

Re: Revision for “*Helicobacter pylori* infection with Atrophic Gastritis: An independent risk factor for colorectal adenomas” (WJG 56160)

Dear Editor in Chief Lian-Sheng Ma

We thank you and the reviewers for giving us the opportunity to revise our manuscript. We have carefully studied the comments raised by the reviewers and editors, and revised the paper accordingly. The following are point-by-point responses to the editors' and reviewers' comments.

Should you have any questions, please contact us without any hesitation.

We look forward to your favorable decision.

Yours truly,

Weihong Lin, MD

Department of Medical Care (physical examination) Center, the First Affiliated Hospital of Wenzhou Medical University. No. 2 Fuxue Lane, Wenzhou 325000, China.

E-mail: linweihong @wmu.edu.cn

Reviewer 1

Number ID: 03733959

This research studied the correlation between *Helicobacter pylori*, atrophic gastritis and colorectal adenomas. Authors conducted a retrospective study on 6018 health-check population, using Logistic regression mode to study the association between the *Helicobacter pylori*, atrophic gastritis and colorectal adenomas, and found that *H. pylori*-related AG is to be an independent risk factor for colorectal adenomas in China. Thus the study suggests that colonic polyps should be screened by colonoscopy in patients with HP-positive atrophic gastritis. In this study, we have some questions need to be reply.

First, in table 4-6, authors discussed the association among *helicobacter pylori* infection, atrophic gastritis, and colorectal neoplasm. In terms of grouping, it was divided into four groups: the non-polyp group, the non-adenomatous polyp group, the adenoma group, and advanced adenoma group. But the adenoma group included the advanced adenoma group, we suggested the comparison among the non-polyp group, the non-adenomatous polyp group and the adenoma group, and then further compared the non-advanced adenoma group and advanced adenoma group. Or authors can directly compare the association among the non-polyp group, the non-adenomatous polyp group, non-advanced adenoma group and advanced adenoma group.

Answer: Thank you for your positive comments. In our study, the aim is to investigate whether *H. pylori* infection, AG and *H. pylori*-related AG increase the risk

of colorectal adenomas. Furthermore, advanced adenoma group draw more clinician's attention. Subgroup analysis was performed for further explore the association between advanced adenoma and H. pylori infection with AG. In the logistic analysis, the non-polyp group was defined as reference group for comparison with adenoma group and advanced adenoma group, respectively.

Second, authors defined the advanced colorectal adenoma as an adenoma that had high-grade dysplasia, was ≥ 10 mm in diameter, significant villous component or any combination thereof. In the chapter "Baseline characteristics of eligible Subject ", it said there were 143 advanced adenomas. But in the table 2, we found that villous adenoma, Size of adenoma ≥ 10 mm and High-grade dysplasia were not calculated into advanced group. Please regroup correctly. Looking forward to the author's reply.

Answer: Thank you for your comments. The advanced colorectal adenoma was defined as an adenoma with high-grade dysplasia, was ≥ 10 mm in diameter, significant villous component or any combination thereof. Some subjects may have more than one diagnostic condition, but only calculated in to advanced group as one patient.

Reviewer 2

Number ID: 00068978

I read with great interest the manuscript by Chen et al. entitled: Helicobacter pylori infection with Atrophic Gastritis: An independent risk factor for colorectal adenomas.

It is true that HP has been implicated in the pathophysiology of numerous extragastric diseases (neurological, dermatological, hematologic, cardiovascular, metabolic, allergic, hepatobiliary) with numerous review articles published over the last years. Regarding CRC adenomas/cancer data are still scarce and contradictory. So this study, even a retrospective one, holds some scientific merit. However, I have some minor comments that need to be addressed.

