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Comments

Review A

I applauded the team's successful results for the patient with high operative risk using a non-intubated VATS approach.

The manuscript was well written, and indicated the advantage of a non-intubated VATS approach for fragile patients. I have some comments to make the manuscript more sophisticated.

1. Please clarify the indication of a non-intubated VATS approach in the author's institution with several references.

2. A non-intubated VATS approach has not been widespread yet worldwide because this approach has the difficulty to perform. Please describe the difficulty and disadvantages in this approach.

The authors wish to thank the Reviewer for his/her kind comment.

Reply 1: Thank you for your suggestion. We clarified the indication of non-intubated VATS approaches in 168-171 lines.

Reply 2: Thank you for your observation. We reported the major limitation of the widespread use of this procedure in 172-175 lines.

Review B

Non-intubated VATS is a safe and feasible alternative for diagnostic and also therapeutic procedures (thymectomies, lobectomies, ...).

It's important to give more explanation about surgical technique (uni/multiportal accesses) and anesthetic technique (local/regional blocks, opioids and other drugs used...).

As the atuhors comment the patient was obese and that complicates the non-intubated technique, it's important to comment about the length of surgery the supply of oxygen and the saturation of the patient.

The authors wish to thank the Reviewer for his/her kind comment.

Reply: Thank you for your comment. We have enhanced the requested information. In particular, the anesthetic technique is described in 114-120 lines, the surgical technique is reported in 121-129 lines, and it was a bi-portal access.

Review C

This reviewer is a strong advocate of not intubated video-assisted thoracic surgery. The technique has proven to be safe and effective, eliminating the need for deep anesthesia with paralysis, drying of the airways, potential intubation trauma, and slow recovery of postoperative strength. It therefore appears to be a particularly good technique for older adults. However, a relative paucity of thoracic surgeons worldwide routinely employee non-intubated VATS. Some of this appears to be due to inertia, as excellent experienced surgeons seem hesitant to even try such procedures. The present case report is thus valuable in bringing the technique back into the front of thoracic surgeons' thoughts.

A few comments:

1. Some geriatricians might replace the word "fragile" with the word "frail." Both are understandable.

2. Abbreviations should be spelled out for clarity the first time that they are used. The authors have generally done this although they have not with PONV.

3. A brief description of the intraoperative sedation and analgesia employed would be useful to the reader.

4. Reference 19 is incomplete.

5. The translation of the manuscript into English is imperfect, slightly awkward in areas, but is always understandable.

The authors wish to thank the Reviewer for his/her kind comment.

Reply 1: Thank you for your observation. We have replaced the word fragile with the word frail.

Reply 2: Thank you for your suggestion. The abbreviations PONV has been replaced with its equivalent (i.e., "postoperative nausea and vomiting").

Reply 3: Thank you for your comment. We inserted a brief description of the intraoperative sedation and analgesia employed in 114-120 lines.

Reply 4: Thank you for your remark. For Reference 19, we have added the journal, volume, and page information; Reply 5: Thank you for your evaluation. We revise the manuscript, hope to have improved the translation.

Review D

It is my great honor to read this interesting report. I have some comment to improve this manuscript.

The authors wish to thank the Reviewer for his/her kind comment.

#1. The abstract should be structured with background, case description and conclusions, as in Guidelines for Authors. Methods and results are not suitable for case reports.

Reply 1: Thank you for your indication. We revised and modified the manuscript accordingly.

#2. The good reason that justifies publication of the current case report is unclear in the Introduction part. I guess this case would teach us something new, unknown or rare, which previous literatures have not described well. Please write it after the review of previous literatures (lines 61-69 on page 3). Manifesting it in the Introduction part will focus on the feature of the case and make this case report more attractive, logical and friendly to readers.

Reply 2: Thank you for your suggestion. Historically, surgical lung biopsy in suspected ILD was afflicted by a not minimal risk of postoperative morbidity and mortality for a diagnostic procedure. Similarly, numerous contraindications were individuated for surgical lung biopsies, such as Obesity, low DLCO and FEV1, Age, Cardiological comorbidity, previous neoplasm, and respiratory restrictive pattern. As we try to clarify in our report, the peculiarity of the case we reported is the concomitant presence of two possible pulmonary pathologies in a patient with multiple features that, historically, could contraindicate this specific kind of surgery (age, obesity, cardiological comorbidities, restrictive pulmonary pathology, previous cancer). We believe that the report, as the special issue in the object, could demonstrate that with the non-intubated approach, we could overcome these contraindications even concomitant on the same patient.

We have specified the peculiarity of the case report in 90-93 lines.

