Peer Review File

Article Information: https://dx.doi.org/10.21037/vats-23-31

Review comments

Reviewer A

Thank you for giving me the opportunity to review the manuscript.
The metasestectomy has an important role to control the oncological progression and contributes to prolonging the prognosis in several types of cancers. In this article, the author
described the role of segmentectomy in this situation.
I have several questions and recommendations as below.
1. The author mentioned, “Anatomical lung resections, although technically more demanding, may present some advantages over wedge resections, both for oncological and post-surgical results.” In lines 77-78.
To our best knowledge, there have been no highly-evidenced studies describing the superiority of segmentectomy to wedge resection in pulmonary metastasectomy. Please show the references if there have been such studies you know.
In my opinion, anatomic segmentectomy is technically more difficult than wedge resection. Moreover, anatomic segmentectomy requires exposure of hilar structures such as pulmonary vessels and bronchi, which will be disadvantage of the following surgical resection because metastasectomy is sometimes repeated.
Therefore, wedge resection might be better in metastasectomy.

2. The author mentioned “If palpation is not possible and other strategies for marking and locating the nodules not readily available, resection following anatomic landmarks can be achieved with or without 3D modelling and reconstruction.”. I totally agree with this opinion. Therefore, robotic approach should be applied to the only segmentectomy when performing metastasectomy.

3. The author mentioned “Satoshi Shiono et al., in their study, showed significantly increased postoperative complications in patients submitted to segmentectomy ($p< 0.001$) compared to wedge resections. However, they did not present any death 30 days after surgery and only 2 (0. 4%) occurred 90 days after surgery (8).”
I think the increase of morbidity is sufficiently problematic although the author might insist the safety of segmentectomy compared to wedge resection.

4. At the moment, the advantage of segmentectomy, compared to wedge resection, is that surgical margin can be ensured when the target tumor is located deeply in lung parenchyma. The author should describe it.

Answer A:

I am very grateful for the review. Regarding the first question, in the text we refer to the fact that anatomical segmentectomies are beneficial, especially in patients with central lesions that would require a lobectomy and also in those who present poor respiratory function tests.
Lines 116-120 explain this idea ("Another advantage of anatomical segmentectomies is the possibility to resect central lung metastases or those not peripherally-located. With anatomical segmentectomy, it is possible to resect the metastasis with oncologically acceptable margins and preserve the rest of the healthy lung parenchyma, providing better lung function (10,11) and decreased risk of complications."). In addition, there are studies such as those discussed in lines 90 to 99 with good results for anatomical segmentectomy.
Thanks for your opinion. Morbidity above all refers to air leakage and especially in complex cases of segmentectomies with more than one intersegmental line.
Line 205 to 214 "Satoshi Shiono et al. conducted a retrospective study comparing segmentectomies with wedge resections in patients with lung metastases; the recurrence rate of the resection margin was higher in patients who underwent wedge resection compared to segmentectomy (7. 3% versus 2. 0%; P = 0. 035). Multivariate analysis revealed that segmentectomy was a significant favorable factor for recurrence (hazard ratio: 0. 63, 95% confidence interval: 0. 44–0. 87, P = 0. 210 005), but not for overall survival (hazard ratio: 0. 65, 95% confidence interval: 0. 38–1. 05, P = 0. 080). What they observed was that patients undergoing segmentectomy developed 212 prolonged air leak more often. (5. 1% vs. 1. 8%) (P = 0. 048). In addition, the disease-free time at 5 years was 48. 8% in patients with segmentectomy and 36. 0% in patients with wedge resections (8)." ,
We described in that lines 116 to 120: "Another advantage of anatomical segmentectomies is the possibility to resect central lung metastases or those not peripherally-located. With anatomical segmentectomy, it is possible to resect the metastasis with oncologically acceptable margins and preserve the rest of the healthy lung parenchyma, providing better lung function (10,11) and decreased risk of complications."

Reviewer B

The revision touches on an interesting topic, but in my opinion a major revision needs to be done.
The authors have not mentioned importants trials such as VIOLET trial, and Pulmicc trial.
The authors should also go into more detail about the techniques used to locate pulmonary nodules, as small nodules and the centroparenchymal nodules are difficult to palpate through VATS approach

Answer B

I am very grateful for your review. Regarding the VIOLET trial, it has not been included because patients with lung cancer are compared VATS versus thoracotomy, not lung metastases. Regarding the Pulmicc trial, it was Stopped because of poor and worsening recruitment.

