Reviewer’s report

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

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Reviewer: Abbas Abbas

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

I do have several comments and questions which fall in the area of major revisions required.

1. There are several references to GERD and Barrett’s esophagus in the paper. On page 3, last paragraph: “…..Clinical and experimental data suggest that gastroesophageal reflux disease and Barrett’s esophagus, both of which are associated with inflammation of the esophageal squamous epithelium, are the major risk factors for esophageal cancer, which suggests that chronic inflammation promotes the development of esophageal cancer [20].”

And page 8, first paragraph: “….The chronic inflammation that is present in Barrett’s esophagus creates an environment suitable for DNA damage and altered expression of genes involved in cellular proliferation, inhibition of apoptosis, stimulation of angiogenesis and cellular transformation [26].”

This is not really relevant to the development of esophageal squamous cell carcinoma and has not been shown to be a predisposing factor. In fact esophageal squamous cell carcinoma is surprisingly rare in the setting of Barrett’s disease, even suggesting a possible protective effect against squamous cell cancer. These references should be either omitted or a clear explanation of why this may be relevant placed in the manuscript.

2. 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.

3. 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. I would recommend stating how many patients were excluded and exactly what the reason for exclusion was, in addition to whether or not they had a SAA level checked and what it’s value was.

4. 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. This should include the overall survival of each group instead of just showing it on a survival curve.

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Acceptable

Statistical review: Yes, but I do not feel adequately qualified to assess the statistics.

Declaration of competing interests:

I declare that I have no competing interests