Any of the following characteristics: Size: >3 cm but ≤5 cm. Airway location: invasion of the main bronchus (regardless the distance to the carina) or presence of atelectasis or obstructive. Pneumonitis that extends to hilar region (whether it is involving part or the entire lung). Local invasion: visceral pleura (PL1 or PL2). Subdivisions: T2a (3 cm < size ≤4 cm or cannot be determined) and T2b (4 cm < size ≤5 cm).
T3	Any of the following characteristics: Size: >5 cm but ≤7 cm. Local invasion: direct invasion of chest wall (including superior sulcus tumors), parietal pleura (PL3), phrenic nerve, or parietal pericardium. Separate tumor nodule(s) in the same lobe of the primary tumor.
T4	Any of the following characteristics: Size >7 cm. Airway location: invasion of the carina or trachea. Local invasion: diaphragm, mediastinum, heart, great vessels, recurrent laryngeal nerve, esophagus or vertebral body. Separate tumor nodule(s) in an ipsilateral different lobe of the primary tumor.

(Oncologist. 2018 Jul; 23(7): 844–848.)

3. The authors determine the subsegmental planes using only the intersubsegmental pulmonary veins as a landmark? In a video on VATS, the authors used the inflation-deflation demarking line. Did the authors use a narrow binding image following intravenous ICG injection after targeted pulmonary artery division? If so, please include how to detect intersegmental or inter subsegmental plane in Operative Techniques.

Response: Thank you so much for this important point. To identify intersegmental planes, we used the inflate-deflate technique. Once all hilar structures were interrupted, ventilation was returned to both lungs, using 100% oxygen and inflating lungs entirely (including target segments). One-lung ventilation mode was then resumed after 10 to 15 minutes. The targeted segments were still inflated, but the remaining lung in the ipsilateral chest cavity was collapsed. Demarcations between target segments and remaining lung materialized thereafter, enabling dissection of intersegmental planes using staple or electrocautery. In our department, we use a narrow binding image following intravenous ICG injection after targeted pulmonary artery division. However, in these cases, intravenous ICG injection method was not used. And to provide more information to the readers, we have added more details to the Methods part. (Changes in the text: Page8 Line180~182)

4. The port sites and robotic instruments for both VATS and RATS should be described in Methods. Please cite previous papers if the authors cannot provide this information due to the character limit.

Response: Thank you so much for this important point. We totally agree with this comment. And we have added some citations for more information due to the character limit. (Changes in the text: Page7 Line171~175)

5. Was the intersubsegmental plane divided by staplers? This issue should be described in Operative Techniques.

Response: Yes, the intersubsegmental plane was divided by staplers, and we have further described it in the Operative Techniques part. (Changes in the text: Page8 Line180~182)

6. How did the authors examine LN invasion? Were all dissected nodes examined by the frozen section histopathology? Moreover, how did the authors examine the surgical parenchymal margin? The authors should describe the methods in detail in Methods

Response: Thank you so much for this important point. The surgical parenchymal margin was determined by intraoperative frozen section examination, and the pathological outcomes were confirmed by postoperative pathological paraffin section. We have added these information to the Methods part. (Changes in the text: Page8 Line184~188)

7. These issues should be described in Methods.

Response: Thank you so much for this important point. We totally agree with this comment and we have fully revised our manuscript to address these issues.

8. In the VATS group, did all patients receive an uniportal VATS approach? This is not mentioned in Methods.

Response: Yes, all patients receive an uniportal VATS approach in VATS group. And we have added this information to the Methods part. (Changes in the text: Page7 Line174)

9. The authors state that the number of LNs dissected was higher in RATS. Did the authors perform the same constant, standardized lymph node dissection in both uniportal VATS and RATS? How did the authors determine the extension of ND? Which ND was selected, ND2a-1, ND2a-2 or ND1b? If the authors did not always perform the standardized lymph node dissection, the comparison between VATS and RATS is inaccurate. Without some clear criteria, the surgeon may refrain from

dissecting lymph nodes in areas that are difficult to dissect with uniportal VATS.

Response: Thank you so much for this important point. In our department, the standardized lymph node dissection is performed based on NCCN guidelines. It was imperative to first confirm N0 status. Not only N2 lymph nodes but also No. 12 and 13 lymph nodes were sampled for frozen section examination. If results were positive, we converted to lobectomy and systematic lymph node dissection. According to the NCCN guidelines, one or more nodes should be sampled from all mediastinal stations. For right-sided cancers, an adequate mediastinal lymphadenectomy should include stations 2R, 4R, 7, 8, and 9. For left-sided cancers, stations 4L, 5, 6, 7, 8, and 9 should be sampled. Patients should have N1 and N2 node resection and mapping (American Thoracic Society map) with a minimum of 3 N2 stations sampled or a complete lymph node dissection, which means N1 and N2 node resection and mapping should be a routine component of lung cancer resections, and a minimum of three N2 stations sampled or complete lymph node dissection. we have added this information to the Methods part. (Changes in the text: Page8 Line184~188)

During lymph node harvest, a lung grasper in arm 3 was used to expose the surgical field. A unipolar cautery hook or Cadiere forceps in arm 1 and a bipolar cautery grab in arm 2 were used for sharp or blunt dissection. When all lymph nodes along the pulmonary arteries, veins, and bronchus were removed, this facilitated the dissection of hilar structures, which can be stapled, ligated, or clipped (titanium clip or Hem-o-lok [Teleflex, Morrisville, NC]) according to the specific conditions.

