Author’s response to reviews

Title: Uniportal versus multiportal video-assisted thoracoscopic anatomical resection for NSCLC: a meta-analysis

Authors:
Yueren Yan (1141946212@qq.com)
Qingyuan Huang (huangqy0808@163.com)
Han Han (hhan94@outlook.com)
Yang Zhang (fduzhangyang1987@hotmail.com)
Haiquan Chen (hqchen1@yahoo.com)

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Dear Editors and Reviewers

Thanks for all the valuable comments concerning our manuscript entitled “Uniportal versus multiportal video-assisted thoracoscopic anatomical resection for NSCLC: a meta-analysis”. We highly appreciate all reviewers’ efforts on helping us improve this manuscript. All comments were carefully reviewed and we have tried our best to revise the manuscript accordingly. The detailed amendments are listed below:

Response to Reviewer#1’s Comments:

Reviewer #1’s Comment 1: You mention uniportal as a recent development yet state it has been around for approaching 20 years?
Response to Reviewer #1’s Comment 1: Thanks for your kind suggestion and question. In about 2000, the uniportal video-assisted thoracoscopic surgery (U-VATS) proposed by Dr. Rocco was used for wedge pulmonary resection. This technique was gradually applied to the anatomical lung resection for lung neoplasm after about one decade.

Reviewer #1’s Comment 2: I have repeated your search and have identified a couple of studies from December 2019 and wonder if there will be value from including these?
  o https://pubmed.ncbi.nlm.nih.gov/32030232
Response to Reviewer #1’s Comment 2: Thanks for your constructive suggestion. We checked the paper mentioned above and found that the article authored by Al-Ameri (Al-Ameri et al., 2019) met our inclusion criteria. Our meta-analysis aims to reveal the comparison between U-VATS and M-VATS for anatomical lobe or segment resection of lung cancer, however, the paper authored by
Yameen (Bin Yameen et al., 2019) included some patients undergoing wedge resection, so it does not meet our inclusion criteria. We included the article authored by Al-Ameri, updated our results, and changed the search date to December 31, 2019.


Response to Reviewer #1’s Comment 3: We sincerely appreciate the valuable comments. We have checked the literatures and referenced them into the discussion part in the revised manuscript.

Reviewer #1’s Comment 4: There are some alignment issues in table 1 and 2 (e.g. table 1 between lobe and seg columns)
Response to Reviewer #1’s Comment 4: Thanks for your kind suggestion, and we are very sorry for our mistake. We’ve modified the format of Table 1 and Table 2 in this article.

Reviewer #1’s Comment 5: - Forrest plots are low resolution but I guess that may be the pdf conversion.
Response to Reviewer #1’s Comment 5: Thanks largely for your suggestion. We have used the PDF conversion to improve the resolution of forest plots in this article.

Reviewer #1’s Comment 6: You find no differences, but I note that there are some that approach significance e.g. pain. There are some differences in this meta-analysis to others published with several seeming to favour uniportal. I wonder if the discussion could be expanded specifically explaining why you think that there are these differences. Why is there so much heterogeneity between studies - looking at the titles of some of the included studies, it would appear that the learning curve for uniportal is included and perhaps that may be contributory? Are there other reasons? As a reader I want to understand why several meta-analyses have favoured uniportal but yours does not...
Response to Reviewer #1’s Comment 6: Thanks for your constructive suggestion and question. I reviewed the previous meta-analyses including the meta-analyses mentioned above. We conclude that our meta-analysis is different from others’ for these following reasons:
1)Several pervious meta-analyses (Lazar et al., 2017; Abouarab et al., 2018; Ng et al., 2019) included more studies and patients than us and performed some results that favour uniportal. However, these meta-analyses were not focused on non-small cell lung cancer and included many studies on benign diseases. Compared with surgery for benign diseases, lung cancer surgery requires a radical resection of the primary lesion and lymph node dissection. Therefore, the scope of surgery and the degree of trauma are relatively large. In this situation, the perioperative outcomes of U-VATS may be better.
2)In addition, the present meta-analysis is focused on anatomical pulmonary resection segmentectomy or lobectomy for patients with NSCLC, while some previous meta-analyses included patients undergoing wedge resection.
3)Besides, some articles included in several previous meta-analyses have overlaps in study population. For instance, there are three studies (Liu et al., 2014; Liu et al., 2016; Shih et al., 2016)
related to our topic published by the same clinical institution, and the patients included in the three articles have a relatively large overlap. Their results all found U-VATS better. If repeated results are included, the conclusion of the meta-analysis would be biased.