#3. The Discussion part lacks discussion on the current case. Your description is limited in review of previous literatures. The novelty or rareness, which I mentioned above, should be discussed and reinforced with quoting literatures.

Reply 3: Thank you for your comment. We improved the discussion section accordingly in 182-184 lines.

#4. When you use abbreviations, you must obey the rule in Guidelines for Authors. "All abbreviations should be defined when they are first used in the text unless the abbreviation is a standard unit of measurement and a list of full terms should be provided in the manuscript" (quoted from Guidelines for Authors). For example, "BMI", "CT", "PET", "FDG", "SUV", "FVC", "FEV1", "DLCO", "VATS", "MI", "IPF", "PONV", "NSCLC" and "XR" appear before (or without) spelling out full form. In addition, "pulmonary interstitial disease" (in line 71 on page 3) cannot be abbreviated as ILD.

Reply 4: Thank you for your observation. All abbreviations have been replaced with the full term.

#5. In lines 76 and 78 on page 4, you specified the years when the patient suffered from MI (1993 and 2019) and bladder cancer (2021). I think that the exact periods of these diseases did not influence the clinical course of lung disease in this case. If so, these periods should be deleted, because describing these unnecessary data might lead to identification of the patient. If the periods are needed to be described, it is better to use expressions, such as "3 years before ~" or "when he was ~ years old".

Reply 5: We agree with your observation. As the reviewer points out, it could be useful to know the date of the primary tumor that metastasized to pulmonary parenchyma. We have changed this information as recommended using the expression "one year ago" (line 97).

#6. It should be clearly described whether sarcoma in the left lung was diagnosed as primary lung tumor or metastatic lesion from extrapulmonary origin (scalp or somewhere).

Reply 6: Thank you for your indication. The sarcoma in the left lung is a metastatic lesion from extrapulmonary origin. We have added this information in lines 142-143

#7. Although you wrote "bladder cancer", some readers might consider the possibility that bladder tumor metastasized to the lung. Description on histology of the bladder tumor will avoid potential misunderstanding. Reply 7: Thank you for your remark We agree to specify the histology: the bladder tumor was the epithelial type; we have added this information in line 98. The histology of lung cancer is sarcoma, compatible with pulmonary localization of pleomorphic sarcoma.

#8. Anesthetic detail of the surgery is not mentioned in the Case Description. Awake VATS is performed under various anesthetic strategies. Anesthetic approach is as important as surgical maneuver in awake VATS. It is preferable to describe anesthesia and analgesia, even if the description is brief. In addition, if you mention oxygen saturation during surgery, it is better to describe the way of oxygen administration (room air, nasal cannula, face mask, and so on).

Reply 8: Thank you for your observation. We inserted a brief description of the intraoperative sedation and analgesia employed in lines 114-120.

#9. Please describe the spirometric data on which diagnosis of restrictive pattern was made. In addition, although DLCO is mildly impaired, values of FVC and FEV1 written in the Abstract seem good enough to undergo surgery under general anesthesia. Based on this issue, please explain why you did not choose general anesthesia.

Reply 9: Thank you for your request. According to our previous published experience (18), we decided, after multidisciplinary discussion and to comply with patient's willings, to performe an awake video-assisted thoracic surgery.

#10. If you want to include the spirometric data (FVC and FEV1) in the Abstract, you should also write them in the Case Description. In my opinion, these data may not be necessary in the Abstract.Reply 10: Thank you for your observation. We inserted the spirometric data also in the case description.

#11. Description on management of "high creatinine levels" (lines 102-104 on page 5) is redundant but obscure. It is unclear whether renal dysfunction was preoperatively diagnosed or whether acute kidney injury occurred postoperatively. If "high creatinine levels" did not affect surgical procedure or postoperative treatment, it may not be described. If renal dysfunction seriously affected clinical course, please describe it briefly. The diagnosis which experts of nephrology and urology made would be helpful to understand the situation.

Reply 11: Thank your suggestion. The high creatinine levels was an occasional finding that not affect surgical procedure or postoperative treatment, but they extended the hospital stay to perform specialist evaluations. Since they did not influence the patient's outcome and are not related to surgery, we have removed it.

#12. You wrote histological findings of lung parenchyma other than neoplasm in detail in lines 108-110 on page 5.

Assumed readers of this journal are surgeons, who are not familiar with histological findings of ILD. If you want to describe it in detail as in the current manuscript, you should add a microscopic picture in the manuscript. In addition, please write the diagnosis. Was it IPF?

Reply 12: Thank you for your observation. We added the diagnosis in lines 141-146. Unfortunately, we don't have a microscopic picture of this case.

