

Reviewer A

I read with interest this review that describes the long-term oncologic outcomes of RATS lobectomy. Methods and statistics for systematic research are correct; however, some major issues need to be solved:

Comment A1: In some meta-analyses and studies analyzed in the paper, the patients were not divided according to preoperative conditions, such as spirometry values and comorbidity, but were subdivided only according the surgical approach. These limits should be specified in the discussion.

Reply A1: Thank you for this important point. The limitations have been revised to reflect this.

Comment A1: As highlighted in some reviews and meta-analyses included in the paper, the data relating to recurrence and DFS of the robotic technique, compared with VATS, cannot be considered definitive, as RATS has been developed in the last few 15 years and many data about survival outcomes are lacking in the study included in this review. Therefore, RATS long-term oncologic outcomes are not yet definitively comparable with the data relating to open surgery or VATS, which are numerically and historically much more, thus more accurate for recurrence, OS and DFS.

Reply A2: The authors agree with the reviewer that not enough high quality data has been produced to show definitive results and claim superiority for VATS versus robotic lobectomy with regard to oncologic outcomes. Nevertheless, we do think that this paper is the starting point for an important discussion which will only continue to increase in relevancy as robotic approaches are more widely adopted and longer term data is produced.

Comment A3: OS is not the best endpoint for oncologic outcomes, since patients may die for causes other than related to lung cancer. To overcome this bias, did you search for cancer-specific survival endpoint?

Reply A3: Thank you for this question, we note in the paper that OS is a problematic endpoint due to the reasons that the reviewer commented upon. We thus looked for and reported disease-free survival, which was the best representation of cancer specific survival outcomes and found a slight advantage with robotic lobectomy in 3 meta analyses.

Comment A4: There is a lack of high-quality RCTs and one of the two presents in literature, the ROMAN study, did not have oncologic outcome as primary endpoint, as well as it failed to accrue

and was closed prematurely. Given all these premises (point 2, 3 and 4), in the discussion session the authors should stress the concept that there is not yet strong evidence about oncologic efficacy of RATS technique in lung cancer, thus it is really premature to withdrawn conclusions about superiority of RATS compared to VATS for best long-term outcomes.

Reply A4: Thank you for this astute comment regarding the ROMAN trial which we also stated in section 4.5 of the paper. Our discussion aims to provide objective evidence without unfounded claims that there is strong evidence to indicate oncologic superiority with robotic lobectomy.

Moreover, some data are missed and should be implemented:

a) Did any patient of the selected studies undergo adjuvant therapy?

Reply: Of the included studies, there were 4 that reported rates of adjuvant therapy. The ROMAN study showed that 12% of VATS patients and 9% of robotic patients underwent adjuvant therapy (p=0.69). The comparative analysis by Merritt et al showed equivalent rates between VATS and robotic groups (29%), but a statistically significant higher rate in the open group (31%). They posit that the higher rate of adjuvant therapy in the open group may be associated with the larger preoperative tumor size seen. Shagabayeva et al showed that rates of adjuvant radiation (6%) and adjuvant chemotherapy (31%), and immunotherapy (<10%) were similar between the VATS and robotic groups, but there was a difference in the rate of adjuvant chemotherapy (6.2% in VATS vs 8.4% in robotic, p=0.04). The time from surgery to adjuvant treatment for both groups was not significantly different at 40-43 days. Lastly, Sesti et al showed no difference in rate of adjuvant therapy between the two groups at 20%.

b) Did any case undergo pre-operative multidisciplinary tumor board discussion?

Reply: Tumor board discussion information was not included in any manuscript.

Reviewer B

Thank you for this scoping review of the very important topic of robot assisted thoracic surgery. It is indeed the task of surgeons, as users of the robotic and/or video assisted technique, to report the importance of the techniques for the patients.

I do have a couple of comments:

Comment B1: please correct all spelling mistakes

Reply B1: All spelling mistakes have been addressed.

Comment B2: In the introduction the early studies of Melfi and Park are mentioned. One should not forget that since the early 2000's the Da Vinci robotic platform (at that time the Si generation) of Intuitive Surgical Inc. the development of the systems have resulted in the X and Xi systems.

Especially the latter has improved technical issues drastically. During analysis of the literature this is also a matter we need to take into account.

Reply B2: This point is very well-taken and is now reflected in the introduction of the paper.

Comment B3: Upstaging of lymph node status is a surrogate marker of quality of the surgical work that has been done. But upstaging depends also on the preoperative staging, which should be performed according to the guidelines. Lastly, as the robotic technique facilitates more accurate and precise dissection (of the nodes) it should be commented on by the authors what is said in the literature on keeping the capsula of the nodes intact as opposed to damaging the nodes and delivering them in morsels. Does this possibly affect survival and local recurrence.

