

Reviewer #1:

**Scientific Quality:** Grade D (Fair)

**Language Quality:** Grade B (Minor language polishing)

**Conclusion:** Major revision

**Specific Comments to Authors:** Gastric cancer is one of the most prevalent cancers in the world, especially in East Asian countries. Many studies have shown that eradicating *Helicobacter pylori* can reduce the risk of gastric cancer. For patients who have received endoscopic treatment for early gastric cancer, many studies have also suggested that *Helicobacter pylori* eradication treatment can reduce the risk of metachronous gastric cancer. This study included 24 clinical studies and analyzed the data of 9182 patients with early gastric cancer after endoscopic operation. The authors found an inverse association between the eradication of *H. pylori* and progression to metachronous gastric cancer in patients with a history of ERs. They suggested that eradicating *H. pylori* after primary gastric cancer can reduce the risk of metachronous gastric cancer and increase survival in gastric cancer patients. There were some problems: This study included 9182 patients. The content of data analysis and discussion is too simple.

The follows information that readers may interested in, such as: The gender and age distribution of patients, location of gastric cancer of patients with metachronous gastric cancer.

What gastric locations' metachronous gastric cancer can be reduced by *Helicobacter pylori* eradication?

**Response:** Unfortunately, there is no detailed information about the location of the reduction of gastric cancer in stomach after *H. pylori* eradication. Therefore, in future studies, more research should be done on the recent puzzle. However, in most of studies pepsinogen I/II ratio and the rate of atrophy of antrum and corpus led to the development of metachronous gastric cancer in patients with *H. pylori* eradicated infection.

“In some cases, the eradication effect of *H. pylori* has not been able to prevent metachronous gastric cancer in patients with ERs.” What are the characteristics of these patients? What are the possible reasons?

**Response:** Thank you, this comment was noted in text.

Reviewer #2:

**Scientific Quality:** Grade C (Good)

**Language Quality:** Grade A (Priority publishing)

**Conclusion:** Minor revision

**Specific Comments to Authors:** This is a well written paper (correspondence) on the role of *Helicobacter pylori* (HP) eradication in preventing metachronous gastric cancer after endoscopic resection.

The relationship between HP infection and metachronous carcinoma following endoscopic resection of EGC was recently well described by the following paper, that the Authors should cite: Basso L, Gallo G, Biacchi D, Carati MV, Cavallaro G, Esposito L, Giuliani A, Izzo L, Izzo P, Lamazza A, Polistena A, Tarallo M, Micarelli A, Fiori E. Role of New Anatomy, Biliopancreatic Reflux, and *Helicobacter Pylori* Status in Postgastrectomy Stump Cancer. *J Clin Med* 2022 Mar 9;11(6):1498. doi: 10.3390/jcm11061498. PMID: 35329824; PMCID: PMC8952228.

**Response:** This reference was cited in text.

Besides, it would be interesting to mention (with one reference) the possible role of HP in many types of extra-gastric disease, which issue remains still inadequately researched: Mladenova I. Clinical Relevance of *Helicobacter pylori* Infection. *J Clin Med* 2021 Aug 6;10(16):3473. doi: 10.3390/jcm10163473. PMID: 34441769; PMCID: PMC8396975. I think that future research should address the above.

**Response:** This reference was cited in text.

I think references 7, 8, and 20 should be re-edited. As for the rest this is a well written and well searched correspondence that, after the above minor revision, should be accepted for publication.

**Response:** These references were re-edited.

Reviewer #3:

**Scientific Quality:** Grade B (Very good)

**Language Quality:** Grade A (Priority publishing)

**Conclusion:** Minor revision

**Specific Comments to Authors:** The authors does a good job summarizing a range of literature on the association between H. pylori eradication and the recurrence of metachronous after endoscopic resection in an East Asian population. Overall, this work is well done. Although I am positive about this manuscript, I have few general criticisms that I ask the authors to take to heart. They are somewhat related to one another. The discussion part, and therefore the reading, is a bit choppy and was not thoroughly written. Since this manuscript was presented as a letter to the editor, authors personal opinion as regard the subject under discussion becomes indispensable. Other specific comments and suggestions are listed below:

1. The authors stated that “In 1994, the International Agency for Research on Cancer (IARC) of the World Health Organization (WHO) announced that the bacterium was considered a group I gastric carcinogen (3).” However, the reference provided (1991) doesn’t match the subject under discussion as it appears too backward to correctly validate the statement.