#13. There seems to be several types and sizes of Alexis wound protector/retractor. Please specify which type you used.

Reply 13: Thank you for your recommendation. We specified which type we used in line 121.

#14. It is unclear what information you want readers to obtain from figures. It is better to make figures and figure legends more descriptive. In Figures 1 and 3, each image should have legend.Reply14: Thank you for your advice. We have added some short legends to the images.

#15. Is there any reason that figures in Figure 1 have different tones ("lung tone" and "mediastinal tone")? It would be better to use images in "lung tone" to indicate pulmonary lesion.Reply 15: Thank you for your indication. We have changed the images in "lung tone" accordingly.

#16. Is reference no.131 in line 124 on page 6 mistaken for no. 11 or 13? Reply 16: Thank you for your remark. The mistake has been corrected.

#17. The location of the incision ("between on the middle line" in line 88 on page 4) is unclear. Was the incision made in middle axillary line or midclavicular line? Please also describe which intercostal space the incision was located at.

Reply 17: Than you for your request. We have added this information in 121-122 lines.

Review E

First of all I would like to commend the authors on a very well written manuscript. Unfortunately the authors do not add new aspect to what we already know about non-intubated minor lung surgery. Larger series have dealt with potential advantages of non-intubated diagnostic procedures in ILD patients and compared the outcome with those undergoing conventional VATS (Grott M, Wimmer CD, Kreuter M, Prasse A, Eichhorn ME, Eichhorn F, Herth FJF, Seeliger B, Kriegsmann K, Schmidt W, Koenigsfeld K, Zardo P, Winter H. Surgical Lung Biopsy for Interstitial Lung Disease: A Two Center Propensity Score Matching Analysis. Respiration. 2022;101(10):910-917. doi: 10.1159/000525903. Epub 2022 Aug 25. PMID: 36007492.) and the authors' group analyzed the effects of obesity on the outcome of minor non-intubated lung surgery.

The authors wish to thank the Reviewer for his/her kind comment.

Reply: Thank you for your observation. Historically, surgical lung biopsy in suspected ILD was afflicted by a not minimal risk of postoperative morbidity and mortality for a diagnostic procedure. Similarly, numerous contraindications were individuated for surgical lung biopsies, such as Obesity, low DLCO and FEV1, Age, Cardiological comorbidity, previous neoplasm, and respiratory restrictive pattern. As we try to clarify in our report, the peculiarity of the case we reported is the concomitant presence of two possible pulmonary pathologies in a patient with multiple features that, historically, could contraindicate this specific kind of surgery (age, obesity, cardiological comorbidities, restrictive pulmonary pathology, previous cancer). We believe that the report, as the special issue in the object, could demonstrate that with the non-intubated approach, we could overcome these contraindications even concomitant on the same patient.

We have specified the peculiarity of the case report in 90-93 lines.

Editorial Comments

1. Please confirm if the Figures are original and have not been published before; Reply 1: The Figures are original and have not been published before.

 Please make a revision to the main text especially the Discussion section as the similarity rate is a little bit over the requirement (20% while the current one is 25%). Attached please see the similarity report;
Reply 2: Thanks for pointing that out. We revised the Discussion section.

3. Please make some adjustment to the Abstract according to the journal instruction and Structured as: Background (state what is known and unknown; why the case report is unique and what it adds to existing literature)

Case Description (describe the patient's demographic details and main history, the main diagnosis, interventions, outcomes and follow-ups)

Conclusions (summarize the main take-away lesson, clinical impact and potential implications). Reply 3: We revised the manuscript accordingly.

4.Consider a more informative title, using the PICO (patient, intervention, control, outcome) guidance; Reply 4: We revised the title.

5.In the abstract, also specify if there was any adverse event. If none, just state there was none. Reply 5: We specified that there were no adverse events. 6.In the "Case Presentation" section, further specify whether the patient is followed up and how everything was going (e.g., any adverse events or unanticipated events);Reply 6: We revised the manuscript accordingly.

7. Limitation of this case report is required in the Discussion; Reply 7: We added limitations in 189-191 lines.

8.We highly recommend a flow diagram that highlights the whole case report; Reply 8: We added the diagram that highlights the case report.

9. Please confirm if the study was conducted in accordance with the Declaration of Helsinki (as revised in 2013) and add this statement together with the Declaration Of Patient Consent into the Method section in the main text; Reply 9: We improved the manuscript accordingly

10.For Reference 19, please add the journal, volume and page information; Reply 10: We corrected reference 19.

11.Please complete <u>the attached Conflict of Interest Form</u> and send back all authors' forms. Reply 11: We attached all forms in the submission.