Author's response to reviews

Title: Preoperative serum carcinoembryonic antigen, albumin and age are supplementary to UICC staging systems in predicting survival for colorectal cancer patients undergoing surgical treatment

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Author's response to reviews: see over
Dear Reviewers:

Thank you for your valuable comments on our manuscript. We have made changes and corrections to our article accordingly, and below are our point-by-point replies:

**Reviewer 1:**

1. We much appreciate your question and interest regarding our manuscript entitled “Preoperative serum carcinoembryonic antigen, albumin and age are supplementary to UICC staging systems in predicting survival for colorectal cancer patients undergoing surgical treatment”. As per your comments, serum LDH may be an important factor of prognosis in some disease. Serum albumin measurement is one of the routine laboratory examinations in preoperative evaluation of CRC patients in Taiwan, however, serum LDH measurement is not a routine laboratory examination. Consequently, we cannot provide detailed analysis of serum LDH level in CRC patients for the prediction of survival at this time. Actually, several previous studies have stated that preoperative serum albumin level is an important predictor in predicting operative mortality in CRC patients (Cerdan FJ, Diez M, Gomez JJ, Balibrea JL: The prognostic value of common predictive variables in rectal cancer. Rev Esp Enferm Dig 1995; 87 (3):205-10; Stephan G, Sibylle M, Edwin B, Gerd S, Christiane M, Sonja A, Farzin A, Stephan R, Wilfried B, Matthias F, Reinhardt W: Survival Prediction in Terminally Ill Cancer Patients by Clinical Estimates, Laboratory Tests, and Self-Rated Anxiety and Depression. J Clin Oncol 2007; 25 (22): 3313-20).

2. We have further analyzed the prognostic factors of stage II and III colorectal cancer patients in Tables 6 to 9. The only significant prognostic factor for both cancer-specific and overall survival rates in stage II and III colorectal cancer patients were pre-operative serum CEA level. Meanwhile, age over 65 years was also an
independent prognostic factor of overall survival for stage II and III CRC patients. We have added this information to our Results and Conclusion sections.

3. The English writing of the manuscript has been reviewed by a local foreign consultant, and the certificate is also enclosed.

**Reviewer 2**

1. We have added cancer-specific and overall survival curve graphics in Figures 1 & 2 as per your comments. CRC patients with serum CEA levels < 5 ng/ml ($P < 0.001$; Figure 1a) or albumin levels $\geq 3.5$ gm/dl ($P < 0.001$; Figure 1b) had a significantly greater cancer-specific survival rate than those with serum CEA levels $\geq 5$ ng/ml or albumin levels $<3.5$ gm/dl respectively. Moreover, CRC patients with age < 65 years ($P < 0.001$; Figure 2a) or serum CEA levels $< 5$ ng/ml ($P = 0.003$; Figure 2b) had a significantly greater overall survival rate than those with age $\geq 65$ years or serum CEA levels $\geq 5$ ng/ml respectively.

2. The postoperative outcome of patients with colonic and rectal cancers was not significantly different in the present study despite patients with rectal cancer likely receiving a multidisciplinary treatment with, e.g. neoadjuvant radio chemotherapy and/or adjuvant chemotherapy. From Table 2, the 5-year cancer-specific survival rates on colonic and rectal cancer patients were 58.48% and 65.18% respectively ($P = 0.082$). In Table 4, the 5-year overall survival rates on colonic and rectal cancer patients were 55.67% and 62.26% respectively ($P = 0.064$). No significant differences in cancer-specific and overall survival rates between colonic and rectal cancer patients were observed. Accordingly, we presented our results in overall colorectal cancer patients.

3. In the Conclusion section on page 16, we have modified the original sentence to a more significant message of “Of these factors, preoperative serum CEA level is the
only significant prognostic factor of cancer-specific and overall survival for patients with stage II and III CRCs. Preoperatively, the identified prognostic factors supplementary to the UICC staging system may be potentially useful in improving the prediction of cancer-specific survival and overall survival in CRC patients.” In fact, the main purpose of our current study is to determine additional and powerful prognostic factors for patients with CRC, especially preoperatively.

Reviewer 3

1. As per your concern, we have further analyzed the prognostic factors of stage II and III colorectal cancer patients in Tables 6 to 9. The only significant prognostic factor for both cancer-specific survival and overall survival rates in stage II and III colorectal cancer patients were pre-operative serum CEA levels. We have added this information to our Results and Conclusion sections.

We sincerely appreciate your comments. They were very helpful in enabling us to present our study in a form suitable for publishing in the BMC Cancer Journal.

Yours truly,

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