

PEER-REVIEW REPORT

Name of journal: *World Journal of Gastroenterology*

Manuscript NO: 70510

Title: Inverse correlation between gastroesophageal reflux disease and atrophic gastritis assessed by endoscopy and serology

Provenance and peer review: Unsolicited manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 03731081

Position: Peer Reviewer

Academic degree: MD

Professional title: Professor

Reviewer's Country/Territory: Russia

Author's Country/Territory: South Korea

Manuscript submission date: 2021-08-13

Reviewer chosen by: AI Technique

Reviewer accepted review: 2021-08-13 19:17

Reviewer performed review: 2021-08-14 15:45

Review time: 20 Hours

Scientific quality	<input checked="" type="radio"/> Grade A: Excellent <input type="radio"/> Grade B: Very good <input type="radio"/> Grade C: Good <input type="radio"/> Grade D: Fair <input type="radio"/> Grade E: Do not publish
Language quality	<input checked="" type="radio"/> Grade A: Priority publishing <input type="radio"/> Grade B: Minor language polishing <input type="radio"/> Grade C: A great deal of language polishing <input type="radio"/> Grade D: Rejection
Conclusion	<input checked="" type="radio"/> Accept (High priority) <input type="radio"/> Accept (General priority) <input type="radio"/> Minor revision <input type="radio"/> Major revision <input type="radio"/> Rejection
Re-review	<input type="radio"/> Yes <input checked="" type="radio"/> No

Peer-reviewer statements	Peer-Review: [<input checked="" type="radio"/>] Anonymous [<input type="radio"/>] Onymous Conflicts-of-Interest: [<input type="radio"/>] Yes [<input checked="" type="radio"/>] No
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SPECIFIC COMMENTS TO AUTHORS

This manuscript is very interesting and relevant. Contains very important information on the prevention of gastric and esophageal cancer. To confirm the diagnosis of GERD, the authors used risk factors: age, gender, anthropometric data, metabolic syndrome, smoking and many others. Authors explain regarding causality among H. pylori infection, atrophic gastritis, and GERD. I agree with the authors that their results findings must be confirmed through prospective clinical trials. The Kimura-Takemoto visual endoscopic method used in the manuscript is very subjective. I recommend that the authors continue a similar study using the endoscopic morphological method - Updated Kimura-Takemoto classification of atrophic gastritis. This is important in the second step for the accurate diagnosis of atrophic gastritis after serological screening.

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Title: Inverse correlation between gastroesophageal reflux disease and atrophic gastritis assessed by endoscopy and serology

Provenance and peer review: Unsolicited manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 02954019

Position: Editorial Board

Academic degree: MD, PhD

Professional title: Associate Professor

Reviewer's Country/Territory: Japan

Author's Country/Territory: South Korea

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Reviewer chosen by: AI Technique

Reviewer accepted review: 2021-08-15 05:00

Reviewer performed review: 2021-08-15 06:37

Review time: 1 Hour

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input checked="" type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input checked="" type="checkbox"/> Rejection
Re-review	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No

Peer-reviewer statements	Peer-Review: [<input checked="" type="checkbox"/>] Anonymous [<input type="checkbox"/>] Onymous Conflicts-of-Interest: [<input type="checkbox"/>] Yes [<input checked="" type="checkbox"/>] No
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SPECIFIC COMMENTS TO AUTHORS

This is a potentially interesting manuscript describing the associations between reflux esophagitis and gastric atrophy defined by endoscopy as well as serology. However, there are several points that concern me. Major point In evaluating the atrophic status of stomach using serology by using pepsinogens, we must consider the past history of H. pylori eradication. Several studies (APT 20Suppl1:25-32, 2004, JGH doi:10.1111/jgh.15017) reported that pepsinogens normalize after successful eradication, suggesting that evaluation of atrophy status merely by pepsinogens is not always correct if subjects with post eradication are not excluded. I strongly recommend to exclude subjects with successful eradication history. The result of this study seems to be incorrect, and more sharp correlation would be obtained if excluding subjects with past successful eradication history. Correlation between serological atrophy and reflux esophagitis has been already reported by several investigators (J Korean Med Sci 32:796-802, 2017, World J Gastrointestinal Endosc 16;71-7, 2011, Int J Biol Markers 25; 207-12, 2010). Thus, regrettably, this manuscript does not offer any new information to the field.

