

## Peer Review File

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### Reviewer A

Interesting and well-done paper.

Reply: We thank the reviewer for the positive feedback.

### Reviewer B

The authors conducted a systematic review and meta-analysis on the long-term outcomes of RATS versus VATS for non-small cell lung cancer, using data from 2015 patients. No significant differences were observed between RATS and VATS in OS, DFS, rates of postoperative complications, prolonged air leak, conversion rates, and operative times. However, RATS was associated with a shorter hospital stay compared to VATS.

The strength of this study lies in its rigorous data collection method for meta-analysis. Although similar studies exist, this study reinforces the finding that there is no superiority in long-term outcomes between VATS and RATS. Therefore, the reviewer has a few minor comments on this study.

1) The authors note that RATS is associated with a shorter length of stay compared to VATS and suggest that this difference might be due to the fact that institutions adopting new robotic technologies may have concurrently implemented different discharge protocols, such as ERAS, that facilitate earlier discharge in patients undergoing RATS. This might be a reasonable assumption, but it seems challenging to explain the results of significant differences between the two modalities reported in many studies based solely on this factor. Could there be other potential reasons, such as RATS offsetting hospitalization costs with the surgical costs?

Reply: We appreciate this suggestion. We modified our discussion around the LOS which now reads as follows: *“Interestingly, the LOS was noted to be shorter in the RATS group despite similar post-operative complications. We hypothesize that this difference might be to the fact that the institutions while adopting the new robotic technologies might have also adopted different discharge protocols including ERAS that facilitated earlier discharge in patients undergoing RATS. Another potential explanation regarding the LOS could be that hospitals utilizing RATS may attempt to offset the surgical costs with the hospitalization costs.”*

2) In the highlight box, the authors state that further evidence is warranted from randomized clinical trials. However, due to the widespread use of both approaches, conducting prospective trials may no longer be feasible. Please consider revising this sentence.

Reply: We thank the reviewer for this comment. After performing a search in the literature, we identified more than three ongoing RCTS (ROMAN Study, RAVAL trial, RVlob Trial). These studies have reported only the short-term outcomes so far and the long term survival outcomes are anticipated to be published soon. That is the main reason we have included the sentence in our highlight box.

We have edited the sentence in our highlight box according to the reviewer’s suggestion. The sentence now reads as follows: *“While further evidence is warranted from high quality studies, utilization of one approach over the other should be tailored according to the surgeon’s and the center’s experience.”*

## Reviewer C

This manuscript has fatal bias. A critical issue is lymphadenectomy. The authors stated that there was a significant difference in the number of lymph nodes dissected between RATS and VATS, but when extracting articles, they did not include terms related to dissection such as "systemic lymphadenectomy." Therefore, it is likely that some papers do not perform proper dissection. Also, regarding the length of hospital stay after surgery for RATS, it seems that early discharge is intentionally encouraged in order to control the high cost.

RATS generally has more ports and longer operating time than VATS. It is difficult to think that RATS has better results, and it is thought that the underlying background bias has a great influence.

Reply: Thank you for your review and raising concerns about potential biases in the manuscript. We appreciate your critical evaluation and would like to address the points you have raised.

Regarding the issue of lymphadenectomy, RATS is credited to offer advantages in terms of improved visualization, increased dexterity, and enhanced surgical precision, which could potentially facilitate more robust lymph node dissection. We acknowledge that the authors did not include specific terms related to lymph node dissection in the search strategy and therefore the following sentence was added to our limitations:

We incorporated only studies reporting on the long-term outcomes in our final synthesis. This way we excluded some studies reporting on early outcomes, however, we believe that this way our results are impart decreased risk for selection and confounding biases.