Reviewer C

In this review, The authors mentioned the benefit of minimally invasive surgery (MIS) for lung metastasectomy. As they mentioned, though lung metastasectomy should be less invasive, clear evidence of benefit from MIS for metastasectomy is yet to be reached. Therefore, this review would be useful in summarizing the previous reports. However, there are some shortcomings in this manuscript.

1. Is this a "systematic" review? I'm sure that systematic review resembles meta-analysis with respect to its method. However, there was no mention of methodology, including what kind of databases were used, and the inclusion criteria were adapted.

2. In line 73, the recommendation based on expert consensus was referred to, but no citation was given.

3. In line 125, it is unclear what conventional treatment means. Does it mean chemotherapy?

4. In line 129-131, I can't make out the relevance between the availability of palpation during surgery and undetectable nodules by CT scan.

Answer C

Excuse me, there is a narrative review.

Long-term results of lung metastasectomy: prognostic analyses based on 5206 cases. The International Registry of Lung Metastases. J Thorac Cardiovasc Surg 1997;113:37-29549.

Casiraghi M, De Pas T, Maisonneuve P, et al. A 10-year single-center experience on 708298

lung metastasectomies: the evidence of the “international registry of lung299 metastases”. J Thorac Oncol 2011;6:1373-8.

Onaitis MW, Petersen RP, Haney JC, et al. Prognostic factors for recurrence after pulmonary resection of colorectal cancer metastases. Ann Thorac Surg 2009;87:1684-8

Actually, it refers to chemotherapy.

Some surgeons are of the opinion that in order to be able to resect all pulmonary nodules, open surgery is necessary to be able to palpate with the hand and therefore be able to detect nodules that we would not detect with minimally invasive surgery. Sometimes fewer nodules appear on the CT than there really are when the lung is touched with the hand.

Reviewer D

Dear Authors

the idea is interesting but there is a fundamental weak point.
Line 79 The authors wrote: The objective of this systematic review is to understand ..... etc.

COMMENT: unfortunately, this is not a systematic review as the author wrote, and it is not a narrative review. Please follow the guidelines for a systematic and narrative reviews.
References 2,6,9,20,31 are also incomplete. Moreover, VATS published a very good special issue on Lung metastasectomy. https://vats.amegroups.com/post/view/vats-in-lung-metastasectomy.

Thank you for sending this paper to VATS

Answer D:
I am very grateful for the review.
That´s a mistake. It is a narrative review.
Added definition of narrarive revision of the VATS amegroups guidelines for authors.
"We strongly welcome the submission of narrative reviews, although our editors may still consider traditional reviews for publication. A narrative review aims to provide readers with a cutting-edge, scholarly, evolving developments and evidence-based overview on a clinical or mechanistic subject by searching, selecting, compiling, and summarizing the available literature. Through a narrative review, readers could gain a more comprehensive and enlightening knowledge on a particular field. A narrative review is less methodologically demanding than a systematic review, as it does not require a search of all literature in a field, nor does it necessarily require a rigorous appraisal on the included literature."
Reference 2: Rusch, Valerie W. "Pulmonary Metastasectomy". *Chest*, vol. 107, núm. 6, 1995, pp. 322S-331S, doi:10.1378/chest.107.6_supplement.322s.
Reference 6: Liu, Tianyu, et al. "Anatomical Resection Improves Disease-Free Survival after Lung Metastasectomy of Colorectal Cancer". *Cancer Management and Research*, vol. 13, 2021, pp. 9429–9437, doi:10.2147/CMAR.S341543.

Reference 9: Berry, Mark F. “Role of Segmentectomy for Pulmonary Metastases”. *Annals of Cardiothoracic Surgery*, vol. 3, núm. 2, 2014, pp. 176–182, doi:10.3978/j.issn.2225-319X.2014.02.08.
Reference 20: Bédat, Benoît, et al. “Segmentectomy by Video-Assisted Thoracic Surgery for Pulmonary Metastases”. *Video-Assisted Thoracic Surgery*, vol. 6, núm. 0, 2021, pp. 7–7, doi:10.21037/vats-2020-lm-05.
Reference 31: Bawaadam, Hasnain, et al. “Lung Nodule Marking with ICG Dye–Soaked Coil Facilitates Localization and Delayed Surgical Resection”. *Annals of Thoracic Surgery Short Reports*, vol. 1, núm. 2, 2023, pp. 221–225, doi:10.1016/j.atssr.2023.02.010.