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Provenance and peer review: Unsolicited manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 06136279

Position: Peer Reviewer

Academic degree: MD

Professional title: Doctor

Reviewer's Country/Territory: Japan

Author's Country/Territory: South Korea

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Review time: 10 Days and 14 Hours

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input checked="" type="checkbox"/> Grade A: Priority publishing <input type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input checked="" type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Re-review	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No

Peer-reviewer statements	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
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SPECIFIC COMMENTS TO AUTHORS

Han et al. systematically showed that atrophic gastritis, in both endoscopically and serologically, could be an independent protective factor against GERD. Their review was retrospective but it was a very large study in the general population, and very significant in terms of the prevalence and severity of GERD were shown according to the extent of atrophic gastritis. Their article has been well elaborated and of sufficient quality to be reported. Although the study seemed to have conducted in a well-organized manner, further revisions are desirable for publication. Major comments: 1. The authors conclude that atrophic gastritis is an independent protective factor for GERD and that the cost of maintenance anti-reflux therapy should be taken into account when considering the cost-effectiveness of H. pylori eradication therapy. The primary goal of H. pylori eradication therapy is to improve atrophic gastritis and to reduce carcinogenic risk and associated mortality, and it is clear from previous studies that eradication therapy can reduce cancer deaths (ref 1,2). As the authors mentioned, it is a well-known fact that eradication therapy carries the risk of exacerbation of GERD, while this is a benign disorder, and in most cases, it can be sufficiently controlled by acid secretion inhibitors. It seems clear which is the higher priority, controlling cancer death with eradication therapy or avoiding the risk of exacerbation of benign disease. The author declared that eradication interventions should be cautious given the risk of GERD, but I think this is a dangerous claim to readers. With or without GERD, I believe that the advantages of eradication therapy and to improve mucosal atrophy take precedence over the disadvantages, but what do authors think? It is desirable to specify the author's view on eradication therapy. Ref. 1) Li WQ, et al. BMJ. 2019; 366:l5016. 2) Take S,

et al. J Gastroenterol. 2020; 55: 281- 288. 2. The authors examined atrophic gastritis in two directions: endoscopic and serological. Did the serological and endoscopic evaluations match in the same case? Previous reports has also pointed out that the Pepsinogen method may result in false negatives especially in cases after eradication, and the accuracy of either method is limited. Whether there was a reliable correlation between these two methods in the cases in this study should be showed in Tables or Figures. 3. In Discussion, the authors stated that it may be possible to assess the risk and severity of GERD with only a simple serological test (page 16, line 28-29). As shown in Figure 5, it may be true that patients with SAG tend to have a lower prevalence of GERD, but in the end, GERD can only be diagnosed endoscopically. So picking up patients without SAG as GERD high risk would only increase the burden of excessive endoscopy after all. It seems that there is a limit to picking up patients at risk of GERD serologically, and I think that it may be sufficient to recommend endoscopy to patients with GERD-related symptoms. It is desirable to clearly state the clinical significance of performing a serological risk assessment of GERD. Minor comments: 1) In Figures 3A and 6, it is necessary to show the unit of the vertical axis. Why is the vertical axis of Figure 3A up to 9 and of Figure 6 up to 10?

RE-REVIEW REPORT OF REVISED MANUSCRIPT

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Manuscript NO: 70510

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Peer-review model: Single blind

Reviewer's code: 06136279

Position: Peer Reviewer

Academic degree: MD

Professional title: Doctor

Reviewer's Country/Territory: Japan

Author's Country/Territory: South Korea

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Reviewer chosen by: Jing-Jie Wang (Online Science Editor)

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Scientific quality	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input checked="" type="checkbox"/> Grade A: Priority publishing <input type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input checked="" type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Peer-reviewer	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous



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statements

Conflicts-of-Interest: [] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

The authors responded appropriately to the reviewers' suggestions, and it seems that all necessary corrections were addressed. This research is now considered to be suitable for publication.