Author's response to reviews

Title: Elevated levels of serum amyloid A indicate poor prognosis in patients with esophageal squamous cell carcinoma

Authors:

Jun-Ye Wang MD (wangjy@sysucc.org.cn)
Yu-Zhen Zheng MMed (zhengyzh@sysucc.org.cn)
Juan Yang MMed (juanyang85@gmail.com)
Yue-Hao Lin BS (linyh@sysucc.org.cn)
Shu-Qin Dai MMed (daishq@sysucc.org.cn)
Ge Zhang PhD (zhangge@mail.sysu.edu.cn)
Wan-Li Liu PhD (liuw@sysucc.org.cn)

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Author's response to reviews: see over
11th of July 2012

Dear Editor,

Please find enclosed the edited manuscript in Word format.

Title: Elevated levels of serum amyloid A indicate poor prognosis in patients with esophageal squamous cell carcinoma.

Author: Jun-Ye Wang, Yu-Zhen Zheng, Juan Yang, Yue-Hao Lin, Shu-Qin Dai, Ge Zhang, and Wan-Li Liu

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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

A Reviewer: Hiroya Takeuchi
Q: Did all patients and healthy donors participate in the study after signing an informed consent?
A: We confirmed that this study was approved by the Institute Research Ethics Committee of the Cancer Center of Sun Yat-Sen University and informed consents were obtained from all participants before theirs sera were used. Thank you for your advice. We have modified the article according to the suggestion (page 5, paragraph 2, last sentence).

B Reviewer: Abbas Abbas
Q1: There are several references to GERD and Barrett’s esophagus in the paper, but this is not really relevant to the development of esophageal squamous cell carcinoma and has not been shown to be predisposing factor. These references should be either omitted or a clear explanation of why this may be relevant placed in the manuscript.
A1: Thank you for your attention to our article. It is an objective suggestion. Based on it, we omitted these references to prevent mistake derives from subjective assume.

Q2: It would be interesting to relate the many known causes of elevated SAA, e.g. atherosclerotic disease, steroids, COPD, glaucoma, etc. The absence or presence of these factors in each group of patients should then be stated.
A: You are right that many diseases such as atherosclerotic disease and COPD have been found elevated serum SAA levels in these patients. By re-examination of all enrolled people’s records, there were 2 cases with atherosclerotic disease and 6 cases with COPD in group with serum SAA levels ≧8.0mg/L; there were 3 cases with atherosclerotic disease and 4 cases with COPD in group with serum SAA levels <8.0mg/L (see page 4, paragraph 2, sentence 3); there were 1 case with atherosclerotic disease and 2 cases with COPD in healthy cohort (see page 4, last paragraph, last sentence). No glaucoma was found in all patients. Other diseases that would potentially cause elevation of SSA were not recorded.

Q3: Exclusion criteria included “patients with inflammatory diseases”. Were these patients excluded before or after the SAA level was measured? Were these exclusions mainly from one group rather than the other? If there is a large number of patients with elevated SAA in the group with better outcomes, this would have changed the results of the analysis.
A: Since white blood cell count is the general indicator of inflammatory, and SSA level would be elevated in inflammatory situation. Patients with elevated white blood cell count (>10 × 10^9/L) were considered with inflammatory diseases and were excluded before the measurement of SAA (see page 4, paragraph 2, first sentence). We are sorry to not address in the primary article.

Q4: In the results section, there is mention of the statistically significant differences in survival between the 2 groups of elevated and non-elevated SAA. In figure 2, the 80 month survival (>6.5 years) of patients with Stage III-IV seems to be almost 40%. That of patients with N1 disease was 45% and that of patients with T3-T4 was 60%. These rates are very different from any previously reported series and should be clearly discussed in the results section. These results are very impressive and the survival data should be discussed in detail.
A: The unusual prognosis in stage III and stage IV patients may contribute to our results. First, a minority of the whole cohort of stage III-IV (29/101, 28.7%) with non-elevated SAA levels showed the 40% of 80 month survival. The majority of the stage III-IV showed a 10% 5-yr survival rate, agreed with previous studies. Second, development of surgical resection and superiority of multimodality therapy had prolong the survival time of patients with esophageal carcinoma. In the article of Lerut et al [1], the 5-yr survival rate of stage III and stage IV esophageal carcinoma is 36.8% and 13.3%, which is rather better than ours. Finally, our small sample size may be biased in some extent. Thus, we added a survival graph to compare prognosis between different stages and find that, the predicted five-year overall survival rate of the entire cohort, stage I cohort, stage II cohort, stage III cohort and stage IV cohort was 41%, 65%, 60%, 40% and 0% (See figure 2, ).

Thank you again for publishing our manuscript in the BMC Cancer.

Sincerely yours,
Wan-li Liu: Clinical Laboratory Medicine, Sun Yat-sen University cancer center, 651 Dongfeng Road East, Guangzhou 510060, China. Tel: 86-20-8734-3199; Fax: 86-20-8734-3199; E-mail: liuwl@sysucc.org.cn
Ge Zhang: Department of Microbial and Biochemical Pharmacy, School of Pharmaceutical Sciences, Sun Yat-sen University, No.132 Waihuandong Road, University Town, Guangzhou 510006, China. Tel: 86-20-39943021; Fax: 86-20-39943021; E-mail: zhangge@mail.sysu.edu