10. I don't think single port VATS CAS is still common, so please include it in your manuscript. In addition, the number of dissected lymph nodes by VATS is less than that by RATS; isn't it because of single port VATS?

Response: Thank you for your question. Single port VATS CAS may not as common as other methods, to our knowledge, there are still some reports about this kind of method. Chang CC, et al [1] have reported that single-port video-assisted thoracoscopic surgery subsegmentectomy is safe and feasible for small-sized lung lesion, providing the benefit of minimal invasiveness, preservation of pulmonary function, and clearance of lymphatic drainage at the intersegmental plane.

In our previous work [2], we have reported early outcomes of robotic versus uniportal video-assisted thoracic surgery for lung cancer. Judging from the short-term outcomes, both RATS and UVATS are safe and feasible for non-small-cell lung cancer treatment. In particular, RATS is better able to reduce bleeding and complete lymphadenectomy than UVATS. According to this research, RATS might improve the dissection of LNs stations. However, whether the number of dissected lymph nodes by VATS less than that by RATS is due to single port VATS still needs further investigation.

[1] Chang CC, Yen Y T, Lin C Y, et al. Single-port video-assisted thoracoscopic surgery subsegmentectomy:

The learning curve and initial outcome[J]. Asian Journal of Surgery, 2019, 43(5).

[2] Yang S, Guo W, Chen X, et al. Early outcomes of robotic versus uniportal video-assisted thoracic surgery for lung cancer: a propensity score-matched study. Eur J Cardiothorac Surg 2018;53:348-52.

11. In line 234, readmission occurred in the RATS group because of multiple small discrete lung nodules distributed throughout both lungs, resulting in a second operation. What were the lesions and how were they resected?

Response: Thank you for your question. This patient had her first surgery on 24th July, 2020. The pulmonary nodule was on the left lung and the patient underwent a S6+S8a RATS CAS. The pathological outcome was adenocarcinoma. On 9th November, 2020, the patient had another video-assisted surgery (S8 segmentectomy), and the lesion was on right lung, which was also adenocarcinoma.

12. In Table 1, there are more cases in the VATS group where only the subsegments are resected. So it seems that subsegmentectomy is associated with more lymph nodes than only subsegmental resection because the more peripheral bronchi were dissected. Do the authors have any opinions?

Response: Thank you so much for the question. It seems that there are more cases in the VATS group where only the subsegments are resected (In our perspective, RATS group where only the subsegments are resected are 9, while VATS group are 16) in Table2. However, after the statistical analysis, there actually is no significant difference between two groups(χ^2 tests, P=0.109). Since it has not come to our attention until you mentioned it, we would very much like to appreciate your question and we hold the view that it need more studies to confirm their correlations.

13. Is the excision method "S6a + S7+8" correct? Will there be a margin for S9a and S10a? It's a somewhat incredible combination.

Response: We are regretfully sorry about this typo mistake. We have changed "S6a+S7+8" into "S6b+S7+8" in our manuscript. (Changes in the text: Page19 Line542)

14. The occurrence (%) of postoperative pneumonia was 10% or more in both groups. Why was the rate higher?

Response: Thank you so much for this important point. Postoperative pneumonia (POP) is one of the most common complications in patients with lung cancer (LC) undergoing therapeutic surgical resection. We have checked some studies and found that the reported incidence of POP following LC surgery was quite different and various, ranging from 2.2 to 31.7%[1,2,3,4,5,6,7]. The diagnosis criteria of POP (WS 382-2012) applied in our study were as follows:

(1) Two chest X-ray exams at least and it should meet at least one of the following criteria, including new or progressive and persistent lung infiltrations, shadows,

consolidation, and cavity formation;

(2) Fever (body temperature $>38^{\circ}\text{C}$) and no other clear cause, peripheral blood $\text{WBC}>12\times 10^9/\text{L}$ or $<4\times 10^9/\text{L}$ and aged ≥ 70 years old without other clear cause, and mental changes. At least one of these conditions is met.

(3) The emergence of new phlegm or the change of the characteristics of sputum, or respiratory secretions increase, sputum suction or need number increase, the emergence of new cough, difficulty breathing or breathing rate faster, or the original cough, difficulty breathing or shortness of breath, the lungs or bronchial breath sounds, gas exchange situation worse, Increased oxygen demand or mechanical ventilation support. At least two of these conditions are met.

According to this criteria, the complication rate of POP in our study was much higher than that following VATS lobectomy in some literatures.

[1] Sandri A, Papagiannopoulos K, Milton R, et al. Major morbidity after video-assisted thoracic surgery lung resections: a comparison between the European Society of Thoracic Surgeons definition and the Thoracic Morbidity and Mortality system[J]. J Thorac Dis, 2015, 7(7): 1174-1180.

[2] Schussler O, Alifano M, Dermine H, et al. Postoperative pneumonia after major lung resection[J]. Am J Respir Crit Care Med, 2006, 173(10): 1161-1169.