Reply B3: This dataset does not allow us to assess whether entire lymph nodes or just fragments were removed. The theoretical concept of understaging as a result of leaving nodal fragments behind is difficult to study for many reasons, one being that pathologists also have a practice of taking mere sections of nodes for microscopic review. Thus, the whole process of staging has the potential to be inaccurate on various fronts.

Reviewer C

Drs. Wong and Oh in their manuscript, “Scoping review on long term oncologic outcomes in robotic-assisted lobectomy” have provided a nicely written, concise review on the major multi-center studies and meta-analyses comparing robotic with VATS and open lobectomy.

Overall, I think this is a worthy addition to the literature on this topic given its limited goals. There are a few misspellings throughout the text (ex “thoroscopic” in line 112) that should be corrected.

Comment C: My only comment/question is whether or not the meta-analyses that were cited examined overlapping studies. In that case, citing the number of meta-analyses that supported one viewpoint or another may be misleading, as they may be duplicative.

Reply C: Thank you for the interesting and important question. Of the 69 separate studies that were included across all 10 meta-analyses, 29 (42%) studies were included in more than one meta-analysis. 7 (10%) studies were included in more than 5 meta-analyses, which confirms the reviewer’s comment about the potential bias from duplicative results. We have thus amended the limitations section to specifically address this.

Reviewer D

Robotic lobectomy is quickly becoming the standard of care. This is a very well written, comprehensive and thoughtful for review. I have some very specific comments/questions for the authors:

Comment D1: The organization of the results is a little half hazard. I would present findings as you would find them chronologically (LN count, recurrence rate, DFS, OS) as opposed to presenting survival data first.

Reply D1: Thank you for this comment. We chose to present the results in the particular order in the paper because our primary outcome was OS, DFS, and recurrence; with secondary outcomes being lymph node data and upstaging rate.

Comment D2: Comparison of oncologic outcomes is very interesting and definitely of interest to surgeons wanting to offer the best care to their patients. I cannot find the recurrence data that you cited in your paper from Kent et al. Was this possibly from a different paper?

Reply D2: This is the citation for the Kent paper:

Kent, M. , Hartwig, M. , Vallières, E. , Abbas, A. , Cerfolio, R. , Dylewski, M. , Fabian, T. , Herrera, L. , Jett, K. , Lazzaro, R. , Meyers, B. , Reddy, R. , Reed, M. , Rice, D. , Ross, P. , Sarkaria, I. , Schumacher, L. , Spier, L. , Tisol, W. , Wigle, D. & Zervos, M. (1990). Pulmonary Open, Robotic and Thoracoscopic Lobectomy (PORTaL) Study: Survival Analysis of 6,646 Cases. *Annals of Surgery, Publish Ahead of Print* , doi: 10.1097/SLA.0000000000005820.

Please refer to Table 2.

Comment D3: They representation of Hannas QOL seems biased in your presentation. Specifically, RATs was more expensive but because they reported better QOL at 1 year they extrapolated that there was an improved QAYL. I don't think this means robotic is more cost effective than VATs. If you want to say that, can you elaborate and explain that detail more carefully in the review.

Reply D3: Thank you for this distinction, the early results from the RAVAL trial show an indicator of better patient-reported quality of life indicators in robotic lobectomy, rather than making a definitive statement on the comparative cost effectiveness. Quality is an economic evaluation that takes into account cost, clinical outcomes, and patient-reported quality of life. This change has been made in the paper.

Editorial Comments

Regarding the reporting following the PRISMA-ScR Checklist, please see the comments below.

Comment 1: Methods

1. "We performed a systematic search": only one database was searched? We suggest the authors consider additional databases (e.g., Web of Science, EMBASE, Gray database) or additional search references to achieve "a systematic search".

Reply: This is not an exhaustive systematic review, but rather an invited review article on the topic and therefore we chose to review PubMed. If this was intended to be complete systematic review and meta-analysis, we could consider searching all the above databases. For this invited review, we chose PubMed as there is a large amount of overlap between the databases as listed above. The link below compares Scopus, Web of Science, and Google Scholar. Scopus has more international journals and non-English journals which are not applicable to this review. Web of Science has citations from earlier years than Scopus and more conference proceedings but we are discussing a relatively novel topic which has only

produced studies in the last 15-20 years at most. Google Scholar has the most overlap with PubMed so overall we stand by our protocol.

<https://instr.iastate.libguides.com/c.php?g=901522&p=6492159>

2. Please report language restrictions and publication status.

Reply: Only accepted publications in the English language were included. This is now added in the Methods section.

3. Please specify the full electronic search strategy for at least 1 database.

Reply: Below is the search strategy used for PubMed.

