

Peer review file

Article information: <http://dx.doi.org/10.21037/jtd-20-2759>

Reviewer A

Comment 1: In the literature, there are several retrospective studies and a meta-analysis that compare the single-port technique with the multi-port techniques. Only one prospective, randomized study has been published. Further studies focused on this topic should be prospective, randomized and include a large number of patients so that they can provide significant novelties.

Reply 1: As you pointed out, this was a retrospective, non-randomized, single-institution study. We believe that a multicenter, prospective and randomized trial will be needed in future.

Reviewer B

Comment 1: The fact that prolong stays, mortality, Readmissions are excluded, makes the short-term outcomes comparison unacceptable. I strongly suggest the mean and median length of stay, including all patients, should be reported.

Reply 1: In this study, we focused on acute postoperative pain. Hence, confounding factors that affect the evaluation of postoperative pain were excluded. The mean and median duration of hospital stay of all the patients in the M-VATS group were 5.4 days and 4.0 days, respectively, while those of patients in the U-VATS group were 4.1 days and 3.0 days, respectively.

Comment 2: The authors should explain the surgeons' experience performing the procedure. Were all surgeons performing U-VATS and M-VATS or it was surgeon specific?

Reply 2: M-VATS was performed by two surgeons with intermediate experience and three senior surgeons. U-VATS was performed by two of the three senior surgeons. We have added a description about this in the revised manuscript (Page 7, lines 103-106).

Changes in the text: M-VATS was performed by three senior surgeons and two surgeons with intermediate experience, and U- VATS was performed by two of the three senior surgeons. The surgical procedure was decided by the surgeon.

Comment 3: Were there any conversions from U-VATS to M-VATS during any case?

Reply 3: There were no conversions from U-VATS to M-VATS.

Comment 4: How did authors decide either to perform U-VATS or M-VATS ?

Reply 4: The surgical procedure (U-VATS or M-VATS) was decided by the surgeon.

We have added text about this in the revised manuscript (Page 7, lines 106).

Changes in the text: The surgical procedure was decided by the surgeon.

Comment 5: An editorial review of the manuscript will be helpful.

Reply 5: Thank you. I will consult the editor about this.

Comment 6: What was the conversion rate to thoracotomy in both arms?

Reply 6: The conversion rate was 9.6% in the M-VATS group and 6.1% in the U-VATS group.

Reviewer C

Comment 1: As the authors commented in the limitation section of the discussion, there are many different points in the settings of surgery between U-VATS and M-VATS. The reviewer wants to know who was the operator or operators in U-VATS in this study period. Probably, there might be multiple operators in M-VATS, while the operator in U-VATS might be the senior staff surgeon. This might affect the results even though there might be a learning curve issue in U-VATS. Please clarify this point for the better understanding of this investigation.

Reply 1: As you pointed out, there might be surgeon-related differences in perioperative results. M-VATS was performed by two surgeons with intermediate experience and three senior surgeons. U-VATS was performed by two of the three senior surgeons. We have described this in the revised manuscript (Page 7, lines 103-106).

Changes in the text: M-VATS was performed by three senior surgeons and two surgeons with intermediate experience, and U- VATS was performed by two of the three senior surgeons. The surgical procedure was decided by the surgeon.

Comment 2: It might be better for the authors to perform propensity matched study if possible.

Reply 2: As you pointed out, a propensity matched study would increase the accuracy of comparisons of various surgical outcomes between U-VATS and M-VATS. I will perform propensity score-matched analysis if it is absolutely necessary, although, since this study focuses on postoperative pain, we do not think it is necessary to match propensity scores between the two groups.

Comment 3: According to Figure 1, there were 75 (49+26) patients undergoing thoracotomy. The reviewer wants to know the pain issue of these patients, because the authors discussed the pain issue in the third paragraph in the discussion section (There was no difference by surgical approach in a reference). Especially, the reviewer wants to know the pain issue in the conversion cases.

Reply 3: This study focuses on which approach reduced postoperative pain earlier, M-VATS or U-VATS. The conversion rate was 9.6% in M-VATS (n=21) and 6.1% in U-VATS (n=5). Among them, 17 patients (65.4%) needed analgesic prescriptions for over 10 days after surgery. This is clearly a large number compared to VATS.

