

Peer Review File

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Review comments

Reviewer A

Comment 1:

I would recommend to modify the title of the article (for instance: „Simultaneous minimally invasive bilateral pulmonary metastasectomy“), since a concrete comparison between simultaneous and staged minimally invasive approaches concerning the oncological outcome or postoperative complications is not the focus of this article.

Reply 1:

Thank you for reviewing our manuscript and providing constructive feedback and comments. We agree with you and have changed the title to “Simultaneous minimally invasive bilateral pulmonary metastasectomy.”

Change 1:

The title was changed to “*Simultaneous minimally invasive bilateral pulmonary metastasectomy.*”

Comment 2: The authors should comment on the results of the literature search concerning the number of articles dealing with the concrete topics.

Reply 2:

We agree with your point, and we added the results of our literature search to the manuscript.

Change 2:

We added the sentence to the Review articles section (Line 106-107). “*We identified 629 manuscripts and selected 40 for inclusion.*”

Comment 3: (line 285 – 295) I recommend to leave the sentences concerning bilateral lobectomy for lung cancer, since this is another topic and it would entail further questions that are not addressed here.

Reply 3:

We agree with you and we have deleted the sentences. We have also clarified when the past manuscript on primary lung cancer was utilized in “Review articles section.”

Change 3:

We removed the sentences.

~~“Zheng et al. compared one and two stage surgery groups in intercostal uniportal thoracoscopic bilateral lobectomy for primary lung cancer (25). There were no postoperative mortality and no significant differences in postoperative complications between the two groups. Univariate analysis of the one stage surgery group revealed that preoperative comorbidity, forced expiratory volume in one second (FEV1) of less than 2 liters, FEV1 % of less than 80 percent, and a total of 9 or more segments of lung resection were risk factors for postoperative comorbidities. However, it should be noted that the median age of the patients was 55.93 years and they were highly selected.”~~

We added these sentences to “Review articles section.”

Some of these literature sources included cases of simultaneous bilateral pulmonary resections for primary lung cancer. Due to the limited availability of the literature focusing solely on simultaneous thoracoscopic bilateral pulmonary metastasectomy, we included literature on primary lung cancer only when discussing intraoperative or immediate perioperative outcomes, as the targeted disease may not have a significant impact.

Comment 4: It may be helpful to add tables illustrating the published experiences with different approaches and technical variations such as the subxiphoid approach. I also recommend highlighting boxes summarizing the advantages and disadvantages of simultaneous and staged minimally invasive bilateral metastasectomies.

Reply 4:

We agree with you and have added a table illustrating features of various different approaches to bilateral pulmonary metastases and a highlight box.

Change 4:

We added the Table 1 and a highlight box.

Line 208-209

The clinical features of each surgical approaches were summarized in Table 1.

Table 1 Clinical features of surgical approaches for bilateral pulmonary nodules

surgical approaches	patient's position	changing patient's position	number of incisions	maximal size of incisions	approach to the posterior lung	compression of the heart	connection of bilateral thoracic cavities
conventional multiportal	lateral decubitus	Yes	four or more	N/A	easy	No	No
intercostal uniportal	lateral decubitus	Yes	two	3 to 4 cm	easy	No	No
subxiphoid uniportal with intercostal ports	supine	No	two or more	3 to 4 cm	less difficult	Yes	Yes
subxiphoid uniportal	supine	No	one	3 to 4 cm	difficult	Yes	Yes

N/A, not applicable

Highlight Box

Key findings

Simultaneous minimally invasive thoracoscopic bilateral pulmonary metastasectomy may be safe and feasible and may gain wider acceptance soon.

What is known and what is new?

The minimally invasive approach has been widely accepted as an alternative to conventional metastasectomy through thoracotomy, and the number of simultaneous bilateral surgery has been rapidly increased. Recently, various novel surgical approaches have been reported.

What is the implication, and what should change now?

The short-term outcomes of simultaneous minimally invasive thoracoscopic bilateral pulmonary metastasectomy have been gradually revealed. Further studies are necessary to assess long-term oncological outcomes.

