Peer Review File

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Reviewer A

1. In the abstract, the authors state: 'Malignant pleural mesothelioma is an aggressive cancer for which there remains no standardized treatment regimen, although surgery is essential to achieve tumor control.'
> The role of surgery for early-stage remains somewhat controversial and in more advanced disease, there is no evidence for the benefit of surgery, so this statement is not entirely correct.
- Thank you for this point. The sentence has been modified to be more accurate.
> Platinum plus pemetrexed has been established as the standard first-line regimen (in the non-surgical and surgical setting) since the Vogelzang study; in addition, the Checkmate 743 trial has led to nivolumab/ipilimumab having been registered as first-line treatment, so the 'absence of a standardized treatment regimen' (outside of the surgical setting) is also somewhat incorrect.
- We agree with this point; the intent of these sentences was to reference the controversy around timing of therapies and surgical intervention. The abstract has been slightly modified in attempt to clarify this.

2. This manuscript deals with early-stage, operable mesothelioma, but speaks of mesothelioma in general without clearly defining this. A paragraph on which patients/tumours are surgical candidates is relevant and should be included in this manuscript.
- Agree, this has been added in the introduction.

3. The authors state in the introduction that 'the successful surgical removal of macroscopic disease sets the stage for multimodal adjuvant therapy in this deadly malignancy'. Many multimodality protocols in mesothelioma contain neoadjuvant chemotherapy; therefore, this statement is confusing. Whether neoadjuvant or adjuvant chemotherapy is to be preferred is currently being investigated by the EORTC 1205 trial, which is also trying to standardize/uniformize extended pleurectomy/decortication.
- Thank you for bringing this to our attention; the sentence has been corrected.

4. The authors state in the results that 'an MRI may be useful as well'. Could they explain to the readers the added value of chest MRI, if this is not covered by another review?
- Further explanation on the utility of MRI has been added to the text

5. The authors use a single S-shaped posterolateral thoracotomy in the 5th intercostal space to perform their pleurectomy/decortication. Are there patients in which a second thoracotomy is required to access and remove all pleura and the involved diaphragm?
We do not routinely perform more than one thoracotomy to access the chest.

6. There is much more data available on surgery in MPM, including results from phase II trials (EPP), controversies (MARS trial), and trials in progress (e.g. the MARS2 trial in the UK,

randomizing between surgery (pleurectomy/decortication) and no surgery), but discussing this may not be the goal of this review? I would add a more extensive discussion on surgery, though, as it may substantially increase the quality of the manuscript.
Thank you, we added a reference to the MARS trials. Since there is a separate article to be written on EPP we did not include phase II trials on that technique.

Reviewer B

The authors have attempted a discussion on radical pleurectomy with decortication alongside its technical considerations.

1. The introduction fails to set up the background for discussion, instead the authors reference historical data on EPP and nomenclature, which nomenclature however I think they fail to follow in their main text.

Thank you for this feedback.

2. A few of the papers referenced are fairly old and, surprisingly, the MARS trials are not mentioned at all.

   - References have been updated and include the MARS trial.

3. The discussion is limited to providing a description of a surgical technique in a fairly 'generic' manner. The authors note but don't 'discuss' decisions related to selection, technique and management of patients.

Overall, in its current form, this manuscript does not provide enough arguments to support the attempted discussion and it is restricted mainly in giving an overview of the institution's surgical approach.

We have added additional information regarding the selection and management of the patients. The article discusses the technique of extended pleurectomy/decortication as well as modifications that do not require resection of the diaphragm and/or pericardium.

Reviewer C

In my opinion, this is an excellent review on the merits of lung sparing surgery -and specifically pleurectomy/decortication (PD)- for malignant pleural mesothelioma, with a detailed description of the surgical technique for this procedure.

I have a few questions/comments as follows:

1. Since talc pleurodesis is sometimes applied at thoracoscopy following diagnostic pleural biopsies

in mesothelioma, I wonder about the author´s opinion on this approach, especially when the patient is likely to undergo surgery afterwards. Would previous talc poudrage make PD surgery more difficult or problematic?

- many of us find that talc helps fuse the parietal and visceral surfaces and gives some substance to the tissue that needs to be resected. Many of us feel this makes dissection easier in the setting of minimal disease but may go either way for bigger tumors. Generally, we avoid talc because it's unnecessary in someone who is going to undergo resection.

2. On the last paragraph of the "Introduction and Background" section (page 7, line 1), the authors mention that some of the techniques that might be applied after PD surgery (photodynamic therapy and hyperterthermic intracavitary chemotherapy) "are discussed elsewhere in this issue" (sic). I assume that those specific techniques are discussed in detail in other articles that are probably included in a monographic issue dedicated to treatment of malignant pleural mesothelioma (MPM). This would imply that the interested reader would need to asses those specific articles -besides the current one- to get the full picture on treatment of MPM, However, I believe that adding a comment from the authors on those particular techniques in the present review would be a great help for the interested reader.

- thank you for your comment; due to the particular focus of this manuscript and the complexity of those other mentioned techniques, on completion, the editors will add in specific references as details of these techniques are beyond the scope of this review.

Reviewer D

Thank you for inviting me for reviewing an excellent review article on surgical treatment for malignant pleural mesothelioma (MPM). I enjoyed the manuscript, and strongly agree to the conclusions mentioning that P/D is an appropriate surgical approach for resectable MPM. The authors presented detailed preoperative, intraoperative, and postoperative management, which provide important information to readers of ASJ. However, the authors presented no detailed information about visceral pleurectomy, which is the most critical and important step of P/D. I strongly recommend that authors provide information about surgical techniques of visceral pleurectomy with discussion about its surgical issues.

- Thank you, further information on visceral pleurectomy has been added.