[3] Lee JY, Jin SM, Lee CH, et al. Risk factors of postoperative pneumonia after lung cancer surgery[J]. J Korean Med Sci, 2011, 26(8): 979-984.

[4] Kaneda H, Nakano T, Taniguchi Y, et al. Impact of previous gastrectomy on postoperative pneumonia after pulmonary resection in lung cancer patients[J]. Interact Cardiovasc Thorac Surg, 2012, 14(6): 750-753.

[5] Doddoli C, Thomas P, Thirion X, et al. Postoperative complications in relation with induction therapy for lung cancer[J]. Eur J Cardiothorac Surg, 2001, 20(2): 385-390.

[6] Dominguez-Ventura A, Allen MS, Cassivi SD, et al. Lung cancer in octogenarians: factors affecting morbidity and mortality after pulmonary resection[J]. Ann Thorac Surg, 2006, 82(4): 1175-1179.

[7] White M, Martin-Loeches I, Lawless MW, et al. Hospital-acquired pneumonia after lung resection surgery is associated with characteristic cytokine gene expression[J]. Chest, 2011, 139(3): 626-632.

15. There is no video of RATS. General thoracic surgeons are interested in this procedure. Please add the RATS video.

Response: Thank you so much for this suggestion. We totally agree with this comment, and we have shared an actual video of robotic combined anatomic subsegmentectomy followed by this manuscript.

(Minor comments)

1. In line 382, " ia" should be changed to " Ia". Similarly, in line 393, " i" should be changed to " I".

Response: Thank you for pointing this out. A native English speaker has reviewed the manuscript and we have made some modifications on these inappropriate wording and

typing errors.

2. In reference 11, the authors' names should be described according to the instruction of JTD.

Response: Thank you for pointing this out. We have revised the reference part according to the instruction of JTD.

Reviewer G:

1. The title is a little unclear and I would suggest a change to something like Robotic vs VATS subsegmental resection for early stage lung cancer.

Response: Thank you for the advice. We have made some modification on the title to make it more clear. Still, there is a restriction for abbreviation in Title part and our manuscript mainly focuses on combined anatomic subsegmentectomy, this type of surgery. We respectfully believe that the modified title can be readable to our readers. (Changes in the text: Page1 Line3)

2. The relatively young mean age of the patients is an interesting finding. Can the age range be also stated?

Response: Thank you for your question. As we mentioned in the baseline characteristics of all patients, the tumor size in RATS group is 0.83 ± 0.27 cm and 0.8 ± 0.22 in VATS group. The age range of RATS is 21~65, and the age range of VATS is 29~73. The youngest patient in RATS group are 21 years old and the tumor size is $0.8 * 0.8 * 0.7$, and in VATS group, the youngest patient are 29 years old and the tumor size is $0.9 * 0.8 * 0.8$.

3. Tumor size as expected in small- about 8 mm. Can the range of size be stated?

Response: Thank you for your question. As we mentioned in Question 3, the tumor size in RATS group is 0.83 ± 0.27 cm and 0.8 ± 0.22 in VATS group. The range of tumor size in RATS group is 0.4~1.4cm, and the range of tumor size in VATS group is 0.5~1.3cm.

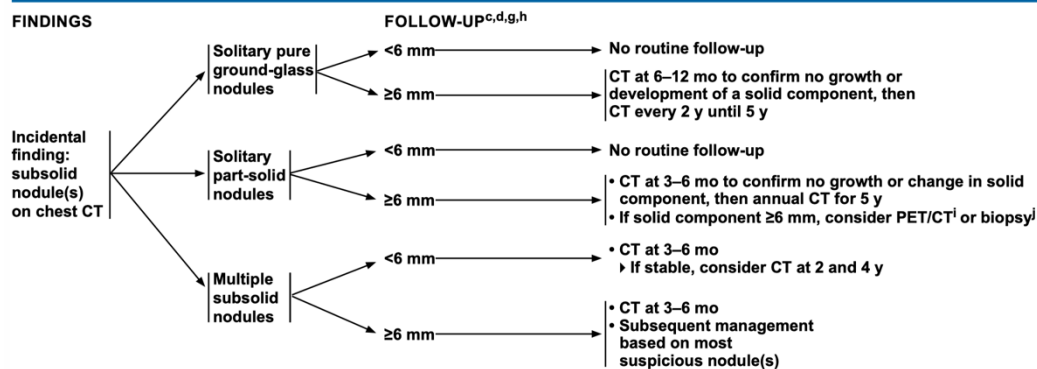
4. What made several of these lesions T1b?

Response: Thank you for the question. We used 8th editions of the TNM for case selection and pathological evaluation. According to this edition, pulmonary nodules which are larger than 1cm but smaller than 2cm can be divided as pT1b.

5. Just because a lesion can be removed, does not mean it should be. Can the authors explain their decision making on when they operate for these 8mm or so lesions?

Response: Thank you for the question. We totally agree with this comment. Criteria

for surgery and follow-up are based on the latest NCCN guidelines for NSCLC. For most of these 8mm or so lesions, they are recommended for a follow-up visit in outpatient department. There are two criteria of surgery for clinical use, one is disease progression in pulmonary nodules during follow-up period, including a sharp increase in tumor size, an increase in aspect of solid lesions, border roughness, vascularization, and pleural traction. The other one is that the patient is too anxious about the tumor lesion and has a strong desire for an operation.



