Peer Review File

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Reviewer A

This is a well-written article, covering all relevant information. I have some minor suggestions, though, and I found a number of small errors.

(41) benign chest diseases > perhaps benign or malignant?. Symptoms of dyspnoea (pleural effusion) or pain (invasion in chest) may also be caused by lung cancer; many asbestos exposed blue-collar workers are also (former) smokers. A presentation also often underestimated is early-stage mesothelioma presenting as primary pneumothorax. In an asbestos-exposed individual with unexplained pneumothorax, vigilance for mesothelioma is essential. Great points, thank you. I incorporated these additions in the Introduction paragraph. (52-54)

(47) tissue diagnosis is critical > in addition, in some countries tissue diagnosis is required to have mesothelioma recognized as an occupational disease for which compensations are provided Added into the Introduction paragraph. Thank you! (57-58)

(114) Unilateral pleural effusion, pleural thickening, and invasion of invasive structures are the usual findings > what is invasion of invasive structures? I assume the authors mean invasion of chest wall or mediastinum? Great catch I have made the adjustment. (205)

(115) Limitations of CT imaging include difficulty estimating chest wall and mediastinal invasion as well as involvement of the peritoneal cavity > CT is also often unable to differentiate between benign and malignant causes of pleural effusion. Thank you (207)

(122) pleural calcification > which is not a symptom of mesothelioma but benign asbestos exposure good point, thank you I've added the clarification (215)

(133) It is difficult to differentiate MPM from other malignancies or even benign disease based only on the above findings > something that is relevant to be mentioned is that a cytological or even biopsy-based diagnosis of mesothelioma in a patient very unlikely to have mesothelioma (e.g. young woman with spontaneous pneumothorax and 'biopsy-proven' mesothelioma) may be a false-positive case, as reactive mesothelium (e.g. after a chest drain) may appear very 'malignant'. It is therefore important to discuss the case multidisciplinary and not to 'believe' the pathologist (who often receives hardly any clinical information). Some cases may be extremely complicated. (227) I agree with the points you have made and that the entire clinical picture needs to be taken into account.

(149) FD- PET followed by thoracoscopy > FDG-PET is correct fixed (244)

(155) FDG-PET had a sensitivity of 88% and sensitivity of 93% for malignant disease > sensitivity

of 88% and specificity of 93%, I assume. If correlated with clinical information (asbestos exposure) performance might even increase, I would guess I completely agree. 253

(163) The role of MRI in diagnosis of MPM is primarily focused on determining resectability > MRI is not routinely used in surgical trials for MPM, a reason being that chest MRI requires an experienced radiologist. 260 great addition

(194) Loss of BAP1 and deletion of p16 seen in mesothelioma but not reactive mesothelial cells could be a useful adjunct for cytologic diagnosis > our pathologist considers loss of BAP-1 in pleural effusions sufficient to confirm the diagnosis I was trying to list both, rather than imply that both are needed. I clarified. Thanks! (137)

(197) Core needle biopsy is an option for diagnosis > agree, but there are several reasons why we usually prefer a thoracoscopy: more tissue (molecular testing becoming more and more important), invasive evaluation of the extension of the disease (important in early-stage if surgical multimodality treatment is an option), and the option to perform a talc pleurodesis (given the fact that most patients present with pleural effusions) Thank you I added this to the paragraph discussing thoracoscopy (145)

Reviewer B

The article presented the current TNM and previous staging systems for malignant pleural mesothelioma and radiological and surgical modalities useful to establish the stage of a disease. A histopathological diagnostics is discussed very superficially but it is not the key topic of this paper and may be accepted, in my opinion.

The manuscript is interesting, however, it contains a lot of mistakes or inaccuracies that should be corrected. The most important are:

1. Page 4, Line 72: According to TNM 8 Ed., the stage T2 refers to tumor involving parietal OR visceral pleura and not necessarily both of them as it is suggested in the sentence. (90) I clarified the wording, Thank you.
2. Page 5, Lines 97-98: The sentence is not clear and seems to be incomplete, please, revise it. I have revised this sentence.
3. Page 8, Lines 157-158: A term „sensitivity" is used twice instead of sensitivity and specificity. (253) changed, thank you
4. Page 8, Line 159: Is the mean SUV value „0.8 ±" for benign lesions correctly written? It seems to be incomplete, please, revise it. I have revised the sentence and added the missing metric Thank you (256)
5. Page 11, Lines 232-233: Mesothelin can be expressed by the tumors/tissues and not by patients. The sentence is inconsistent. I have clarified this sentence (177)

There is also a number of linguistic mistakes that should be proofread. Thank you for this feedback.

We have gone over the manuscript again critically looking for these mistakes.

Reviewer C

The article is a good comprehensive review of the literature.

I would recommend rearranging the staging into clinical TNM, and pathological stage , currently the surgical staging is in the clinical stage and pathological is defined later. Thank you for this comment. I have rearranged the text.

Also the paper would benefit from adding tables with a comparison. I have added 3 tables detailing the comparison of the 7th and 8th editions in respect to TNM.

Lastly , volumetric staging has also been proposed and would merit inclusion for completion. Please see below references. I have added volumetric staging under its own heading. Thank you for the references.

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