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RESPONSE TO REVIEWERS

REVIEWER A

The manuscript tries to address the role of the imaging in the management of malignant pleural effusion caused by unknown primary tumor. The topic is actual and interesting, considering the great number of MPE caused CUP that could be found currently. The manuscript appears as an accurate overview of the literature, but there are some concerns and questions that should be clarified.

Comment 1: The text presents several grammar errors and a friendly language, I suggest a revision by mother tongue reviser.

Reply 1: I'm completely agree with you. The text was corrected by mother tongue reviser

Comment 2: Material and methods should be more precise and theoretically it may allow a reproduction of the result that authors found.

Reply 2: You are right. I modified the "Methods" section as you suggested. I inserted "search strategy", "study selection" and "data extraction"

Comment 3: The analysis of the PET and CT scan role is quite messy moreover, indications, timing, advantages and risks should be described thoroughly.

Reply 3: As you suggested, I corrected the analysis description of the total-body PET/CT and CT. However, the available Literature on the role of the two techniques in the malignant pleural effusion (MPE) in the course of cancer unknown primary site (CUP) is very poor and no clear indications are available

Comment 4: Conclusions are not supported by data reported.

Reply 4: Although some papers reported good specificity and sensitivity values (Table1), PET/CT is not the first step in the differential diagnosis of pleural effusion. Based on my analysis review CT scan should be used in the first instance

REVIEWER B

The manuscript is focused on the role of CT Scan and the 18F-FDG PET/CT in the management of malignant pleural effusion caused by unknown primary tumor. The topic is extremely specific, and authors provided an accurate overview of the literature adding interesting comparative tables. Nevertheless, there are some concerns.

Comment 1: The text should be checked by a mother tongue reviser because there are several grammar error and incorrect sentences.

Reply 1: You are right. I modified the paper as you suggested. The paper was checked by mother tongue reviser

Comment 2: The introduction is too generally and informative, it may be set more on the topic and with a critical and scientific appearance.

Reply 2: As you suggested, I modified the introduction. I'm agree with you but the Literature is very poor regarding to diagnostic strategy in MPE patients due to CUP.

Comment 3: Methods does not allow a correct definition of the real method used by authors in this article due to absence of inclusion and exclusion criteria of the articles reported.

Reply 3: I'm agree with you. I modified the "methods" section by inserting three subparagraphs "search strategy", "study selection" and "data extraction".

Comment 4: In the PET/CT paragraph are reported different articles focused on the role of PET/CT in the management of MPE but they are described in unorganized manner and it is not clear the real role and the effectiveness of the PET/CT.

Reply 4: As suggested, I checked the PET/CT paragraph. Actually, PET/CT is not the first step in the differential diagnosis of malignant from benign pleural effusion. The PET/CT could be useful in the localization of the tumor primary site.

Comment 5: In the discussion chapter, conclusions are not supported by the previous analysis. It appears clear the CT scan role in the early management of MPE but the PET/CT role is discussed lightly and unclearly. Moreover, their role in the CUP is barely analyzed.

Reply 5: Thank you for you precious comment. Although some papers reported good specificity and sensitivity values, PET/CT does not provide more informations than CT in the differential diagnosis of pleural effusion and PET/CT is more expensive. In the Literature does not exist

articles that explain the role of PET/CT and CT in MPE patients with CUP and then, I mainly focused my analysis in the ability of the two radiological techniques in differentiating malignant from benign pleural effusion