(NCCN Guidelines Version 1.2022 for NSCLC)

6. Please include a comparable robotic video.

Response: Thank you so much for this suggestion. We totally agree with this comment, and we have shared an actual video of robotic combined anatomic subsegmentectomy followed by this manuscript.

7. Please include a diagram (in addition to nomenclature) for the resections. This will be helpful and educational.

Response: Thank you so much for this suggestion. We totally agree with that a diagram for the resections will be helpful and educational. Actually, in our previous study, we had provided a full introduction about how these resections were performed [1]. In this case, we focused more on the clinical early outcomes between these two methods (RATS and VATS). For more information for the readers, we have added some details and citations in the Methods part. (Changes in the text: Page 7 Line 171~177)

[1] Li C, Han Y, Han D, et al. Robotic approach to combined anatomic pulmonary subsegmentectomy: Technical aspects and early results. *Ann Thorac Surg* 2019;107(5):1480-1486.

8. Paper needs formal statistical review.

Response: Thank you for the suggestion. We have our manuscript formal statistical reviewed.

9. More details on direct, indirect and total cost needs to be provided if this is to be included.

Response: Thank you for the suggestion. The indirect costs referred to the sum of all additional costs for the hospital that was comprised of overhead cost and amortization of surgical equipment, including of the purchase and maintenance of minimally invasive platforms. The indirect cost associated with the amortization of surgical equipment was unified within each approach, which was around \$300 for video-assisted surgery and \$4300 for robotic surgery. The standard charges for the amortization of the surgical equipment were decided by the Shanghai Municipal Government. We, as a public hospital, strictly followed the unified charging standard instead of independent pricing. We have provided a more detailed explanation of the indirect costs in the manuscript. (Changes in the text: Page6~7 Line164~169)

10. I am surprised a model S robot is being used- can the authors confirm this. I did not think these are made/serviced anymore.

Response: As we mentioned in the methods part, the da Vinci S/Si system (Model S/Si) was used in this study. We preferred using 4 arms and an auxiliary port for CAS. The 12-mm camera port was on the eighth intercostal space of the midaxillary line. The 15-mm auxiliary port, 8-mm arm 2 port, and 8-mm arm 3 port were all on the eighth intercostal space (anterior axillary line, posterior axillary line, and 2 cm from the spine, respectively). The 8-mm arm port 1 was on the fifth intercostal space of the anterior axillary line.

The current and more advanced da Vinci Xi system gained new features including rotating boom-mounted arms with better dexterity and patient clearance, improved stapling capabilities, integration with fluorescence imaging, improved camera optics, and a redesigned smaller endoscope which can be inserted through any 8 mm robotic port. Compared with the older da Vinci S/Si system used in this trial, these new features of the Xi system could potentially improve maneuverability and dexterity, shorten docking and operating time, and reduce surgical trauma. The more sophisticated robotic system may also reduce the risk of conversion to an open thoracotomy and improve surgical capabilities especially for challenging cases. However, there are also different opinions. Some surgeons may think the main difference between the most recent system and the older ones is the ability of the console surgeon to perform stapling of the vascular structures. Despite this, many surgeons including one of the authors (A.E.A.) continue to prefer bedside stapling.

11. the question becomes the value of this type of complex surgery. Is there ANY benefit the authors can show in terms of lung function to a segmentectomy. Are we doing more harm than good?

Response: Thank you for the question. We are so sorry that we have no evidence to

confirm that there is any benefit in terms of lung function to a segmentectomy, because it's not common to have postoperative pulmonary function tests in our department. According to a study published in Journal of Cardiothoracic Surgery [1], while there was no significant difference of the postoperative FEV1 of each lobe between the CAS and single segmentectomy, the value of the CAS was higher than that of the multiple segmentectomy with marginal significance ($p = 0.07$). Their data indicated that the CAS is useful for preservation of pulmonary function of each lobe by avoiding the multiple segmentectomy especially in patients with small sized tumors with likely pathological N0 involving multiple segments of the right upper lobe.

[1] Yoshimoto et al. Combined subsegmentectomy: postoperative pulmonary function compared to multiple segmental resection. Journal of Cardiothoracic Surgery 2011 6:17.

12. Need line by line review and revision by a native English speaker.

Response: Thank you for pointing this out. A native English speaker has reviewed the manuscript and we have made some modifications on these inappropriate wording and typing errors.

Reviewer H: The authors retrospectively evaluated oncological safety, the early results in short term, and cost-benefit of combined anatomic subsegmentectomy using RATS and VATS methods in early NSCLC. They found that higher cost was observed in RATS group compared to VATS group. RATS might contribute to the potential improvement of N1 and N2 lymph node retrieval.

Despite the complexity of the technique, the authors were able to perform good operations, which was excellent. I have the following concerns.

1. I think the introduction is too long for the readers. The author needs to make the introduction more concise.

Response: Thank you so much for this suggestion. We have fully revised our manuscript and made some modifications on the introduction part to make it more concise and readable. (Changes in the text: Page4~5 Line70~104)

2. The authors evaluated the number of dissected lymph node. Similarly for N2, what is the difference by definition between N1 lymph nodes and N1 stations?

