

Dear Reviewer:

Thank you for your letter and for the reviewer's comments concerning our manuscript entitled "Diagnostic value of elevated serum carbohydrate antigen 125 level in sarcoidosis" (ID:75582). Those comments are all valuable and very helpful for revising and improving our paper, as well as the important guiding significance to our research. We have studied the comments carefully and have made corrections which we hope meet with approval. The main corrections in the paper and the responses to the reviewer's comments are as follows:

Reviewer 1#:

Response to comment: The manuscript titled "Diagnostic value of elevated serum carbohydrate antigen 125 level in sarcoidosis" is interesting. Report classification: Good. I accept the publication of manuscript. The authors must: add exclusion criteria, correct some spelling errors and adapt some references to the guide of the journal.

Response to Reviewer 1#:

1. Add exclusion criteria

Response: We gratefully appreciate your valuable suggestion. Thank you for your comments. Because the purpose of this study was to investigate whether the serum CA125 level of patients with sarcoidosis can be used as a potential biomarker for disease diagnosis, it is necessary to exclude diseases that may cause elevated CA125 levels and the differential diagnosis of sarcoidosis. Previous research have found that pulmonary tuberculosis and tumors including ovarian cancer can cause elevated serum CA125 levels, so it is necessary to exclude such diseases. We added the exclusion criteria for this study in the patients section of the method section, including 'Exclusion criteria included the coexistent diagnosis of cancer, tuberculosis, or any other rheumatologic diseases, or missing clinical data.'

2. Correct some spelling errors

Response: We gratefully thanks you for the precious time the reviewer spent making constructive remarks. Based on your suggestion, we have revised the article for expression and language errors. We resubmitted the revised article for polish and got the relevant certificate.

3. Adapt some references to the guide of the journal

Response: Thank you so much for your careful check. We have rechecked the references in this article and adjusted the format and content of the references according to the journal guidelines. On request, we make adjustments to the text font. In addition, because of content adjustments, we have added two references that are background descriptions of the definition and incidence of the scadding's classification of stage IV pulmonary sarcoidosis.

Response to Reviewer 2#:

1. The author should explain why Scadding's classification is classified between as 0-3 and not 0-4.

*Response: We totally understand the reviewer's concern. Patients with stage IV sarcoidosis mainly present with irreversible pulmonary fibrosis, and the proportion of patients with this type is relatively small compared with the patients with previous stages. Because of the 108 patients with sarcoidosis included in this study, there were no patients with stage four. This may be related to the less frequent occurrence of stage IV patients in the population. Hok Sreng Te et.al conducted a retrospective data collection and analysis of 187 subjects with biopsy-proven sarcoidosis at a tertiary center. Among their result, they reported 4 cases of Stage IV among 184 sarcoidosis patients (1). In the future, we should include more patients and explore the differences in CA125 levels between patients in this stage and those in other stages. We should present it in the Results and explain and describe the issue in detail in the Discussion. We've added descriptions in the result 'CA125 expression was closely associated with clinical features of sarcoidosis' section, including 'Scadding's classification for the total 108 patients led to 2 patients being classified as Stage 0, 35 as Stage I, 49 as Stage II, 22 as Stage III, and 0 as **Stage IV.**' And we added possible explanations for this result in the discussion section, including 'However, none of the patients included in this study were defined as stage IV of Scadding's classification, which may be related to the lower incidence of sarcoidosis with pulmonary fibrosis features on chest imaging [27, 28]. In the future, more patients with Scadding stage IV need to be further included to explore the differences in CA125 levels with patients with other stages.'*

1. Te HS, Perlman DM, Shenoy C, Steinberger DJ, Cogswell RJ, Roukoz H, et al. Clinical characteristics and organ system involvement in sarcoidosis: comparison of the University of Minnesota Cohort with other cohorts. BMC Pulm Med. 2020;20(1):155.

27.Scadding JG. Prognosis of intrathoracic sarcoidosis in England. A review of 136 cases after five years' observation. Br Med J 1961; 2: 1165-1172 [PMID: 14497750 DOI: 10.1136/bmj.2.5261.1165]

28.Iannuzzi MC, Rybicki BA, Teirstein AS. Sarcoidosis. N Engl J Med 2007; 357: 2153-2165 [PMID: 18032765 DOI: 10.1056/NEJMra071714]

2. "In the current study, we evaluated the serum CA125 levels in a cohort of 108 sarcoidosis patients and compared the results to those from a cohort of 112 healthy controls. This represents, to our knowledge, the first retrospective study evaluating the association of the levels of CA125 with clinical characteristics and suggesting that CA125 could be a potential diagnostic biomarker in sarcoidosis." paragraph should be moved to materials and methods.

Response: We gratefully appreciate your valuable suggestion. It is really

inappropriate to put this paragraph of text in the background section. Our study included 108 patients with sarcoidosis and 112 healthy controls, and their serum CA125 levels were measured. We revised the language and placed the main content in the methodology section.

Again, thank you for giving us the opportunity to strengthen our manuscript with your valuable comments and queries. We have worked hard to incorporate your feedback and hope that these revisions persuade you to accept our submission. Thanks again to the reviewers and editors for your hard work! Best wishes to you!

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