Author’s response to reviews

Title: 18F-fluorodeoxyglucose–positron emission tomography/computed tomography for the diagnosis of polymyalgia-like illnesses: A retrospective study

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Author’s response to reviews:

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BMC Rheumatology
Editor
Dr. James Mockridge

Dear Dr. Mockridge

Please find our revised manuscript entitled “18F-Fluorodeoxyglucose–Positron Emission Tomography/Computed Tomography for the Diagnosis of Polymyalgia-like Illness,” which we would like to submit for publication in BMC Rheumatology as a concise communication. Our manuscript includes two figures and three tables.

The answers to the reviewers and revised points are attached below.

The symptoms of various inflammatory conditions such as infection, vasculitis, arthritis, myositis, and neoplasms may be similar and sometimes fulfill the diagnostic criteria of PMR. Therefore, it is often difficult to distinguish PMR from the so-called “polymyalgia-like illness”. 18F-FDG–PET/CTs has been adapted for diagnosing PMR, and FDG accumulation in the PMR-specific sites has been reported. Moreover, to the best of our knowledge, there are no imaging studies that have compared PMR and polymyalgia-like illness.

In the present study, we compared the FDG–PET/CTs findings between PMR and polymyalgia-like illness. Interestingly, patients with polymyalgia-like illness showed significantly low FDG accumulation in PMR-specific sites. Various patterns of FDG uptake in patients with polymyalgia-like illness revealed the diversity of pathogenesis in similar clinical presentations. Moreover, along with the
current diagnostic criteria, the accumulation pattern of FDG in PMR-specific sites may increase the accuracy of diagnosing PMR.

We believe that the findings that have been described in the present study will be of special interest to the readers of BMC Rheumatology.

The manuscript has not been submitted and is not currently being submitted elsewhere until a decision has been made as to its publication in Rheumatology and no portion of the data has been or will be published in proceedings or transactions of meetings or symposium volumes. All the authors have read the manuscript and have approved this submission.

We would be grateful if the manuscript is reviewed and considered for publication in Rheumatology.

Thank you very much for your consideration.

Sincerely yours,

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Answer to the reviewers

We appreciate the reviews of our manuscript. We have revised our manuscript in accordance with the advice and insights of the reviewers, as discussed below.

For reviewer 1:

We appreciate your advice and suggestions. As per you suggestions, we have made several revisions to the manuscript and hope that its quality has been improved accordingly.

Major concerns.

Some parts of the manuscript are quite difficult to read. In particular, some sentences that might need clarification or rephrasing are:

1. In the abstract, the explanation of the visual score (the comparison with the liver uptake) and, in the results, the part on "FDG-accumulation"

Response: We have added the VAS score in the method section of the abstract and modified the result section to indicate that FDG accumulations were recognized at the PMR-specific sites (page 2, lines 32-34 and 39-40).
2. Page 3 line 52: "The diagnostic criteria consist of non-specific symptoms and laboratory signs of inflammation": these are not the diagnostic criteria rather the clinical presentation; some of these features are included in different sets of diagnostic criteria.

Response: Because the symptoms of PMR are similar to those of other inflammatory diseases, we have deleted this description (page 3, line 52).

3. Page 3 line 63: I would use "the presence of uptake" rather than "positive results"

Response: We have corrected this phrase according to your suggestion (page 3, lines 62-63).

4. Page 4 line 77: "we also evaluated their condition" is not clear

Response: We have included some details to clearly explain what the “condition” meant in the methods section (page 4, line 76-77).

5. Page 5 line 120: instead of "Ps" I would rather use "p values"

Response: We have made this change according to the reviewer’s suggestion (page 6, line 122).

6. Page 7 line 145: I would add "mean" between "the" and "value".

Response: We have corrected the same accordingly (page 7, line 147).

7. Page 2 line 30: "FDG-PET/CT scan" instead of "FDG-PET/CTs"

Response: We have made the changed according to the reviewer’s suggestion (page 2, line 29, and page 4, line 95).