Response: Thank you for the question. N1 stations means N1 nodes, which lie distal to the mediastinal pleural reflection and within the visceral pleura. N2 stations means N2 nodes, which lie within the mediastinal pleural envelope. The number of N1 lymph nodes means the total quantity of dissected N1 lymph nodes, and the number of N2 lymph nodes means the total quantity of dissected N2 lymph nodes.

3. There is a large difference in medical costs between the two groups. Unfortunately, this result is not even reflected in the conclusion. A minor change should be made by including this result in the conclusion.

Response: Thank you so much for this suggestion. We totally agree that there is a large difference in medical costs between the two groups and it should be reflected in the conclusion. As we mentioned in the conclusion part(last 3th paragraph), we made some comments about the economic viability of these two methods. Still, to make these comments more concise and readable, we have made some modifications on this part. (Changes in the text: Page12~13 Line321~334)

4. Is VATS single port or multi-port? Does the VATS approach include single-port or multi-port, although the same surgeon performed the procedure in this paper?

Response: Yes, all of VATS are single-port. Although single port VATS CAS may be not as common as other methods, to our knowledge, there are still some reports about this kind of method. For example, Chang CC, et al [1] have reported that single-port video-assisted thoracoscopic surgery subsegmentectomy is safe and feasible for small-sized lung lesion, providing the benefit of minimal invasiveness, preservation of pulmonary function, and clearance of lymphatic drainage at the intersegmental plane.

[1] Chang CC, Yen Y T, Lin C Y, et al. Single-port video-assisted thoracoscopic surgery subsegmentectomy: The learning curve and initial outcome[J]. Asian Journal of Surgery, 2019, 43(5).

5. The most important aspect of segmentectomy is the surgical margin. In particular, RATS has the disadvantage that it is difficult to confirm the localization of the tumor intraoperatively because the surgeon does not have the sense of touch. Is there anything you have done to secure the surgical margin? For example, marking with a hook wire, assembling a surgical strategy with 3D-CT.

Response: Thank you for pointing this out. We hold the same view that one of the most important aspect of segmentectomy is the surgical margin. In our department, it is common to have the patients to be marked with a hook wire(In this study, RATS group:43.33%, VATS group:32.35% P=0.47), and 3D-CT is a routine test for patients who are going to undergo the operation.

6. How did you identify the segmental lines during surgery? Did you use injection of ICG? Did you create an air-containing collapse line, which is difficult to create under the artificial pneumothorax used in RATS?

Response: Thank you so much for this important point. To identify intersegmental planes, we used the inflate-deflate technique. Once all hilar structures were interrupted, ventilation was returned to both lungs, using 100% oxygen and inflating lungs entirely (including target segments). One-lung ventilation mode was then resumed after 10 to

15 minutes. The targeted segments were still inflated, but the remaining lung in the ipsilateral chest cavity was collapsed. Demarcations between target segments and remaining lung materialized thereafter, enabling dissection of intersegmental planes using staple or electrocautery. In our department, we use a narrow binding image following intravenous ICG injection after targeted pulmonary artery division. However, in these cases, intravenous ICG injection method was not used. And to provide more information to the readers, we have added more details to the Methods part. (Changes in the text: Page8 Line180~183)

7. I think early pneumonia after pneumonectomy by minimally invasive approach is generally much less common. Is there a reason for the high frequency of postoperative pneumonia?

Response: Thank you so much for this important point. Postoperative pneumonia (POP) is one of the most common complications in patients with lung cancer (LC) undergoing therapeutic surgical resection. We have checked some studies and found that the reported incidence of POP following LC surgery was quite different and various, ranging from 2.2 to 31.7%[1,2,3,4,5,6,7]. The diagnosis criteria of POP (WS 382-2012) applied in our study were as follows:

(1) Two chest X-ray exams at least and it should meet at least one of the following criteria, including new or progressive and persistent lung infiltrations, shadows, consolidation, and cavity formation;

(2) Fever (body temperature $>38^{\circ}\text{C}$) and no other clear cause, peripheral blood $\text{WBC}>12\times 10^9/\text{L}$ or $<4\times 10^9/\text{L}$ and aged ≥ 70 years old without other clear cause, and mental changes. At least one of these conditions is met.

(3) The emergence of new phlegm or the change of the characteristics of sputum, or respiratory secretions increase, sputum suction or need number increase, the emergence of new cough, difficulty breathing or breathing rate faster, or the original cough, difficulty breathing or shortness of breath, the lungs or bronchial breath sounds, gas exchange situation worse, Increased oxygen demand or mechanical ventilation support. At least two of these conditions are met.

According to this criteria, the complication rate of POP in our study was much higher than that following VATS lobectomy in some literatures.

[1] Sandri A, Papagiannopoulos K, Milton R, et al. Major morbidity after video-assisted thoracic surgery lung resections: a comparison between the European Society of Thoracic Surgeons definition and the Thoracic Morbidity and Mortality system[J]. J Thorac Dis, 2015, 7(7): 1174-1180.

[2] Schussler O, Alifano M, Dermine H, et al. Postoperative pneumonia after major lung resection[J]. Am J Respir Crit Care Med, 2006, 173(10): 1161-1169.