Reviewer B

Comment 5:

Your conclusion is, that bilateral minimally invasive thoracoscopic pulmonary metastasectomy is safe and feasible, but you have not discussed the number of lesions being a limitation, nor did you discuss histology of the primary being a risk factor for missing small lesions (e.g. sarcoma metastases) and your own experience of 8 cases does not allow any general promotion of for bilateral VATS procedures.

Please discuss the number of metastases as limitation for VATS procedures and histology and than specify your conclusions.

Reply 5:

Thank you for your constructive comments. As you pointed out, the number of pulmonary metastases and the histology of the primary lesion were not discussed in this manuscript. We primarily focus on surgical procedures, intraoperative/ perioperative management, and short-term perioperative outcomes of bilateral surgery. As you mentioned, the surgical indications, including the number of metastases and the histology of the primary lesion are very important topics when discussing about pulmonary metastasectomy. However, these were not addressed in the context of bilateral metastasectomy. And the past literature focused primarily on surgical procedures and perioperative short-term outcomes. Therefore, we have incorporated your comments into the sections “Extent of lung resections,” and “Conclusion.”

Change 5:

We have added these descriptions to “Extent of lung resections” section.

Generally, the number of pulmonary metastases and the histology of the primary lesion are considered to have a significant impact on the prognosis of patients with pulmonary metastases. However, many studies have suggested that the number and histology themselves may not be the sole independent factors limiting pulmonary metastasectomy.

We have also added these sentences to Conclusion.

However, the surgical indications, including the number of pulmonary metastases and the histology of the primary lesion, as well as long-term outcomes, were not extensively discussed in the reviewed articles. Further studies are necessary to evaluate the surgical indications and assess long-term oncological outcomes, including a comparison of simultaneous and staged thoracoscopic bilateral pulmonary metastasectomy.

Comment 6:

Line 144: check the meaning of "chest all invasion"

Reply 6:

Thank you for your comments. The word "invasion" was changed to "damage."

Change 6:

The word "invasion" was changed to "damage." Line 153.

Comment 7:

Line 293: check the meaning of "comorbidities" (complications? morbidity?)

Reply 7:

We have eliminated the sentences include "comorbidities" according to the comments 3.

The term "complications" in Line 339 in the revised manuscript was changed to "morbidity."

Change7:

The term "complications" in Line 339 in the revised manuscript was changed to "morbidity."

Reviewer C

Comment 8:

However, even if minimally invasive surgery has gained popularity due to its undoubted advantages on the postoperative course, some of the studies you cited question the oncological results and outcomes derived from the inability of parenchyma palpation and there is no agreement one way or the other, if the undetected nodules have or have not a prognostic impact.

For example, a recent review of PM for sarcomas (<https://dx.doi.org/10.21037/asj-21-68>) explores the same topic applied to a specific pathology, both on the side of techniques and the oncological indications.

In my opinion, your paper deserves to be published with minor revisions, principally

expanding the discussion on whether or not this technique should be used and for what type of patients: it's not clear indeed in your center when you perform this kind of surgery.

Reply 8:

Thank you for providing insightful comments. The surgical indications, including the number of pulmonary metastases and the histology of the primary lesion, were not extensively discussed in this review as we primarily focused on surgical procedures and perioperative short-term outcomes. However, it is worth noting that several of the reviewed articles suggested that the number and histology may not be independent factors limiting pulmonary metastasectomy. Therefore, we have incorporated your comments into the sections “Extent of lung resections,” and “Conclusion.”

Change 8:

We have added these descriptions to “Extent of lung resections” section.

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Reviewer D

Comments 9:

It would be useful to expand the discussion focusing on methods for pre/intraoperative nodules finding (eg: radioguided Surgery)

Reply 9:

Thank you for your suggestion. We agree with you and have incorporated this comment into the topic “Surgical approaches.” (Line 224-227)

Change 9:

We added “*As another approach for unpalpable nodules, Kawada et al. reported the intrathoracic stamping method, which avoids puncturing the lung. In Japan, virtual-assisted lung mapping (VAL-MAP) using three-dimensional images and*

bronchoscopic dye injection has been widely accepted as a safe and reproducible procedure.” To Line 224-227.