Peer Review File

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Reviewer A

Authors report a retrospective comparison between traditional VATS and tubeless VATS for mediastinal diseases resection. The series is large but not homogeneous being the comparison between group with some differences (age, ASA score...) underlining the first bias of the study (retrospective fashion).
I have some other comments:
1. The English is poor and need a major revision: a lot of misspellings and grammar mistakes are present.

Response： Thank you for your comment. We have fixed the language and the logic, please kindly check.

Change in text: We have fixed the language.

2. It is unclear the technique and the devices used: do the authors use the CO2 insufflation during anterior mediastinal masses resection? If yes, do they have problem in tubeless technique? Do the authors use energy devices (i.e. Harmonic Ultracision, radiofrequency, other) in their procedures in order to reduce bleeding or serous production?

Response： Thank you for your comment. Sure, we used the energy devices (i.e. Harmonic Ultracision, Electrocantery). However, we didn't use CO2 insufflation during anterior mediastinal masses resection.

Change in text: Energy devices (Harmonic Ultracision) was used to reduce bleeding or serous production during surgery.

3. No clear complications related to the intubation, venous or urinary catheterization seem present in the standard group: the authors should better comment on that.

Response： Thank you for your comment. We will describe the complications related to the intubation, venous or urinary catheterization in results. Please kindly check.

Change in text: 5/43 (11.6%) patients in traditional group suffered from sore throat, while only one patient (2.3%) in tubeless group has the same symptom. No venous or urinary catheterization related morbidity was recorded in either group.

Reviewer B

This is an article about the advantages of non-incubation of patients affected by a mediastinal tumor. There are numerous works on non-intubated patients undergoing lung resection. The work has important limitations, it is a retrospective paper without randomization On the other hand, we cannot know if the patients to be compared are similar. Non-tubed patients are younger and have less comorbidity except for the presence of high blood pressure. On the other hand, although the differences between both procedures in time are minimal, the work does not analyze other aspects like the size of the tumor that could influence the course of the intervention Logically simplify the procedure and these reasons may explain an earlier discharge in non-intubated patients.

There are two very important aspects of non-intubated patients during the surgical procedure not resolved at work.

1. How to resolve an accident during the intervention? if necessary how to intubate the patient in the context of an operative accident?

Response： Thank you for your comment and question. If hypoxemia or hypercapnia or other indicated conditions for conversion occur during the surgery and cannot be resolved after non-invasive management, the anesthesiologist must be able to switch the anesthesia mode and perform tracheal intubation. The single lumen endotracheal tube + bronchial blocker is preferred. Given there is Intra-airway hemorrhage, lung

isolation can be achieved by double lumen endotracheal intubation. The single-lumen tube should be inserted under the guidance of a fiber optic bronchoscope when the patient is in a lateral position, which is more difficult than normal practice. To achieve this a small pillow should be placed under the head to allow the front, bottom perspective of the mouth and nose to stay up and the head and neck should be parallel to the central axis of the body. We added this in methods.

Change in text: If hypoxemia or hypercapnia or other indicated conditions for conversion occur during the surgery and cannot be resolved after non-invasive management, the anesthesiologist must be able to switch the anesthesia mode and perform tracheal intubation. The single lumen endotracheal tube + bronchial blocker is preferred. Given there is Intra-airway hemorrhage, lung isolation can be achieved by double lumen endotracheal intubation. The single-lumen tube should be inserted under the guidance of a fiber optic bronchoscope when the patient is in a lateral position, which is more difficult than normal practice. To achieve this a small pillow should be placed under the head to allow the front, bottom perspective of the mouth and nose to stay up and the head and neck should be parallel to the central axis of the body.

2 How to safely select patients who may be candidates for this type of resection without intubation?

Response： Thank you for your comment and question. For the patients selection, we evaluated all patients who could be potentially treated with tubeless VATS, the criteria are as follow: age<60, BMI<25, no cardiopulmonary dysfunction, ASA status ≤2, no obvious invasion to other organs. Patients met the criteria were asked to sign the informed consent to accept tubeless technique, patients who refused would get the conventional intubated surgery. We have mentioned this in manuscript, please see the highlight in manuscript (Method).

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Patients met the criteria were asked to sign the informed consent to accept tubeless technique, patients who refused would get the conventional intubated surgery.

Reviewer C

I found your paper interesting. I have some questions.