[3] Lee JY, Jin SM, Lee CH, et al. Risk factors of postoperative pneumonia after lung cancer surgery[J]. J Korean Med Sci, 2011, 26(8): 979-984.

[4] Kaneda H, Nakano T, Taniguchi Y, et al. Impact of previous gastrectomy on postoperative pneumonia after pulmonary resection in lung cancer patients[J]. Interact Cardiovasc Thorac Surg, 2012, 14(6): 750-753.

[5] Doddoli C, Thomas P, Thirion X, et al. Postoperative complications in relation with induction therapy for lung cancer[J]. Eur J Cardiothorac Surg, 2001, 20(2): 385-390.

[6] Dominguez-Ventura A, Allen MS, Cassivi SD, et al. Lung cancer in octogenarians: factors affecting morbidity and mortality after pulmonary resection[J]. Ann Thorac Surg, 2006, 82(4): 1175-1179.

[7] White M, Martin-Loeches I, Lawless MW, et al. Hospital-acquired pneumonia after lung resection surgery is associated with characteristic cytokine gene expression[J]. Chest, 2011, 139(3): 626-632.

8. Did you use robotic staplers for all staples in RATS? Did the assistant only change the robotic forceps and not manually control the non-robotic staplers from the outside?

Response: Thank you for the question. No, we do not use robotic staplers in RATS. The assistant not only need to change the robotic forceps but also need to manually control the non-robotic staplers from the outside.

9. Is S1a+S2a an error for S1a+S2b in Figure 2?

Response: No, it is S1a+S2a of right lung.

10. The format of the references are messy. Please modify them to fit the regulations.

Response: Thank you for pointing this out. We have fully revised and modified them to fit the regulations.

11. There are many inadequacies in the citation of abbreviations and formal names. The authors need to review the entire text with rigorous notes.

Response: Thank you for pointing this out. We have fully revised and modified them to fit the regulations.

12. This is the first time computed tomography is used in a sentence. Please add the abbreviation (CT) in parentheses after this word. CT is used later in the text. Computed tomography in Page6 Line112 is used for the second time, so only the abbreviation is needed.

Response: Thank you for pointing this out. We have add the abbreviation (CT) in parentheses after this word to make it concise and readable.

13. Since VATS in Page5 Line101 is a first-time citation, please add its official name. Please add the abbreviation (RATS) after robotic-assisted thoracic surgery in Page5 Line107.

In Page5 Line108, video-assisted thoracic surgery should be changed to VATS.

Please add the official name for 3D in Page5 Line108.

The robotic-assisted thoracic surgery and video-assisted thoracic surgery in Page6 Line128-129 should be abbreviations only.

The combined anatomic subsegmentectomy in Page 6 Line 135-136 should be abbreviations only.

Page 3, line 56 and Page10 Line 242

Larger is a typo. Please change it.

Response: Thank you for pointing this out. We have fully revised and modified them to fit the regulations.

Reviewer I: The authors retrospectively investigate perioperative outcomes in patients who underwent lung subsegmentectomy through VATS or RATS. In comparison between RATS and VATS, the authors found that RATS was associated with similar perioperative outcomes compared to VATS except for lymph node assessment, in which RATS had better lymph node retrieval than VATS. Following issues should be addressed before publication.

1. Since this is not a randomized control trial, it would be important to clarify any potential factors causing patient selection bias. The authors should describe patient selection criteria for VATS or RATS.

Response: Thank you so much for this important point. We totally agree it is important to clarify any potential factors causing patient selection bias. And for more information, we have added the patient selection criteria for VATS or RATS in the Methods part. (Changes in the text: Page6 Line138~143)

2. In the Methods section, descriptions for operative techniques are not adequate. The authors should at least add explanations for the following surgical aspects in both VATS and RATS: 1) surgical incisions; 2) details for surgical instruments; 3) how to identify intersegmental and inter-subsegmental planes; 4) how to “accurately separate” the intersegmental and inter-subsegmental planes; 5) lymph node dissection or sampling.

Response: Thank you so much for this suggestion. We totally agree with that descriptions for operative techniques will be helpful and educational for the readers. Actually, in our previous study, we had provided a full introduction about how these resections were performed [1]. In this case, we focused more on the clinical early outcomes between these two methods (RATS and VATS). For more information for the readers, we have added some details and citations in the Methods part. (Changes in the text: Page7~8 Line171~189)

[1] Li C, Han Y, Han D, et al. Robotic approach to combined anatomic pulmonary subsegmentectomy: Technical aspects and early results. *Ann Thorac Surg* 2019;107(5):1480-1486.

3. I understand that a surgical video for RATS combined subsegmentectomy is available in the previous publication (Li H et al. Ann Thorac Surg 2019). However,

it would be better to include videos for both RATS and VATS in this paper.

Response: Thank you so much for the advice. We totally agree with this comment, and we have shared an actual video of robotic combined anatomic subsegmentectomy followed by this manuscript.

4. Please describe whether the authors perform preoperative simulation and/or intraoperative navigation. If so, please describe the details of them.

Response: Thank you so much for the question. It's very common to make these 3D-CT figures in our department, because it does help the surgical procedures. For example, 3D-CT figures can bring a better view and understanding of the location of pulmonary nodule. Some patients sometimes will need hook-wire localization before surgery. However, we do not perform the intraoperative navigation. Our attached videos have shown the details of these techniques, I am sure the readers can find a lot benefits from them.