4) Compared with previous meta-analyses, our meta-analysis has been the largest one on the comparative clinical outcomes between U-VATS and M-VATS anatomical resection for lung cancer. Relevant explanations for why there are some differences in this meta-analysis to others published with several seeming to favour uniportal have added to the discussion section. (Line 194-200)

In addition, high heterogeneity does lead to biased results. We agree that the learning curve is a cause of high heterogeneity. We believe that there are two other main reasons for the heterogeneity: one is that the included studies in our meta-analysis come from different institutions in different countries, and the surgical techniques are different. Besides, only four included studies are prospective in design, and the majority is retrospective which is of lower quality and inevitably introduce potential biases and heterogeneity to the results. (Line 233-238) By the virtue of high heterogeneity, random effect model was used to analyze the results.

Reviewer #1’s Comment 7: There are some grammatical errors throughout and there may be benefit from seeking a native English speaker reviewing the manuscript.
Response to Reviewer #1’s Comment 7: Thanks for your kind suggestion. We feel really sorry for our mistakes. We do invite a friend of us who is a native English speaker from USA help polish our article. And we hope the revised manuscript could be acceptable for you.

Response to Reviewer #2’s comments:
Reviewer #2’s Comment 1: The tables in Fig 2 and 3 reads very poorly and must be revised.
Response to Reviewer #2’s Comment 1: Thanks for your question, and we are really sorry for our mistake. We have used the PDF conversion to improve the resolution of forest plots in the revised manuscript.

Reviewer #2’s Comment 2: I think the authors rightly point out that single port is usually adopted by surgeons who are already well trained multiport surgeons, making them more experienced than the multiport surgeons? I assume that the authors do not have data on experience-level in the two procedures.
Response to Reviewer #2’s Comment 2: Thanks for your kind suggestion. We admit that due to the lack of evaluation of experience levels in the relevant literature, it is indeed too arbitrary to infer that “U-VATS is usually performed in experienced hands”. We considered that some of our included studies did not control the same surgeon to perform these two procedures, which would bring potential bias to the results of our study. And we added this limitation to our discussion section. (Line 232-233)

Reviewer #2’s Comment 3: Were there any other measurements that could have been included, like cosmetic result?
Response to Reviewer #2’s Comment 3: Thanks for your question. Cosmetic result is indeed an essential perioperative result. We reviewed all the studies included. However, only one study gave the outcomes about cosmetic result. (Liu et al., 2016) At the meantime, we are also interested in the comparative outcomes of some other parameters, such as the positive margin and the long-term
survival. Unfortunately, there are so few included studies reported them that we could not perform a meta-analysis of these outcomes. Thus, further studies on these outcomes are warranted.

Reviewer #2’s Comment 4: Do the articles include any selection criteria for the two procedures that should be analyzed?
Response to Reviewer #2’s Comment 4: Thanks for your kind suggestion. The present meta-analysis focused on anatomical pulmonary resection segmentectomy or lobectomy for patients with NSCLC, while some previous meta-analyses included patients undergoing wedge resection. Lobectomy and segmentectomy are anatomical pulmonary resection, but wedge resection is not an anatomical resection. Our selection criteria were just focused on lobectomy or segmentectomy, the standard procedures for curative surgery for NSCLC. (Line 199-200)

Reviewer #2’s Comment 5: Can the authors make some comments about potential advantages and disadvantages of the two methods?
Response to Reviewer #2’s Comment 5: Thanks for your constructive suggestion. According to this meta-analysis, U-V ATS might have some potential advantages over M-VATS in reducing postoperative pain and drainage duration, even though these advantages are not significant. M-VATS, as a standard surgical procedure for NSCLC, has reliable safety and feasibility proved by several large-scale randomized controlled trials. Comparatively, there is still lack of evidence that U-VATS can be less invasive without compromising the long-term survival. We add relevant comments to the discussion section(Line 219-224)

Reviewer #2’s Comment 6: Does there exist in the papers any data about cost of the disposable equipment necessary?
Response to Reviewer #2’s Comment 6: Thanks for your question. The expenses of surgical disposable equipment exactly influenced the feasibility of the operation. Dr. Rocco reported that “One disadvantage of uniportal VATS procedures is represented by the higher costs of the rotulating instruments.” (Rocco et al., 2004) We reviewed all the studies included. Unfortunately, there were no relevant data on the cost of the disposable equipment reported by the studies included. Thus, further studies are still needed.

Reference: