

Peer Review File

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Review comments

Reviewer A

The role and benefit of minimally invasive repeat metastasectomy

The topic is an interesting one.

However, your article seems not to underline the right issues.

Reply: *Most parts of the write up has been edited and re-written to highlight the issues especially pertaining the role of minimally invasive surgery mentioned in a sub paragraph in Discussion/Main body.*

First of all, current evidence is that multiple (>3) metastasectomy is safer with a hybrid MIS (thus allowing palpation of the lung).

RPM with MIS is a safe procedure, but re-VATS is not realistic, with the risk of being time-consuming and of missing nodules.

This is the opinion of several authors, and the related bibliography is missing in your paper.

So the choice could be a hybrid procedure.

Reply: *This shortfall in multiple lesions in the lung was addressed in the paragraph under Discussion/ Main body under subtopic 'role of minimally invasive surgery'*

Reviewer B

Dear authors,

I agree with your argument. I only think that the article should be corrected by a writer for clarity. This is just an addition of summaries of different studies.

Reply: *There are no RCT and limited study availability making the write up challenging. Second, repeat pulmonary metastasectomy data were within studies studying pulmonary metastasectomy in general rather specifically. Third is, this is a narrative review and not a systematic review whereby I had to quote studies as accurately as possible to not alter original findings and results.*

Reviewer C

Thank you very much for providing me with the opportunity to review this manuscript. Several comments are listed below for the authors' consideration.

1. The discussion part is not well written. The title is “The role and benefit of minimally invasive repeat pulmonary metastasectomy”, but less than half of the discussion part is on minimally invasive surgery.

Reply: *The whole discussion has been rewritten with specific subtopic addressing this issue ‘Role of minimally invasive surgery’.*

2. Survival benefit for repeat pulmonary metastasectomy is influenced by the primary tumor histology. The first paragraph of the discussion part needs to be revised, taking this point into account.

Reply: *There is a sentence addressing the tumor histology affecting survival outcome in introduction. This issue has been discussed in further detail in Discussion/ Main body under subtopic ‘role of repeat pulmonary metastasectomy in various primary cancers.’*

3. Abbreviations should be used more properly.

Reply: *The abbreviations errors in the manuscript has been corrected.*

Reviewer D

Thank you for the opportunity to review the manuscript with title: The Role and Benefit of Minimally Invasive Repeat Pulmonary Metastasectomy.

The study investigates a very interesting aspect of the pulmonary metastasectomy. However, changes in the manuscript are requested. The authors performed a general analysis concerning repeated metastasectomy. I think that they should more concentrate on analyzing in a special section study, that are associated with repeated metastasectomy with VATS (VATS-RPM). Here, if possible, a comparison between VATS and open thoracotomy should be made. Results and conclusions of studies that investigate VATS-RPM could be analyzed in a separate table. As the article is mainly a narrative review, if all changes in the manuscript are not possible, it should be included in a separate section of limitations.

Reply: *Table 2 in this review addresses the results of RPM. However, when comparing VATS and thoracotomy, the available results available are all comparing just pulmonary metastasectomy in general. No studies provide data mentioning repeated pulmonary metastasectomy using thoracotomy versus VATS approach. Hence this study discussed this issue. Agree this is the limitation of the study and this has been addressed in subtopic ‘Role of minimally invasive surgery’ under Discussion/ Mainbody.*

Reviewer E

Dear Authors,

I have read with interest your manuscript on repeated pulmonary metastasectomy (RPM), since I'm very fond of this topic. The aim of the work is undoubtedly

fascinating, since the role of VATS and other minimally invasive techniques in pulmonary metastasectomy is highly debated. Anyway, I have several concerns on this work, which are worth to be considered.

Major concerns

The work, although being intended as a narrative review of minimally invasive approach applied to RPM, does not deeply analyze this specific topic, rather generally talking about the RPM and confining the minimally invasive approach only to a chapter.

Reply: *The chapter has been expanded and many more citations have been added to make minimally invasive approach more comprehensive. There is a subtopic discussing minimally invasive approach in Discussion/Mainbody.*

The available minimally invasive techniques are not adequately discussed (eg. RATS?).

Reply: *There is a paragraph discussing this topic in the ole of minimally invasive surgery.*

Some authors believe this technique should be reserved to extremely selected cases with few known lung metastasis (1-2 nodules), since in case of higher number of nodules, the benefit of palpating the lesions and performing precision nodulectomy through mini-thoracotomy still defeat the benefits of VATS. This point is not even considered in the work.

Reply: *This point is mentioned in second paragraph, in the subtopic 'Role of minimally invasive surgery'.*

Is there different OS for RPM applied to different histologies? Are there indications on applying VATS only in selected histologies?

Reply: *This issue is addressed in Discussion/ Main body whereby there is a subtopic on the 'Role of repeat pulmonary metastasectomy in various primary cancers.'*

Lines 173-175; why do you assert that? The cited references (15, 17, 34) do not even discuss on VATS topic.

Reply: *This has been deleted and only relevant points are discussed in a more systematic manner.*

I think that before concluding as this work has done ("it can be safely concluded MIS...could achieve metastasis detection for removal...in a safe and effective manner), deeper discussion should be performed.

Reply: *This has been done and mentioned in conclusion.*

Minor concerns

Table 1 has to be fixed, in line 1, 4 and 7 n° of procedures and n° of patients are inverted.

Reply: *This has been corrected*

English language has to be completely revised.

Reply: *This has been corrected with aid of English language department.*

Good luck!

Best regards.