5. Please add explanations for "internal staplers."

Response: Thank you so much for the question. "internal staplers" actually means regular staplers which are the routine used in robot-assisted surgery. To make it more concise and readable, we have deleted the word "internal".

6. Unless there is a specific need to use the term of surgeon, it would be better to use surgeon instead of chirurgion.

Response: Thank you for pointing this out. A native English speaker has reviewed the manuscript and we have made some modifications on these inappropriate wording and typing errors.

7. The authors may want to rewrite the following sentence (lines 184-187, page 8) because it would be hard to understand its meaning. "Compared with segmental resection, subsegmental resection requires a more delicate operation, often dissecting the target bronchi and blood vessels from one segment to another, while combined subsegmental resection requires dissecting the bronchi and blood vessels from 2 to 3 target subsegments."

Response: Thank you for pointing this out. A native English speaker has reviewed the manuscript and we have made some modifications on these inappropriate wording and typing errors.

8. In the following sentence (lines 187-190, page 8), please clarify the true meaning of parenchymal and bronchial margins. Frozen analysis for close margin? "All operations of enrolled patients were mainly carried out by one single practiced

chirurgeon. If there were enlarged resected nodes (e.g., >1 cm) or parenchymal and bronchial margins, a frozen section analysis would be performed.”

Response: Thank you for pointing this out. We have fully revised and modified them to be more concise and readable. (Changes in the text: Page7~8 Line171~189)

Reviewer J: Thank you for submitting this paper to the Journal of Thoracic Disease, I was pleased to receive it as a reviewer and read it with great interest.

The authors demonstrated that RATS and VATS anatomic sub-segmentectomy is safe and feasible for 62 patients with early-stage NSCLC. In addition, RATS might contribute to the potential improvement of N1 and N2 lymph node retrieval. This paper is well written and beneficial for our readers, however, I have several concerns about this article.

1. As you have already mentioned, this is a small number of retrospective study. I think there is a lot of bias in this study and seems difficult to mention the oncological results because of the short follow-up period. In addition, I don't think the prognostic value of lymph node dissection for NSCLC has been proven even if RATS might contribute to the potential improvement of N1 and N2 lymph node retrieval.

We have easily expected that the RATS sub-segmentectomy was safe and feasible for the patients with early-stage NSCLC compared to VATS from your previous report (J Thorac Cardiovasc Surg. 2020 Nov;160(5):1363-1372.).

Response: Thank you so much for the question. We totally agree that it seems difficult to compare the long-term oncological results because of the short follow-up period. In our manuscript, we aimed to analyze the perioperative outcomes and early results of these two methods. We hold the same opinion that long-term follow-up should be carried out to get more concise and scientific oncological results of these two methods, and we are now doing these parts.

As we mentioned in the discussion part, the patient's potential survival benefit from the additional number of LNs and stations dissected from the RATS group may have been negligible. Dezube et al. [1] recently reported a correlation between the number of LNs harvested and long-term survival according to the National Cancer Database, and they found that the optimal number of LNs dissected is 4 for lobectomy, with no survival benefit when additional LN sampling was performed. Further studies, preferably randomized controlled trials, are required to clarify the clinical relevance between the improved LNs harvest and long-term survival in the RATS group.

In our previous work [2], we have proved that segmentectomy with robotic and VATS are safe and feasible for early-stage NSCLC treatment, and a robotic approach might lead to a better N1 lymph node dissection. However, to the best of our knowledge, no evidence has confirmed whether or not the RATS CAS could offer the same perioperative and oncological results as VATS CAS. Due to this, we respectfully believe that this manuscript are

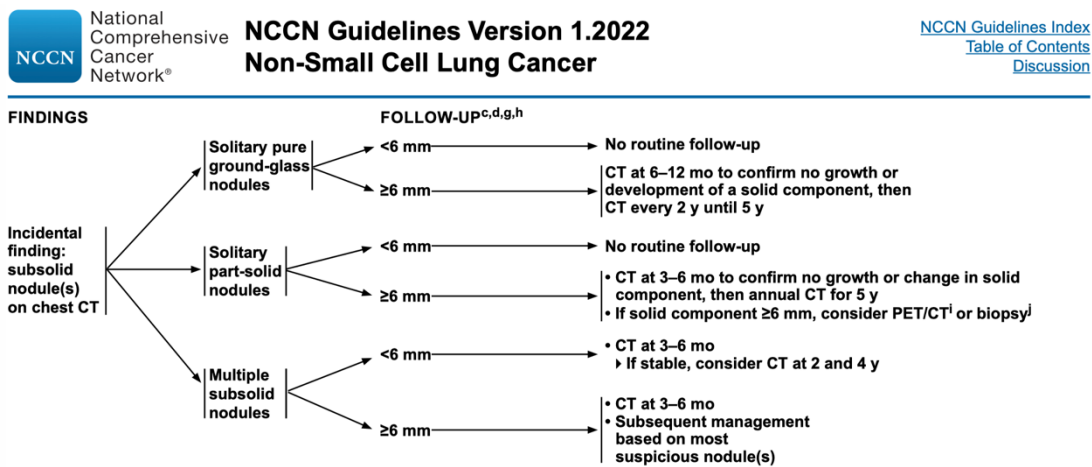
meaningful and beneficial for the readers.