- According to a previously published consensus (your reference 16), your tubeless VATS group means tubeless SV-VATS (or NI-VATS) is that correct? I believe it would be better to use an standardized surgical nomenclature

Response： Thank you for your comment and question. Together with the international experts, we have published two expert consensuses; one is the non-intubated spontaneous ventilation VATS for primary spontaneous pneumothorax (PSP), and another is the tubeless VATS protocol for simple thoracic surgery (reference 16).

Non-intubated spontaneous ventilation is anesthesia technique, while the tubeless VATS is an enhanced recovery after surgery (ERAS) protocol, which includes non-intubated spontaneous ventilation anesthesia, no central venous catheter and urethral catheter during operation and no chest tube after surgery. We have observed and published the use of non-intubated spontaneous ventilation anesthesia in mediastinal tumor resection in 2019; in this study, we would like to make a summary on the use of total tubeless VATS protocol for this population. We added a description in background, please refer.

Reference:

1 He J, Liu J, Zhu C, et al. ***Expert consensus on spontaneous ventilation video-assisted thoracoscopic surgery in primary spontaneous pneumothorax (Guangzhou***). Ann Transl Med 2019;7(20):518. doi: 10.21037/ atm.2019.10.08

2 He J, Liu J, Zhu C, et al. ***Expert consensus on tubeless videoassisted thoracoscopic surgery (Guangzhou)***. J Thorac Dis 2019;11(10):4101-4108. doi: 10.21037/jtd.2019.10.04

3 Liang H, Liu J, Wu S, Zhang Y, Liu H, Yang H, Zhao Y, Hao Z, Liang W, He J. ***Nonintubated Spontaneous Ventilation Offers Better Short-term Outcome for Mediastinal Tumor Surgery***. Ann Thorac Surg. 2019 Oct;108(4):1045-1051. doi: 10.1016/j.athoracsur.2019.04.052. Epub 2019 Jun 7. PMID: 31181206.

Change in text: Non-intubated spontaneous ventilation is anesthesia technique, while the tubeless VATS is an enhanced recovery after surgery (ERAS) protocol, which includes non-intubated spontaneous ventilation anesthesia, no central venous catheter and urethral catheter during operation and no chest tube after surgery. Our team have demonstrated that non-intubated spontaneous ventilation is safe and may associated with better short-term outcomes for mediastinum tumor resection. However, there is no comparative study to describe the entire tubeless VATS procedure applied in mediastinal neoplasms. Hence, we aim to further analyze the application of tubeless VATS in mediastinal neoplasms surgery.

- On results, you report " bleeding 7.79 vs 8.53 ml", are this numbers correct? Which are your ranges?

Response： Thank you for your comment and question. We checked the original number again, the mean volume of intraoperative bleeding is (7.79 ± 6.73 vs 8.53 ± 7.56 ml, P = 0.361), the range is 2-250ml and 2-300ml, respectively. We added the standard deviation (SD) for the outcome. We also added SD for all continuous variables in manuscript, please kindly check.

Change in text: Patients in the tubeless group had similar intraoperative blood loss (7.79 ± 6.73 vs 8.53 ± 7.56 ml, P = 0.361) with traditional practice group. Anesthesia time (177.63 ± 84.77 vs 202.53 ± 101.54 min; p=0.004) was shorter in tubeless group, while operation time (90.95 ± 63.01 vs 101.47 ± 56.34 min; p=0.109) were similar.

- In the same consensus, it is stated that this approach is only for simple surgeries.

In this order of ideas, simple VATS procedures usually do not require central venous catheters nor urethral catheterization; despite this, you conclude that avoiding those

monitoring is a main advantage of tubeless VATS. Does this have more to do with complexity of the procedures and/or medical condition of the patients rather than the surgical approach? Can you comment on this?

Response： Thank you for your comment and question. We admit your comment. In the current thoracic surgery, mechanical induced one-lung ventilation has become the standard care, and intraoperative monitoring including central venous catheters or urethral catheterization have also been deemed as the routine practice in all thoracic operation. Surgical treatment lacks individualization and precision. The concept of "tubeless VATS" indicated that simple disease condition should receive simple procedure. This study demonstrated that simple procedure (Tubeless VATS) is safe and feasible for simple condition (selected mediastinal tumor resection patients), and the simple procedure might associate with better postopeative short outcomes. However, we should acknowledge that operation safety is the priority.