**Response:** The reference was corrected.

2. The authors stated that “According to previous randomized controlled trials (RCTs), eradication of H. pylori has no effect on preventing the occurrence of primary gastric cancer (5-10).” The references appear to be too old. They should be replaced with more recent papers.

**Response:** These references were replaced with more recent papers.

3. “Fuccio et al. in a recent meta-analysis found that eradicating H. pylori can reduce the incidence of primary gastric cancer by about 35% (11).” There is nothing recent about the work of Fuccio et al. as the work was done and published in 2009. Please provide more recent research.

**Response:** We provided a more recent research (Doorakkers et al, 2018).

4. “ Endoscopic resection (ER) such as endoscopic mucosal resection (EMR) as well as endoscopic submucosal dissection (ESD) is a generally accepted therapeutic strategy for early gastric cancer (EGC); but it seems that the metachronous gastric lesions will develop into dysplasia and also the risk of stomach cancer after EGC (12).” Please this statement should be properly restructured.

**Response:** The statement was restructured.

5. “ Heterogeneity was determined via I<sup>2</sup> value and Cochran’s Q test; the random-effect model was applied in high heterogeneity cases (I<sup>2</sup>>25% and Cochran’s-Q p value> 0.05) according to Dersimonian and Laird method.” Please provide reference.

**Response:** The reference was corrected.

6. “ In the current analysis, we evaluated data of 9,182 cases to determine the efficacy of *H. pylori* eradication in preventing metachronous recurrence.” I am wondering where the figure (9,182) is coming from as it doesn’t tally with the data presented in the table or any other section within the manuscript.

**Response:** We apologize for a mistake. Total *H. pylori* positive samples is 9233, and we replaced old sample size with new one. We also add sample size for each study in Table 1.

7. “ The present findings confirm the results of previous published literatures in relation to clinical efficacy of *H. pylori* eradication in prevention of susceptibility to metachronous gastric cancer in patients received ER.”. Authors should cite the previously published papers.

**Response:** We cited an our related article in this section. Keikha M. The association between *Helicobacter pylori* eradication in peptic ulcer patients and gastric cancer? Investigation in an East-Asian population. Trends in Pharmaceutical Sciences. 2020;6(4):279-82.

8. The discussion isn’t thorough. Also, how does this study compare to other studies in other regions?

**Response:** We searched as much as possible, but did not find do any related studies other than Asian studies. We have included all Asian articles in our study

## Round 2

Gastric cancer is one of the most prevalent cancers in the world, especially in East Asian countries. The authors conducted a comprehensive literature review and meta-analysis study. They found an inverse association between the eradication of *H. pylori* and progression to metachronous gastric cancer in patients with a history of ERs. They suggested that eradicating *H. pylori* after primary gastric cancer can reduce the risk of metachronous gastric cancer and increase survival in gastric cancer patients. This conclusion is conducive to the promotion of *Helicobacter pylori* eradication therapy in countries and regions with high incidence of gastric cancer. "Finally, we selected 23 articles as eligible articles according to inclusion criteria (20-42)."" Of all the studies, fourteen were from Korea, as well as 10 from the Japanese population. " mistake in writing?

**Response:** Dear Editor; Have a good time, we are notified that reviewer code: 03009411 has been provided with comments suggesting a conclusion with minor correction as " Of all the studies, fourteen were from Korea, as well as 10 from the Japanese population. " mistake in writing?". Therefore, this correction could be revised in a pre-proof version. Please accept this version. Sincerely