8. Page 3 line 51: maybe I would consider "stiffness in" rather than "stiffness of"

Response: We have corrected this error accordingly. (page 3, line 51).

9. Page 6 line 141: "out of the 17 patients" or "among the 17 patients" instead of "from"

Response: We corrected this and included “among the 17 patients” in accordance with the reviewer’s suggestion (page 6, line 143).
10. Some general observations: Authors refer to the uptake of the spinous processes, but it is reputedly the uptake of the interspinous bursae

Response: We reread the reviewer’s paper (Arthritis Res Ther. 2014;16[6]:492). We have corrected the term according to the reviewer’s suggestion (page 2, line 31; page 3, lines 59-60 and 62; page 5, lines 101 and 116; page 8, Table 2; page 9, line 172; page 17, line 359).

11. When Authors listed the diagnosis of the control group, the one patient with undefined diagnosis is not mentioned in the abstract.

Response: We apologize for this error; we have included the one case of undefined diagnosis (page 2, line 37).

12. The captions of the tables should not contain results or comments (“We found significant differences between the two groups using the Mann-Whitney U test”) but should be only descriptive

Response: We have corrected the caption of Table 2 in accordance with the reviewer’s suggestion (page 9, lines 165-166).

13. How the Authors define abnormal uptake when using the SUV instead of the visual score?

Response: According to the reviewer’s previous report, we mainly used the visual scoring system because we found no standardized reference values for joint SUVs. We used SUV for comparing the patients with PMR and those without PMR. We have added the explanation in the Methods section (page 5, lines 107-109).

14. The last sentence of the Result section is an interpretation and should be moved into the Discussion section

Response: The content of this sentence already appears in the Discussion section (page 12, lines 222-225); therefore, we have deleted the last sentence of the Results section (page 9, line 166).

15. Page 12 line 228: in my view, this assertion is too strong on the basis of the presented data

Response: We agree with this comment because the population in this study was small and MMP3 values vary widely. We have revised this sentence accordingly (page 12, lines 234–236).

16. Reference 19 should be before the dot.

Response: We have revised this error accordingly (page 11, lines 213-214).
17. I would kindly suggest to the Authors to consider an English language editing.

Response: The manuscript was already reviewed by an expert medical editor in English. However, the review seems to have been inadequate. We have used a commercial proofreading service by an expert medical editor in English again. We hope the manuscript is now better and at least understandable.

For reviewer 2,

We appreciate your advice and suggestions. As per you suggestions, we have made several revisions to the manuscript and hope that its quality has been improved accordingly.

Major Concerns:

1. In table 1, P value about MMP-3 is 0.04, however the authors wrote "the difference was not significant" at p.12 line 229. Considering the result from table 1, it seems to be statistically significance. Why the authors described "not significant."?

Response: We agree with your comment and apologize for using the incorrect word. We hesitated with using “significant” because the population in this study was small, MMP3 values varied widely, and the p value was not that small. We have corrected the manuscript and included the following sentence; “…the serum MMP-3 levels were significantly higher in patients with PMR…” (page 2, lines 37-38, and page 12, lines 234-235).

2. The detailed accumulation sites of non-PMR should be described. There were no FDG accumulation at other site except PMR-specific site such as shoulder, sternoclavicular joint?

Response: We have included a column in the Table S1 listing the FDG accumulation sites other than PMR-specific sites in non-PMR patients, and we have added the explanations in the manuscript (page 9, lines 169-170).

3. The author said that multivariate logistic regression analysis showed that FDG accumulation in the shoulder joints was identified as independent predictor of PMR. The authors have to describe table of multivariate analysis. In this study, the number of patients was very low so, the reliability of multivariate analysis was very low.

Response: We have included a new table (Table 3, page 10), listing results of the multivariate regression analysis, and we have modified the limitations of the multivariate analysis in the discussion section (page 12, lines 224-225).