Reviewer’s report

Title: Polymorphism in COX-2 modifies the inverse association between Helicobacter pylori seropositivity and esophageal squamous cell carcinoma risk in Taiwan: a case control study

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Reviewer: Farhad Islami

Reviewer’s report:

This is an interesting article that reports on the association of Helicobacter pylori infection and polymorphisms in Cox-2, and interaction of these factors, with risk of esophageal squamous cell carcinoma (ESCC) in a Taiwanese population. The study seems to be well-designed, data are clearly presented, and the manuscript is well-structured. Overall, the manuscript is easily readable. However, the wording in several sentences could be improved. Overall, this study addresses an interesting issue in ESCC carcinogenesis.

Some minor essential revisions are required:

1. In the first sentence of the Background section, other high incidence areas should be mentioned (such as central Asia and southern and eastern Africa: Parkin et al 2005). Otherwise, the sentence should be changed to something like: the incidence is high in some geographical areas, such as certain parts of China. A more recent reference should also be used for this sentence.

2. I wonder if the controls were healthy people who underwent routine physical examinations or they were outpatients who referred to a clinic because a health problem. Although polymorphism in COX-2 is not likely to be related to control selection method, the authors should add a few sentences to the Methods to describe the control selection process.

3. In “polytomous logistics regression was applied in the multivariate analysis to determine the risk of contacting the two defined cancer groups”, the word “contacting” was not clear to me, as well as “contracting” in “an increased risk of contracting ESCC” (Abstract).

4. Were the P-values one-sided or two-sided? This should be mentioned in the last sentence of the Methods.

3. One row in Table 4 is redundant. In addition, p for H-W3 should be changed to p for H-W2.

4. Numbers beginning a sentence must be spelled.

5. There are some typos in the text, for example: low-third ESCC, once time per week, remain blood cells.

6. Some words should also be changed, for example: pathologically to histopathologically, computer tomography to computed tomography or computerized tomography, gastroendoscope to gastroscopy or upper
gastrointestinal endoscopy or another relevant term.

7. In the following sentence “It means that H. pylori seropositivity has an inverse association with ESCC risk and it was modified by COX-2 polymorphism, especially in the lower third of the esophagus, the anatomy close to the stomach where H. pylori presented”, the first phrase seems to be a little bit strong; I would suggest changing “means” to “suggests”. In addition, “was” should be changes to “is”. The importance of anatomical proximity to the source of H. Pylori infection is not clear to me. The fact that the lower third of esophagus, compared to upper esophagus, is more exposed to acid (in case of acid reflux) may be more important.

8. Finally, in footnotes of Tables 2 to 4, the authors should provide some information about the covariates (if there were continuous, or describe the categories). If categories in Table 1 were used, the authors could only state this in each footnote.

**Level of interest:** An article of importance in its field

**Quality of written English:** Needs some language corrections before being published

**Statistical review:** Yes, and I have assessed the statistics in my report.

**Declaration of competing interests:**

I declare that I have no competing interests.