Final Search String: 169 results

("Pneumonectomy"[MeSH Terms] OR "lobec*" [All Fields] OR "resect*" [All Fields]) AND ("Lung Neoplasms"[MeSH Terms] OR "lung cancer" [All Fields] OR "lung carcinoma" [All Fields] OR "lung neoplasm" [All Fields] OR "pulmonary cancer" [All Fields] OR "pulmonary carcinoma" [All Fields] OR "pulmonary neoplasm" [All Fields]) AND ("Robotic Surgical Procedures"[MeSH Terms] OR "robot*" [All Fields] OR "da vinci*" [All Fields] OR "davinci" [All Fields]) AND ("thoracic surgery, video assisted" [MeSH Terms] OR "video-assisted thoracoscopic surgery" [All Fields] OR "video-assisted thoracoscopic surgery" [All Fields] OR ("thoracic surgery, video assisted" [MeSH Terms] OR ("thoracic" [All Fields] AND "surgery" [All Fields] AND "video assisted" [All Fields]) OR "video-assisted thoracic surgery" [All Fields] OR "vats" [All Fields])) AND ("outcome assessment, health care" [MeSH Terms] OR "recurrence" [MeSH Terms] OR "neoplasm recurrence, local" [MeSH Terms] OR ("surviv*" [All Fields] OR "recurren*" [All Fields]))

4. For the selection and data collection process, please also specify how many reviewers screened each record and each report retrieved, how many reviewers collected data from each report, whether they worked independently, and any processes for obtaining or confirming data from study investigators (e.g., for "Neither of the 2 RCTs included in this review reported OS for various reasons").

Reply: There was a medical librarian who assisted with gathering relevant sources, and two independent reviewers who screened each record and report retrieved for the inclusion criteria.

5. Does this scoping review have a protocol? Please state it in the text (whether or not it has a protocol).

Reply: The protocol is as described in the Methods section.

Comment 2: Results

6. Please number the table as "Table 1" (line 135 and line 392) and provide the Table Legend.

Reply: The revisions have been made.

7. Please define in the table footnote all abbreviations mentioned in Table 1, such as DFS, OS.

Reply: The abbreviations have been defined under the table.

8. "Prior to 2020, there were few large studies comparing long term outcomes from robotic lobectomy versus VATS, and the best published literature consisted of retrospective studies from several high volume centers(5,6)": We suggest the authors also report the published year and sample size in Table 1.

Reply: The year of publication and sample size have been added to the Table.

9. We suggest the authors also specify the data in Table 1. E.g., Lymph node counts [Hennon et al(25)] - "VATS (11.3) > RATS (10.9), P<0.01".

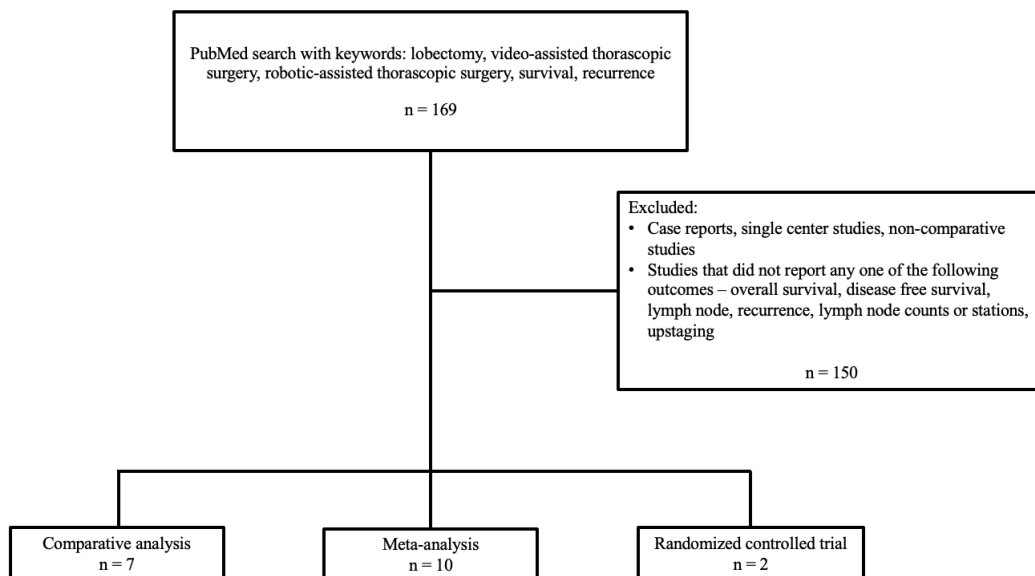
Reply: The data has been specified in the table.

10. "This review article aims to summarize contemporary data on the current state of robotic lobectomy as a maturing procedure, with a focus on oncologic outcomes and long-term survival as compared to traditional open and VATS techniques". Why does Table 1 only summarize the results of VATS and RATS? What about open surgery?

Reply: This review is focused specifically on VATS versus robotic techniques and the sentence as listed above has been amended in the paper.

11. We suggest authors use a flow diagram to state the sources of evidence screened. For the authors' kind reference, specify the number of included studies in the screening and analysis stages. Besides, give reasons and report the numbers for exclusions at each stage too.

Reply: Please see the figure below.



Comment 3: Other Information