[1] Zhang Y, Chen C, Hu J, et al. Early outcomes of robotic versus thoracoscopic segmentectomy for early-stage lung cancer: A multi-institutional propensity score-matched analysis. *J Thorac Cardiovasc Surg* 2020;160(5):1363-1372.

[2] Dezube AR, Mazzola E, Bravo-Iñiguez CE, et al. Analysis of lymph node sampling minimums in early stage non-small-cell lung cancer. *Semin Thorac Cardiovasc Surg* 2021;33(3):834-845.

2. If small lung cancer is detected by CT, how often do you follow up? If there is a highly suspected lung cancer on HR-CT, do you perform surgery immediately or is there a criterion for surgery? Please describe your treatment strategy for a small nodule.

Response: Thank you so much for the question. Criteria for surgery and follow-up are based on the latest NCCN guidelines for NSCLC. For most of patients with small lung cancer, they are recommended for a follow-up visit in outpatient department. There are two criteria of surgery for clinical use, one is disease progression in pulmonary nodules during follow-up period, including a sharp increase in tumor size, an increase in aspect of solid lesions, border roughness, vascularization, and pleural traction. The other one is that the patient is too anxious about the tumor lesion and has a strong desire for an operation.



(NCCN Guidelines Version 1.2022 for NSCLC)

3. Recently, PET/CT is essential for the qualitative diagnosis of small lung cancer. Do you perform PET/CT in such cases at your institution, and if so, please present the SUV-MAX.

Response: Thank you for the question. No, We have not applied PET/CT in such cases in our department.

4. Please describe the surgical margin of the tumor in VATS and RATS, which is a very important factor to evaluate the quality of limited pulmonary resections.

Response: Thank you so much for this important point. We have further analyzed the resection margin of each group and added them into the Table4. (Changes in the text: Page9 Line240; Page21 Line596)

5. Please describe the strategy for the evaluation of lymph nodes (number and station) during surgery. Among 69 patients, 7 cases were converted segmentectomy of lobectomy. Most surgeons would do perform lobectomy in case of positive lymph nodes. How many cases were converted to lobectomy due to the positive lymph nodes, not margin?. I would like to know the details of such cases.

Response: Thank you so much for this important point. 7 conversion cases belong to intraoperative exclusion, which means intraoperative change of surgical plan. In our department, it's common for these patients to take a 3D-CT before surgery, and even more, some patients may have a hook-wire localization. According to preoperative reconstruction of 3D-image and hook-wire localization, subsegmentectomy plus wedge resection sometimes can ensure the safe margin for the patient. Under this circumstance, the CAS procedure will be waived if the patient's consent is obtained. Also, we have added these information in the manuscript. (Changes in the text: Page6 Line142~143)

6. Please identify these 62 patients were durable for standard lobectomy. I understand these procedures in this study were performed as an “intentional” limited resection.

Response: Thank you so much for the question. According to the preoperative evaluation tests, these 62 patients were durable for standard lobectomy. In our department, the patients will be offered some types of surgery to choose based on the preoperative evaluation tests and surgeon's experience. And usually, patients suffered from early-stage lung cancer will be recommended to take a segmentectomy rather than a lobectomy, because there are several clinical trials [1] have proved that segmentectomy can provide similar oncological outcomes and more residual pulmonary parenchyma, which should bring benefits to the patients.

[1] Saji, Hisashi and Okada, Morihito and Tsuboi, et al. Segmentectomy Versus Lobectomy in Small-Sized Peripheral Non-Small Cell Lung Cancer (JCOG0802/WJOG4607L): A Multicentre, Randomised, Controlled, Phase 3 Trial. Available at: <http://dx.doi.org/10.2139/ssrn.3918871>.

7. In patient characteristics, patients' age was much younger (around 50 years old) than I have expected. Is the average age of other lung cancer patients similarly young?

Response: Thank you for the question. No, the average age of other lung cancer patients are not similarly young. As we mentioned in Question 6, in our department, the patients are offered some types of surgery to choose based on the preoperative evaluation tests and surgeon's experience.

8. p.5 line 105-107

With the increasing use of robotic surgery for sub-lobectomy, robotic systems are more likely to promote segmental or sub-segmental pneumonectomy,

→The term “segmental pneumonectomy” seems to be unfamiliar to authors. Is this term correct? (others: p5 line 115)

Response: Thank you for pointing this out. A native English speaker has reviewed the manuscript and we have made some modifications on these inappropriate wording and typing errors.

9. Please let me know if there are any attempts to reduce the indirect cost of RATS.

Response: Thank you for the question. The indirect costs referred to the sum of all additional costs for the hospital that was comprised of overhead cost and amortization of surgical equipment, including of the purchase and maintenance of minimally invasive platforms. To the best of our knowledge, the China-made robot-assisted systems have made rapid progress and advances in recent years. And in our hospital, there are some clinical trials about the application of these China-made robot-assisted systems. It may be a way to reduce the indirect cost of RATS with the promotion of these types of systems, as long as they can bring comparable oncological results compared to da Vinci systems.