Regarding the length of hospital stay after surgery for robotic-assisted thoracic surgery (RATS), we understand your skepticism regarding the superiority of RATS due to its increased ports and longer operating time and we also understand that early discharge may be intentionally encouraged to control costs. Therefore, the discussion around the LOS now reads as follows:

*“Interestingly, the LOS was noted to be shorter in the RATS group despite similar post-operative complications. We hypothesize that this difference might be to the fact that the institutions while adopting the new robotic technologies might have also adopted different discharge protocols including ERAS that facilitated earlier discharge in patients undergoing RATS. Another potential explanation regarding the LOS could be that hospitals utilizing RATS may attempt to offset the surgical costs with the hospitalization costs.”*

## Reviewer D

I would also like to commend the authors for their scholarly work, which presents a systematic review and meta-analysis comparing the outcomes of robotic-assisted thoracoscopic surgery (RATS) and video-assisted thoracoscopic surgery (VATS) in the treatment of lung cancer. In particular, the authors conducted a meta-analysis of 10 studies from the PubMed and Scopus databases in accordance with the recommendations of the PRISMA statement. In total, 1,231 and 814 patients were included in the VATS and RATS groups, respectively. Patients who underwent VATS had similar overall survival compared with those who underwent RATS. The two groups also displayed equivalent outcomes

regarding disease-free survival. Both RATS and VATS had similar postoperative complication rates, prolonged air leak, conversion to thoracotomy, and operative time. However, RATS was found to be superior to VATS concerning length of hospital stay and number of dissected lymph nodes. Therefore, the authors conclude that in patients undergoing lobectomy for non-small cell lung cancer, VATS and RATS have equivalent overall and disease-free survival.

The present manuscript has the potential to make a valuable contribution to the pertinent literature, as it provides a comprehensive and balanced comparison of RATS and VATS in the treatment of lung cancer. Although it lacks novelty, the paper is characterised by an extensive and meticulous analysis of various parameters associated with these two surgical techniques. It not only compares the outcomes of RATS and VATS but also provides a detailed evaluation of the factors influencing these outcomes. This includes operative time, conversion rate to thoracotomy, number of dissected lymph nodes, postoperative morbidity, length of hospitalisation, complications, and cancer recurrence. The authors have also conducted a meta-regression analysis examining the impact of the presence of squamous cell carcinoma in the overall survival and disease-free survival difference between VATS and RATS. This aspect of the study adds a layer of depth to the analysis, providing insights into how specific types of lung cancer may influence the effectiveness of these surgical techniques.

Overall, the manuscript is well-structured and written. The introduction sets the appropriate background even for the reader with little knowledge on the subject matter. The methodology is appropriate for the analysis, and the results are clearly presented with appropriate tables and figures. The findings are discussed within the context of the current literature, and the conclusions drawn are clinically relevant.

Reply: We thank the reviewer for the positive feedback.

1. The manuscript includes a meta-analysis of various studies, and there seems to be a significant heterogeneity in some of the results, as indicated by the I<sup>2</sup> statistic. It would be beneficial if the authors could delve deeper into the potential sources of this heterogeneity. This could include differences in patient characteristics, surgical techniques, or other factors across the studies included in the meta-analysis.

Reply: We thank the reviewer for this valuable comment. We modified our limitations section according to the reviewer's suggestion. The limitation paragraph now reads as follows:

*"There are several limitations in this study that should be acknowledged. First, there are inherent limitations to a study-level meta-analysis as we did not have access to patient-level covariates which could confound our findings. As such no sensitivity analyses examining the impact of certain variables on OS and/or DFS could be synthesized besides meta-regression analyses. It should be clarified that all the operations reported in our study were performed by thoracic surgeon and for that reason our findings may not be generalizable to surgeons who have had different training backgrounds and this might explain the significant heterogeneity noted in some of our results."*

2. The manuscript includes several figures, such as meta-regression analyses examining the impact of the presence of squamous cell carcinoma and the disease's stage on the overall survival and disease-free survival difference between VATS and RATS. It would be helpful

if the authors could provide more detailed explanations or annotations in these figures to make them more accessible to readers who may not be familiar with these types of analyses.

