

Answering Reviewers

Reviewer #1:

Comment. *Excellent article. I agree with everything that the authors wrote. The authors very reasonably and skillfully wrote about the urgent problems, which, as I know, my colleagues are beginning to discuss. My opinion is that this article should be published in the journal.*

Author response: Thank you very much for the comment. We revised the manuscript according to your colleague's suggestions.

Reviewer #2:

Comment. *A comprehensive review evaluating the predictive factors for the development of gastric cancer after H.pylori eradication. The article needs minor English polishing. It is better to use "endoscopic and histological" instead of "clinical", because these are not clinical features. Please find some suggestion in the attached file.*

Author response: Thank you very much for your comments. This is exactly what we aimed for in this review. We asked professional textcheck, and attach the certification. We changed the term to "endoscopic and histological" from "clinical" according to your suggestion. And thank you very much for meaningful suggestions in the attached file. We revised the manuscript accordingly.

Reviewer #3:

Comment. *Helicobacter pylori (H. pylori) infection plays an important role in gastric carcinogenesis. Eradication of H. pylori has been reported to reduce the risk of gastric cancer among asymptomatic individuals in high-risk areas. Therefore, it is advocated to eradication of H. pylori, in clinical work, so as to reduce the risk of gastric cancer. However, the endoscopic appearance of metachronous gastric cancer after eradication treatment becomes atypical, which can easily lead to misdiagnosis. The authors conducted a review article that summarized the clinical characteristics of gastric cancer*

that developed after H. pylori-eradication therapy, as well as the predictors of primary gastric cancer. It may help physicians better understand metachronous gastric cancer after eradication of H. pylori.

Author response: Thank you very much for your detailed comments. This is exactly what we aimed for in this study.

Comment. *However, there are some issues which need to be addressed. 1. In the analysis of the predictive factors of gastric cancer after H. pylori eradication, whether there were analyses on some clinically relevant factors, such as family history, smoking and drinking history and so on. In addition to the characteristics and predictive factors of gastric cancer after H. pylori eradication, is it possible to compare the different prognosis of with H. pylori infection or after H. pylori eradication?*

Author response: Thank you very much for your detailed comments. As for clinically relevant factors, Take et al [32] reported that smoking or alcohol were not risk factors for gastric cancer. Toyoshima et al [55] reported that family history, smoking, and alcohol were not associated with gastric cancer development after eradication in their univariate analysis. Therefore, we did not include these factors as predictors in this article.

The prognosis after eradication is a very important point, however till date, there is also no report which answered this important question. Therefore, we mentioned it in the introduction as below: (page 5 line 8)

Although the effect of *H. pylori* eradication on the prognosis is not determined yet, it is expected that *H. pylori* eradication and elimination within society will lead to less gastric cancer cases and a reduction of medical costs.

Comment. *2. There are a few spelling errors that should be checked carefully and corrected throughout the manuscript.*

Author response: Thank you very much for the comment. We corrected spelling errors throughout the manuscript.

Comment. *3. In addition, the authors cited several articles that they have published in this manuscript.*

Author response: Thank you very much pointing out potential limitation. But, I think that is why we were invited to contribute this review article to *World Journal of Gastroenterology*. Of course we tried to collect as many papers on this specific topic as we could, however, there are few cohort studies evaluating the risk factors for primary gastric cancer development after *H. pylori* eradication. I hope this manuscript will be a help to promoting the investigation of this important research field.