

Dear Editors and Reviewers:

Thank you for your letter and for the reviewers' comments concerning our manuscript entitled "*Pretreatment serum albumin-to-alkaline phosphatase ratio is an independent prognosticator of survival in patients with metastatic gastric cancer*" (Manuscript NO: 72749). All the comments are important guiding significance to our researches. We have made corrections according to the recommendations. Here, we provided below with a brief "List of changes" from the revised manuscript, followed by our point-to-point responses (in blue) to the reviewers' comments.

Best wishes!

Cancer Center of Union Hospital
Tongji Medical College
Huazhong University of Science and Technology
Junli Liu

Reviewer #1:

Scientific Quality: Grade C (Good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Minor revision

Specific Comments to Authors:

1. Research methods and reporting. Authors should have prepared their manuscripts according to manuscript type and the appropriate categories, as follows: (1) CARE Checklist (2013) - Case report; (2) CONSORT 2010 Statement - Clinical Trials study, Prospective study, Randomized Controlled trial, Randomized Clinical trial; (3) PRISMA 2009 Checklist - Evidence-Based Medicine, Systematic review, Meta-Analysis; (4) STROBE Statement - Case Control study, Observational study, Retrospective Cohort study; and (5) The ARRIVE Guidelines - Basic study. Did the author prepare the manuscript according to the appropriate research methods and reporting?

NO

Thanks for the reviewer's positive and constructive comments. We had made some emendations to improve the quality of the article, including corrections of inaccurate description, supplement of additional data.

Reviewer #2:

Scientific Quality: Grade C (Good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Major revision

Specific Comments to Authors: The authors presented a retrospective study relationship between serum albumin / alkaline phosphatase ratio as is an independent prognosticator of survival in metastatic gastric cancer. When we discussed about another kind of metastatic cancer, for example: Metastasis hepatic colon rectal, in this case we have validated the Fong's criteria in the literature. So, it's possible resection of the both tumors and better overall survival / survival disease free. I'd like that authors to explain what's the applicability is in practice? Because in that case the gastric cancer are advanced, with metastasis. If we are knowledge about relationship between serum albumin / alkaline phosphatase ratio as is an independent prognosticator of survival in metastatic gastric cancer, what's the conduct change? I think that if change the conduct, is important. On the other hand if not change, it is just curious. The criteria were validated?

We thank the reviewer for the thoughtful comments. We had analyzed the survival of GC patients received different treatment regimens as recommended. we demonstrated that patients with low level AAPR level received fluorouracil or taxane alone as first-line treatment had a median OS of less than 3 months, while patients received combination chemotherapy had a median OS more than 10 months. This result gave us a hint that for patients with low AAPR was associated with poor prognosis, and stronger treatment regimens were needed to prolong survival time.

We also had read several articles^[1,2] investigating survival after surgical resection of colorectal liver metastasis, which were well-designed and perfected the criteria for resectability of patients with colorectal liver metastasis. Inspired by these studies, we tried to find more meaningful results that may assistant decision-making in practice. At present, the number of metastatic sites is an independent prognostic factor for patients with metastatic gastric cancer. We constructed a AAPR-M system based on AAPR and number of metastatic sites. AAPR-M was superior to the number of metastatic sites for predicting survival. AAPR-M can provide more accurate prognostic information for patients and physicians. (Line 12, Page 11; Fig. 4,5)

Reviewer #3:

Scientific Quality: Grade B (Very good)

Language Quality: Grade A (Priority publishing)

Conclusion: Accept (General priority)

Specific Comments to Authors: The aim of this retrospective study was to investigate the prognostic value of AAPR in distant metastatic GC. This is a well-designed study and the manuscript is well written. When the authors evaluate sub-groups, the number of patients in certain analyzes falls. However, the authors assume this limitation at the end of the discussion.

Thanks for the reviewer's positive and constructive comments.

(1) Science editor:

The authors have performed a retrospective study on patients with metastatic gastric cancer and evaluated the use of the albumin to ALP ratio to determine prognosis. They found a ratio of less than 0.48 was associated liver and bone metastases and a worse prognosis. The findings are interesting. The reviewers have identified that the applicability of the results to patient care should be further discussed in the discussion, given that patients have known metastatic disease. Also the methods suggest patients were contacted by telephone for the study but the methodology suggests the study is retrospective. Please clarify and clarify the duration of follow up.

Language Quality: Grade B (Minor language polishing)

Scientific Quality: Grade D (Fair)

Thanks for the constructive and insightful comment. We had added some discussion in the article (Line 4, Page 15). As for the methods, we often contacted patients by telephone in the routine clinical work to surveillance, regular examination, and appointment. For these patients, the follow-up was on the basis of telephone record. This does not contradict.

(2) Company editor-in-chief:

I have reviewed the Peer-Review Report, the full text of the manuscript, and the relevant ethics documents, all of which have met the basic publishing requirements of the World Journal of Clinical Oncology, and the manuscript is conditionally accepted. I have sent the manuscript to the author(s) for its revision according to the Peer-Review Report, Editorial Office's comments and the Criteria for Manuscript Revision by Authors. Please provide decomposable Figures (in which all components are movable and editable), organize them into a single PowerPoint file. Please authors are required to provide standard three-line tables, that is, only the top line, bottom line, and column line are displayed, while other table lines are hidden. The contents of each cell in the table should conform to the editing specifications, and the lines of each row or column of the table should be aligned. Do not use carriage returns or spaces to replace lines or vertical lines and do not segment cell content.

Thanks for the editor's suggestions. We had edited our tables as required.

- 1 Nathan H, de Jong MC, Pulitano C, Ribero D, Strub J, Mentha G, Gigot JF, Schulick RD, Choti MA, Aldrighetti L, Capussotti L, Pawlik TM. Conditional survival after surgical resection of colorectal liver metastasis: an international multi-institutional analysis of 949 patients. *J Am Coll Surg* 2010; **210**: 755-764, 764-756 [PMID: 20421045 DOI: 10.1016/j.jamcollsurg.2009.12.041].

- 2 Sasaki K, Morioka D, Conci S, Margonis GA, Sawada Y, Ruzzenente A, Kumamoto T, Iacono C, Andreatos N, Guglielmi A, Endo I, Pawlik TM. The Tumor Burden Score: A New "Metro-ticket" Prognostic Tool For Colorectal Liver Metastases Based on Tumor Size and Number of Tumors. *Ann Surg* 2018; **267**: 132-141 [PMID: 27763897 DOI: 10.1097/SLA.0000000000002064].