Comment 4: The reviewer wants to know the pain issue in sequential cases. That is, the reviewer wants to know if the pain in the patients is solely related to the number of ports and is not related with a learning curve in U-VATS.

Reply 4: Patients in the U-VATS group who required analgesic prescriptions were evenly present throughout the period, and the learning curve of U-VATS was irrelevant.

Comment 5: The authors investigated on subacute pain in this study, but chronic pain is also one of the issues in thoracic surgery. It might be better for the authors to add some data on chronic pain if possible. Otherwise, they should comment on this in their discussion.

Reply 5: We're sorry, but this study did not investigate chronic pain. As you pointed out, long-term data, including about chronic pain, is important. We have modified the relevant text, as advised (Page 17, lines 276-277).

Changes in the text: Evaluation of chronic pain and neuralgia is also needed.

Comment 6: The authors should comment on the criteria for U-VATS instead of M-VATS.

Reply 6: The surgical procedure (U-VATS or M-VATS) was decided by the surgeon. We have added some text about this (Page 7, lines 106).

Changes in the text: The surgical procedure was decided by the surgeon.

Comment 7: The reviewer could not find IRB statement in the manuscript.

Reply 7: The study was approved by institutional ethics board of Maebashi Red Cross Hospital (NO.: 2020-17) and individual consent for this retrospective analysis was waived (see Page 18, line 298-300).

Reviewer D

Comment 1: Why did this new technology of U-VATS reduce time compared with the

old technology of M-VATS? Did you say that the experienced surgeons transitioned to U-VATS while the less experienced continue to perform M-VATS ? If that is the case, the improvement was due to experience in surgery and not due to the way the surgery was done. Since it took time to learn the new technique of U-VATS, it would make more sense that U-VATS should take longer time to complete.

Reply 1: M-VATS was performed by two surgeons with intermediate experience and three senior surgeons. U-VATS was performed by two of the three senior surgeons. Hence, the results might have been affected by the fact that U-VATS was performed only by senior surgeons. Other possible factors that might have affected the results are described in the discussion section (Page 16, lines 261-270).

Comment 2: In M-VATS, did you make a bigger incision to remove the specimen? It was not mentioned in the manuscript. I cannot believe that the entire lobe could be removed through a 2 cm incision (unless it was the middle lobe with a really small tumor).

Reply 2: As you rightly pointed out, we did indeed expand the wound as needed to remove the specimen.

Comment 3: How do you explain no difference in blood loss?

Reply 3: There were no significant differences between the groups in intraoperative blood loss and the rate of significant intraoperative bleeding (bleeding from the pulmonary artery or vein that could be managed under VATS). Hence, we believe that

the procedure performed does not affect the amount of bleeding.

Reviewer E

Comment 1: In the paper, the primary and secondary end points are not immediately clear.

Reply1: This study was a retrospective, non-randomized, single-institution study. The primary endpoint was evaluation of which approach reduced postoperative pain earlier and was less invasive for anatomical lung resection.

Comment 2: Postoperative pain has been analyzed during hospitalization and at first visit to the outpatient clinic through the rate of patients requiring analgesic prescriptions over 10 days postoperatively. This is an interesting idea, but to better evaluate postoperative pain it is necessary to evaluate it at 30th and 90Th POD.

Reply 2: We're sorry, but this study focused on acute postoperative pain and did not investigate chronic pain. As you pointed out, long-term data, including chronic pain, is important. We have modified the relevant text, as advised (Page 17, lines 276-277).

Changes in the text: Evaluation of chronic pain and neuralgia is also needed.

Comment 3: In the text is not clear why patients have been treated with one or other approach.

Reply 3: The surgical procedure (U-VATS or M-VATS) was decided by the surgeon.

We added some text about this (Page 7, lines 106).

Changes in the text: The surgical procedure was decided by the surgeon.

Comment 4: The two groups presented relevant numeric differences, this could be sign of a significant bias that is neither explained nor accounted for in the interpretation of the study.

It is not clear if a propensity score matching has been applied to the statistical analysis, making unclear the model specification used and the interpretation of the results.

Reply 4: As you pointed out, a propensity matched study would increase the accuracy of comparisons of various surgical outcomes between U-VATS and M-VATS. I will perform propensity score-matched analysis if it is absolutely necessary, although, since this study focused on postoperative pain, we believe that it is not necessary to match propensity scores between the two groups.