Reviewer E

The authors have written a review to describe the outcomes and approaches in which metastasectomy is treated. I would recommend a table to organize the outcomes so that it could be view with ease.

The discussion was centered on whether segmentectomy should be employed as a treatment for metastatic lesions to the lung. One of the main factor for analysis was recurrence-free survival within the lung. Are there any data out there regarding recurrence of disease that is loco-regional (to the original site of disease) (i.e. colorectal)? I do think the term recurrence-free disease needs to be reclarify to refer to the original disease rather than in relation to the lungs.

It is difficult to discuss a secondary process in terms of whether or not this improved survival due to techniques/approaches alone. Are there any discussions of quality of life, preservation of lung function, time to chemotherapy, avoidance of chemotherapy, or other end points within the literature? Review of these other endpoints/outcomes may provide more granular details into whether a surgeon should spend time performing a more technically challenging operation when we haven't modified the biology of the original disease.

Answer E:
I am very grateful for the review.
Reference is made to deseasse-free time (DFT), understood according to the definition of National Cancer Institute (NIH) as “the length of time after primary treatment for a cancer ends that the patient survives without any signs or symtomps of that cancer”. And it also refers to pulmonary disease-free time (PDFT).
There are studies that evaluate results such as saving the lung parenchyma, such as the reference study 10.

Reviewer F

I would like to congratulate the authors for their great work writing the reviewed manuscript.
I have a few comments which I feel are important to consider during your re-visit for the paper.
Starting with the title where the description of anatomic resection should include, by default, segmentectomy, lobectomy, and pneumonectomy, while your discussion was focused only on segmentectomy and trying to compare the outcomes to wedge resection. I believe you need to change the title to " The role of minimally invasive sublobar resection in pulmonary metastasectomy" or to "The role of minimally invasive segmentectomy in pulmonary metastasectomy".

the second point, you described your study at line 79 as a SYSTEMATIC REVIEW while it's more of a review article. You should provide us with your methadology in a separate section if it is a systematic review.

The third point, your review focused on segmentectomy, as stated above in the first observation. you compared the segmentectomies' oncological outcomes and survival to wedge resection, and you described evidence of segmentectomy by VATS or Robotic to wedge resection. While based on your title, you should include lobectomy and pneumonectomy in your study. I suggest that if you prefer to keep the title without any changes, to include lobectomy and pneumonectomy outcomes in your manuscript or change the title to one of the suggested titles above (first comment) without major changes to the manuscript. I think this point is major and should be considered.
The fourth point is, your references need a further look considering inappropriate citations, as in reference numbers 6, 9, and 20, or repetition, as in numbers 16,18 and 34. Please consider this point, too.

Answer F:
I am very grateful for the review.
We have no problem changing the title. It is more appropriate " The role of minimally invasive sublobar resection in pulmonary metastasectomy"
That´s a mistake. It is a narrative review.
I add the references correctly. It is also true that there are three refernces that are the same.
It should be deleted. We leave references 16 and delete references 18 and 34.
Reference 2: Rusch, Valerie W. “Pulmonary Metastasectomy”. *Chest*, vol. 107, núm. 6, 1995, pp. 322S-331S, doi:10.1378/chest.107.6_supplement.322s.
Reference 6: Liu, Tianyu, et al. “Anatomical Resection Improves Disease-Free Survival after Lung Metastasectomy of Colorectal Cancer”. *Cancer Management and Research*, vol. 13, 2021, pp. 9429–9437, doi:10.2147/CMAR.S341543.

Reference 9: Berry, Mark F. “Role of Segmentectomy for Pulmonary Metastases”. *Annals of Cardiothoracic Surgery*, vol. 3, núm. 2, 2014, pp. 176–182, doi:10.3978/j.issn.2225-319X.2014.02.08.
Reference 20: Bédat, Benoît, et al. “Segmentectomy by Video-Assisted Thoracic Surgery for Pulmonary Metastases”. *Video-Assisted Thoracic Surgery*, vol. 6, núm. 0, 2021, pp. 7–7, doi:10.21037/vats-2020-lm-05.
Reference 31: Bawaadam, Hasnain, et al. “Lung Nodule Marking with ICG Dye–Soaked Coil Facilitates Localization and Delayed Surgical Resection”. *Annals of Thoracic Surgery Short Reports*, vol. 1, núm. 2, 2023, pp. 221–225, doi:10.1016/j.atssr.2023.02.010.