1. Not all patients did the 13-urea test + the gastric histology. As being said by the authors in the ABSTRACT and the MATERIAL AND METHODS section the reader is confused. Besides, it is hard to believe that no patient had a rapid urease test during gastroscopy to confirm HP infection. PLEASE ELABORATE

Answer: Thank you for your comments. H. pylori infection was diagnosed by at least one of two methods (the 13C-Urea breath test, or histological diagnosis of biopsied gastric specimens). Majority of these patients did the 13-urea test and the gastric histology. The urea breath test (UBT) and the rapid urease test (RUT) are the most commonly used diagnostic methods for H. pylori infection and rely on detecting the presence of urease produced by H. pylori. The sensitivity of the UBT is excellent (often exceeding 95 %). The sensitivity of RUT is slightly less (approximately 80–95 %). And Detection of H. pylori infection based on pathological examination was considered as the gold standard. Based on the high sensitivity of UBT and the gastric histology, our center did not a rapid urease test during gastroscopy to confirm HP infection.

2. All patients had an upper and lower endoscopy in 2 days. WHY? what were the indications for that? DO you have a simultaneous endoscopy protocol in your clinic?

PLEASE ELABORATE

Answer: Thank you for your comments. As a large physical examination institution, our center has perfect equipment and standardized procedures. Physical examination is conducted in our center and those who choose to have the package of endoscopy examination can have the endoscopy examination the next day. All the people included in this study had a comprehensive physical examination in our center and completed endoscopy the next day.

3. Why did biochemical parameters such as HDL, LDL etc. were recorded in all patients? Is there some protocol for that as well in your department? Besides that, why did you choose to incorporate them into your manuscript and did not choose other biochemical parameters? PLEASE ELABORATE

Answer: Thank you for your comments. In our center, a physical examination center, blood routine, biochemical indicators, blood lipid and other related examinations were included into routine physical examination items for almost subjects. These items were

people who come to our center for Routine physical examination will basically have.

All inspection reports will be recorded in an electronic file. Lot of evidence has demonstrated that common risk factors, such as metabolic syndrome, family history,

alcohol consumption, diet, and lifestyle contribute to the development of colorectal neoplasm development. Biochemical parameters such as HDL, LDL etc. are part of the metabolic syndrome criteria and had been proved as risk factors for colorectal neoplasm.

4. The authors state that "As a whole, subjects with adenoma had older age, higher BMI, SBP, DBP, TC, TG, LDL, FBG and lower HDL-C." What does BP or biochemical have to do with adenomas? PLEASE ELABORATE

Answer: Thank you for your comments. Comparing the non-polyp group with the adenomas group by Kruskal–Wallis test for continuous variables, subjects with adenoma had older age, higher BMI, SBP, DBP, TC, TG, LDL, FBG and lower HDL-C and a two-side P value of less than 0.05. it may indicate that blood pressure and biochemical indexes are risk factors for adenoma.

5. Figure 1 should be left out

Answer: Thank you for your comments. Figure 1 had been deleted in accordance with your comments.

6. You should start the DISCUSSION section with the paragraph that reads: "Various interpretations may explain the mechanisms by which H. pylori infection and atrophic gastritis increases the risk for colorectal adenomas..."

Answer: Thank you for your positive comments. The first paragraph describes the

relationship between helicobacter pylori and colorectal adenomas. The second paragraph describes the relationship between AG and colorectal adenomas. The third paragraph describes the relationship between *H. pylori*-related AG and colorectal adenomas. After these descriptions, the mechanism is described. Such an arrangement might make more sense.

7. The authors state concluding that "Due to the high prevalence of colorectal adenocarcinoma in Chinese population, strict colonoscopy screening and surveillance is necessary for patients with *H. pylori* infection and especially with *H. pylori*-related AG." GIVEN THE STUDY LIMITATIONS and the fact that data from other studies are inconclusive, the authors should TONE DOWN their concluding remarks. KEEP IN MIND THAT this study pertains only to Chinese patients; Worldwide where the incidence of CRC cancer is different, this CAN NOT BE THE CASE. PLEASE ELABORATE LASTLY, THE MANUSCRIPT HAS TO BE EDITED BY A NATIVE ENGLISH LANGUAGE SPEAKER

Answer: Thank you for your positive comments. The presentation of our analyzable data were derived from a single center and local region in Chinese people, thereby limiting the ability to generalize our finding. So, further multi-centered research should be established to determine the potential association of individuals with other nations and ethnic groups. This had been added into the limitation section. We have revised the manuscript according to your advice.