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- Also, you report fewer wounds in the tubeless group, however there was a bias selection on size of tumor and age between groups; again, it is not clear whether the decision to use fewer incisions is related with complexity of procedure, rather than an implicit advantage of tubeless surgery.

Response： Thank you for your comment and question. For technique requirement, patients underwent tubeless VATS should be young and low BMI, smaller tumor and easier condition for avoiding poor surgical filed. However, the selection bias would

cause the unbalanced outcomes. As the consequence, propensity score matching was used to balance the clinical features pre-operatively, leading to a more objective comparison.

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- Finally, my main concern is that redaction on this paper is essentially the same than a previous paper published about NI-VATS for mediastinal tumors (your reference 14) with many paragraphs all across the paper being identical. Can you comment on this?

Overall, I believe that in the present form the paper it is not suitable for publication, as it seems a copy of the paper mentioned above.

Response： Thank you for your comment and question. I am glad you have read another manuscript (Ann Thorac Surg) from our team. As we mentioned before, Non-intubated spontaneous ventilation is anesthesia technique, while the tubeless VATS is an enhanced recovery after surgery (ERAS) protocol, which includes non-intubated spontaneous ventilation anesthesia, no central venous catheter and urethral catheter during operation and no chest tube after surgery. The article you mentioned studied the use of non-intubated spontaneous ventilation anesthesia in mediastinal tumor resection; in this study, we made a summary on the use of total tubeless VATS protocol for this population. Although the form of the two studies might be identified, the technique content and the essence are totally different.

Reviewer D

Thank you for the opportunity for reviewing this manuscript. In this retrospective single institutional study, the authors demonstrated the efficacy and merits of tubeless VATS for mediastinal tumor resection compared with conventional VATS. Nowadays, less invasive surgical approaches, including uniportal VATS and non-intubated VATS can be applied to thoracic surgery. Moreover, the safety and efficacy of tubeless VATS (without chest drain tube) have recently been reported. The most important thing in surgery should be the safety of patients receiving surgery. In this point, the patient selection for tubeless VATS of the authors seems proper, which is one of the strengths of this study. This paper is well-written; however, there are some points to be elaborated.

1) There are large biases in patient selection since tubeless VATS is only considered among the patients within the criteria such as age<60, BMI<25 and less comorbidities. Is propensity score matching required? Rather, should the comparison be performed among the patients within the criteria for tubeless VATS undergoing and not undergoing tubeless VATS?

Response : Thank you for your comment and question. For technique requirement, patients underwent tubeless VATS should be young and low BMI, in order to avoiding poor surgical filed. However, the selection bias would cause the unbalanced outcomes. As the consequence, propensity score matching was used to balance the clinical features, leading to a more objective comparison.

Change in text: For technique requirement, patients underwent tubeless VATS should be young and low BMI, smaller tumor and easier condition for avoiding poor surgical filed. However, the selection bias would cause the unbalanced outcomes. As the consequence, propensity score matching was used to balance the clinical features pre-operatively, leading to a more objective comparison.

2) In this study, the comparison between the conventional VATS and the tubeless VATS was performed. Were there any cases undergoing VATS without one or two

tubes, like a non-intubated VATS with chest drainage tube or intubated VATS without chest drainage tube, during the study period?

Response： Thank you for your comment. Sure, there were such hybrid technique in real world application. In order to systematically evaluated the tubeless protocol, we only selected patients that underwent total tubeless VATS technique. We will add this in discussion.

Change in text: In order to systematically evaluated the tubeless protocol, we only selected patients that underwent total tubeless VATS technique. A 24-F chest tube was placed at the end of the operation in traditional VATS group. While, neither of these catheters were placed in tubeless group. Whether or not to re-put a chest tube after the operation depends on the patient's status.

3) Indeed, shorter anesthesia time, shorter hospital duration and less postoperative pain are the merits of tubeless VATS. However, the patient satisfaction cannot be evaluated from this study because the re-put of chest drainage tube can decrease the patient satisfaction and the evaluation itself is not actually performed. Please make comments on this point.

Response： Thank you for your comment. We admitted your point of view that patient satisfaction cannot be evaluated easily. We thus plan to develop a randomized controlled trial, aiming to compare the patients report outcomes (PROS) between tubeless group and traditional group. We will add this comment in discussion.

Change in text: Third, patient satisfaction cannot be evaluated objectively. We thus plan to develop a randomized controlled trial, aiming to compare the patients report outcomes (PROS) between tubeless VATS and traditional group.