

ANSWERING REVIEWERS



July 8, 2013

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 3714-revision.doc).

Title: High level of preoperative Carbohydrate antigen 19-9 as a poor survival predictor in gastric cancer

Author: A Ra Choi, Jun Chul Park, Jie-Hyun Kim, Sung Kwan Shin, Sang Kil Lee, Yong Chan Lee, Jae Bock Chung

Name of Journal: *World Journal of Gastroenterology*

ESPS Manuscript NO: 3417

The manuscript has been improved according to the suggestions of reviewers:

1 Format has been updated

2 Revision has been made according to the suggestions of the reviewer

- (1) The title needs to be more specific since the manuscript showed a significant statistical result of the relationship between preoperative CA199 and prognoses, but not the tumor staging. -> We have changed the title as the reviewer pointed out as the followings ; High level of preoperative Carbohydrate antigen 19-9 as a poor survival predictor in gastric cancer
- (2) In the materials and methods, the criteria of inclusion and exclusion of patients may need to be more detailed. ->-> We have stated exclusive criteria. (page 6, line 7~10)
- (3) For example, did the patients included take chemotherapy or other therapies before or after the surgery? Since such interferences are very important factors that influence the survival of people, it will be better if author could show those information in the baseline characteristics-> We have additionally shown in the baseline characteristics (Table 1). However, we did not analyze the factors such as presence of chemotherapy or other therapies after the surgery. Because it might be limitation in our study, we revised and added additional comments. It was mentioned in the limitation (page 14, line 9~19)
- (4) In the section of initial work-up and follow-up, a beginning and ending time point of follow-up could be mentioned. -> We have mentioned a beginning and ending time point of follow-up (page 7, line 15).
- (5) In the statistical analysis section, "DFS was calculated from the date of surgery until the date when those treated for gastric cancer were determined to be free of disease." were mentioned. Most of readers may be confused that how and when to judge a patient was free of disease. Therefore, an explanation or a definition is necessary.-> We have defined DFS as the interval from the operation date to the date of confirming recurrence, death from any cause other than cancer, or last visiting date. (page 8, line 13~15)
- (6) In the result section, the author may show the numbers of the loss and the survival of patients,

both of which will influence the censored value. While too many censored values may affect the use of Cox method and may cause the lack of median survival of DFS, finally impact the test performance.-> We have consulted on this issue to the statisticians. As mentioned in the results, censoring cases have occurred chiefly in the end of the study in OS. Thus the upper limit of the confidence interval in the non-elevated group is not calculated. In the case of DFS, because there are fewer recurrences (80 patients), median survival time could not calculate statistically. The numbers of the censored patients were 408 (83.61%).

- (7) The format of the references was not conformed to the requirement of the journal. The DOI of several articles were incorrect, like reference 5, 12, 14,16,20,25. So the author needs to revise according to the "Instruction to authors" .-> We have corrected DOI of the references.
- (8) The paper is well written, but in the journal of Asia Pac J Clin Oncol (2012 Nov 26), it has been showed that an elevated CA 19-9 concentration was significantly associated with shorter survival. The conclusion is similar to this paper's result. So, the author should explain the superiority compare to the previous study. -> We have reviewed about above-mentioned paper and other journals. We were compared with previous and recent studies in order to emphasize our originality. And we have revised and summarized as followings; Recent study by Jae-Cheol Jo et al^[42] has been reported that an elevated CA 19-9 concentration before chemotherapy was significantly associated with shorter survival especially in metastatic or recurrent gastric cancer. The patients' character of this study is metastatic or recurrent gastric cancer patients. However, our study was designed to analyze treatment-naïve patients who were planning to perform gastrectomy. Therefore, we have the superiority and originality compared to previous studies because of the differences of the subject and focus of study. (page 13, line 14~20) In addition, we noted that our study had mixed model through the matched pair data by age, sex and cancer staging. (page8, line 6)
- (9) Moreover, the sample is relatively small for the conclusions. The multi-center and prospective studies should be designed to certify the prognostic significance of CA 19-9. -> We have described in limitation (page 14, line 18~19)

3 References and type setting were corrected

Thank you again for publishing our manuscript in the *World Journal of Gastroenterology*.

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