Reply: We thank the reviewer for this suggestion. We agree that since our statistical analysis in this paper was extensive and meticulous a lot of plots were ultimately generated. We have provided figure legends in all of our plots and we have also provided a table summarizing all the findings from all the analyses performed to make it more comprehensive and easily understood to the readership. Regarding the meta-regression plots we explained that there were no significant associations between the variables and the outcomes examined. We believe that adding more details on this analysis in our study might overwhelm the overall paper and readership.

3. While the manuscript does a commendable job of comparing RATS and VATS, it might be beneficial to provide a more extensive review of the existing literature. This could include a discussion of previous meta-analyses and systematic reviews, and how the current study adds to or differs from these previous works.

Reply: We thank the reviewer for the suggestion. In the second paragraph of our manuscript we discuss in depth the existing evidence by previous meta-analysis and how our work differs and adds to the literature. In addition, we have included a summary of the findings of all previous meta-analyses in Supplemental table 3.

4. A more detailed explanation of the statistical methods used in the study would be beneficial. This could include a discussion of why certain statistical tests were chosen, the assumptions made for these tests, and how these decisions may impact the results.

Reply: We thank the reviewer for this suggestion. Since our method section is already extensive and the statistical analysis component of it comprised of a total of 650 words and many details regarding the statistics used and the reason they were used are described in that section, we believe that adding extra sentences in our methods would be overwhelming to the readership.

5. The authors could consider expanding their discussion of the implications of their findings for clinical practice and future research. This could include potential ways to address the areas where RATS and VATS showed different outcomes, or suggestions for future studies to further investigate these differences.

Reply: We appreciate this suggestion. We have added the following sentence in our conclusions: “Future research should aim to reconcile conflicting short-term outcomes, optimize postoperative care, explore the impact of lymph node dissection, and assess the role of surgeon training on outcomes. Incorporating patient-centered outcomes, such as patient satisfaction, quality of life, and functional status, in future analyses would add another dimension to the comparison of RATS and VATS. By addressing these areas, surgical techniques can be refined and patient outcomes can be improved.”

6. Given the heterogeneity in some of the results, it might be beneficial to conduct further subgroup analyses. This could involve analysing data based on different patient characteristics, surgical techniques, or other relevant factors. Such analyses could provide more nuanced insights and help identify specific areas where RATS or VATS may be more beneficial.

Reply: Thank you for this comment. The meta-regression analyses were performed in order to address the heterogeneity observed in some of the results and to provide more nuanced insights into the comparisons between RATS and VATS. Since we did not have access to patient level covariates, the meta-regression analysis was used to examine the impact of moderator variables on outcomes and helps identify specific factors that may contribute to the heterogeneity observed across studies.

7. While the manuscript does a good job of comparing clinical outcomes, it might be beneficial to also consider patient-centered outcomes, especially in future analyses. This could include measures of patient satisfaction, quality of life, or functional status following surgery. Such outcomes are increasingly recognized as important measures of surgical success and could add another dimension to the comparison of RATS and VATS.

Reply: We appreciate this suggestion. We have added the following sentence in our conclusions to address the reviewer's comment: "Future research should aim to reconcile conflicting short-term outcomes, optimize postoperative care, explore the impact of lymph node dissection, and assess the role of surgeon training on outcomes. Incorporating patient-centered outcomes, such as patient satisfaction, quality of life, and functional status, in future analyses would add another dimension to the comparison of RATS and VATS. By addressing these areas, surgical techniques can be refined and patient outcomes can be improved."

In conclusion, I would like to reiterate my appreciation to both the editor and the authors for the opportunity to review this manuscript. I believe that the suggested modifications, if implemented, will further improve the quality and impact of the review. I look forward to seeing the revised version and wish the authors success in their ongoing research endeavours.

Reply: We appreciate the feedback by the reviewer.