

## **Reviewer #1:**

**Scientific Quality:** Grade B (Very good)

**Language Quality:** Grade B (Minor language polishing)

**Conclusion:** Minor revision

**Specific Comments to Authors:** The manuscript entitled "Use of alkaline phosphatase to pre-albumin ratio as an independent predictive factor for the prognosis of gastric cancer" contains a series of experiments testing the value of using alkaline phosphatase/per-albumin ratio as a prognostic tool for early diagnosis of gastric cancer condition. After a deep revision, I found this work is interesting with certain novelty. However, some minor concerns are raised to improve this manuscript.

### **1- Minor English language editing is required.**

**Reply:** Thank you for your comments, and we are sorry for the language quality. We have asked the company to further polish and modify the language.

### **2- No sample size calculation**

**Reply:** Thank you for your professional advice. I'm sorry that our presentation is not perfect and we have made the revision of the statement in the material and method section. In total, 985 patients with types of tumors underwent treatment, and we removed the patients who couldn't meet the criteria. Finally, 409 patients were remained. Among the patients, 353 patients underwent surgeries, and 56 patients with metastasis gave up operation.

### **3- Exclusion criteria should contains renal problems and lung problems**

**Reply:** Thank you for your professional advice. We have made the revision of the statement in the material and method section. In our study, we excluded the patients who had other diseases or tumors that could affected the expression of ALP significantly. And the patients we selected had no renal or lung problems, which could affect the expression of ALP or PA.

## Reviewer #2:

**Scientific Quality:** Grade C (Good)

**Language Quality:** Grade B (Minor language polishing)

**Conclusion:** Minor revision

**Specific Comments to Authors:** This is an interesting study that proposes the use of the ALP to prealbumin ratio (APR) as a prognostic marker for gastric cancer (GC) based on 406 patients from their institution. The introduction mentions that ALP has been described as an independent prognostic marker in GC **but it is unclear why the authors would suggest using the APR rather than the ALP directly as the reason for this is not elucidated.**

**(Reply:** Thank you for your professional advice. ALP has been studied as an indicator of prognosis in gastric cancer, although just few such articles. We gave relevant explanations and references in the introduction and discussion section of the article. On the other hand, we considered the prealbumin as an indicator to observe the nutritional status of patients. The combination of ALP and PA may better reflect its predictive function in the prognosis of gastric cancer. In fact, we combined ALP with multiple prognostic indexes which had been applied in GC, such as neutrophils, lymphocytes and so on, but the results were not ideal. Only the combination between ALP and PA was acceptable in prognosis evaluation, so we chose ALP and PA instead of ALP alone for further analysis).

**There was also no mention if this ratio has been explored in other cancers e,g, there has been some studies on lung cancer.**

**(Reply:** Thank you for your professional advice. We searched for relevant articles again but no such articles describing the function of ALP and PA ratio in cancers. We tried several researching strategy including "(alkaline phosphatase[Title/Abstract]) AND (prealbumin[Title/Abstract])", "(alkaline phosphatase[Title/Abstract]) AND (prealbumin[Title/Abstract] AND cancer[Title/Abstract])", "(alkaline phosphatase[Title/Abstract]) AND (prealbumin[Title/Abstract] AND tumor[Title/Abstract])", "(ALP[Title/Abstract]) AND (PA[Title/Abstract] AND cancer[Title/Abstract])", "(ALP/PA[Title/Abstract]) AND cancer[Title/Abstract]", "(ALP/PA[Title/Abstract])", and so on. Maybe our searching strategy is not perfect. We will further study and read other experts' articles to improve our own research).

**It would be also interesting and useful to compare ALP by itself versus APR to understand the added value of the new proposed "marker".**

**(Reply:** Thank you for your professional advice. Firstly, ALP has been studied as an indicator of prognosis in gastric cancer, although just few such articles. Secondly, your professional advice is consistent with our study which we are preparing now. We are collecting the relevant patients for the next comparison of multiple indexes combining with ALP or not, and the exclusive criterial is not same with that in this article).

**The materials and methods section does not clearly state how many of the patients underwent surgery and there was also no description on how raised ALP from liver and bone disorders was excluded, for example, was CT liver done routinely to exclude liver pathology, or was bone scan done to exclude occult bone metastases.**

(*Reply:* Thank you for your professional advice. I'm sorry that our presentation is not perfect and we have made the revision of the statement in the material and method section. In total, 985 patients with types of tumors underwent treatment, and 353 patients underwent surgery. In our study, the patients reserved were GC patients without other tumors, liver or bone diseases, so the patients were excluded once they were diagnosed to have the relevant diseases).

**There was also no mention on whether those with higher ALP later developed bone and liver mets more commonly than those with lower or normal ALP levels.**

(*Reply:* Thank you for your professional advice. In our study, excluding the 56 patients with metastasis when they were in hospital, 3 patients had liver metastasis, 2 patients appeared brain metastasis, 1 patient had pancreas metastasis, 1 patient appeared bone metastasis, and 1 patient had lung metastasis. The patient number was low and the result was not accurate for statistics, so we didn't mention the relationship between APR and the type of metastasis. We will analyze it when the sample size is appropriate for statistics).

**It will be good also to understand if adjuvant therapy was added to any of the patients,**

(*Reply:* Thank you for your professional advice. The patients we chose for the study had no relevant adjuvant therapy and the relevant indexes were collected when they were in hospital in order to avoid the influence of adjuvant therapy)

**and also if nutritional assessment and support was done for any of the patients with low prealbumin.**

(*Reply:* Thank you for your professional advice. Before the surgery, we would assess the patient's relevant indicators, and if there is a low protein condition, we would conduct relevant treatment. In our study, the indicators we collected were pre-treatment data, so it did not conflict with our treatment plan. Secondly, we are now collecting the data of these indicators before and after surgery, but the number of patients is currently small due to different treatment options and various exclusion conditions, and we are still collecting further.)

**There is a need for minor language revision.**

(*Reply:* Thank you for your comments, and we are sorry for the language quality. We have asked the company to further polish and modify the language.)

## Issues raised by *Science editor*

**(1) I found the authors did not provide the approved grant application form(s). Please upload the approved grant application form(s) or funding agency copy of any approval document(s);**

**Reply:** Thank you for your comments. We have prepared the approved grant application form(s) or funding agency copy of any approval document(s). If any problems, please email us with no hesitation.

**(2) I found the authors did not provide the original figures. Please provide the original figure documents. Please prepare and arrange the figures using PowerPoint to ensure that all graphs or arrows or text portions can be reprocessed by the editor;**

**Reply:** Thank you for your comments. We have prepared the original figures as zip file, including PPT and tiff figures. If any problems, please email us with no hesitation.

**(3) I found the authors did not write the "article highlight" section. Please write the "article highlights" section at the end of the main text;**

**Reply:** Thank you for your comments. We have revised the text and added this section in the manuscript. If any problems, please email us with no hesitation.

**(4) please don't include any \*, #, †, §, ‡, ¥, @....in your manuscript; Please use superscript numbers for illustration; and for statistical significance, please use superscript letters. Statistical significance is expressed as aP <0.05, bP <0.01 (P > 0.05 usually does not need to be denoted). If there are other series of P values, cP <0.05 and dP <0.01 are used, and a third series of P values is expressed as eP <0.05 and fP <0.01.**

**Reply:** Thank you for your comments. We have revised the problem in the manuscript. If any problems, please email us with no hesitation.