Number ID: 00052643

"Helicobacter pylori infection with Atrophic Gastritis: An independent risk factor for colorectal adenomas" is an interesting paper. Study is well designed and sample size is wide. I have really appreciated the discussion section.

Answer: Thank you for your positive comments.

Editorial Office's comments

Science Editor: 1 Scientific quality: The manuscript describes a retrospective study of the Helicobacter pylori infection with atrophic gastritis. The topic is within the scope of the WJG. (1) Classification: Grade A, Grade C and Grade D; (2) Summary of the Peer-Review Report: Reviewer# 00052643 thinks this is an interesting paper. This manuscript is well-designed and sample size is wide. Reviewer# 00068978 thinks this study holds some scientific merit. However, there are some minor comments that need to be addressed. The authors need to describe more details in the method section. The language needs a great deal of polishing. Reviewer# 03733959 pointed out this research studied the correlation between Helicobacter pylori, atrophic gastritis and colorectal adenomas. However, there are some points need to be addressed. The questions raised by the reviewers should be answered; and (3) Format: There are 6 tables and 1 figure. A total of 31 references are cited, including 2 references published in the last 3 years. The authors need to update the references. There are no self-citations. 2 Language evaluation: Classification: Grade A, Grade B and Grade C. The authors need to provide the language certificate of professional language

company. 3 Academic norms and rules: The authors provided the Biostatistics Review Certificate, the signed Conflict-of-Interest Disclosure Form and Copyright License Agreement. The authors need to provide the official Institutional Review Board Approval Form of Chinese version, and original informed consent. No academic misconduct was found in the Bing search. The CrossCheck results showed the similarity to be high. According to our policy, the overall similarity index should be less than 30%, and the single-source similarity should be less than 5%. Please rephrase these repeated sentences. 4 Supplementary comments: This is an unsolicited manuscript. The study is without financial support. The topic has not previously been published in the WJG. The corresponding author has not published articles in the BPG. 5 Issues raised: (1) I found the language classification was grade C. Please visit the following website for the professional English language editing companies we recommend: <https://www.wjgnet.com/bpg/gerinfo/240>; (2) I found the authors did not provide the original figures. Please provide the original figure documents. Please prepare and arrange the figures using PowerPoint to ensure that all graphs or arrows or text portions can be reprocessed by the editor; (3) I found the authors did not write the “article highlight” section. Please write the “article highlights” section at the end of the main text; and (4) The authors need to provide the official Institutional Review Board Approval Form of Chinese version, and original informed consent. 6 Re-Review: Required. 7 Recommendation: Conditionally accepted.

Answer: Thank you for your positive comments. We have revised the manuscript according to your advice. First, more details have been added in the method section.

Second, the references have been updated according to your advice. Third, the article has been handed over to a professional company for polishing and there is proof of certificate. Forth, the investigation conforms to the principles outlined in the Declaration of Helsinki. The study was approved by the ethical committee of the First Affiliated Hospital of Wenzhou Medical University Ethical Committee. Fifth, these repeated sentences have been rephrased. Sixth, the “article highlight” section have been added in the article.

(2) Editorial Office Director: I have checked the comments written by the science editor. All of the three reviewers require a re-review.

Answer: Thank you for your comments.

(3) Company Editor-in-Chief: I have reviewed the Peer-Review Report, the full text of the manuscript, and the relevant ethics documents, all of which have met the basic publishing requirements of the World Journal of Gastroenterology, and the manuscript is conditionally accepted. I have sent the manuscript to the author(s) for its revision according to the Peer-Review Report, Editorial Office’s comments and the Criteria for Manuscript Revision by Authors. Before its final acceptance, the author(s) must provide the Chinese version of the ethical approval document. The author(s) must provide the English Language Certificate issued by a professional English language editing company. Please visit the following website for the professional English language editing companies we

recommend: <https://www.wjgnet.com/bpg/gerinfo/240>.

Answer: Thank you for your comments. The investigation conforms to the principles outlined in the Declaration of Helsinki. The study was approved by the ethical committee of the First Affiliated Hospital of Wenzhou Medical University Ethical Committee. Relevant certificates have been submitted.