

Responses to Reviewers' Comments

Thank you very much for reviewing our manuscript and providing valuable comments. Our replies to the comments and questions are as follows.

Round 1

Responses to Reviewer #1:

Reviewer #1:

Scientific Quality: Grade D (Fair)

Language Quality: Grade B (Minor language polishing)

Conclusion: Major revision

Specific Comments to Authors: Atrophic gastritis is the main background for the development of gastric cancer in patients infected with H. Pylory. Eradication therapy (ET) may help reverse the pathological manifestations of H. pylori gastritis and reduce the risk of gastric cancer. In this regard, the search for objective and reliable criteria to assess the effectiveness of ET is important. The authors present the results of a study that is a continuation of a previously initiated study (Nishikawa Y, et al. 2018). Their aim is to evaluate changes in atrophic mucosal patterns (AMPs) observed on blue laser imaging in patients with H. pylori-associated gastritis after ET. Unlike the previous study, in which endoscopic examination before and after ET was performed in only 22 patients, in this study, the authors evaluate the corresponding changes in 101 patients. At the same time, there are a number of unclear points in the manuscript that require clarification and more correct wording.

Abstract

1. The authors state that 771 patients were included in this study, of which 101 patients received endoscopy before and after ET. However, they report 236

patients in their results (76 patients with the Spotty pattern, 90 patients with the Cracked pattern, and 70 patients with the Mottled pattern). It is not at all clear how this number of patients (236) compares with the 771 patients included in the study and the 101 patients who received ET.

2. I believe that the Abstract should include data that relate to both the 771 patients included in the study and data that relate specifically to the 101 patients who received ET.

Reply: Thank you for highlighting that the patient characteristics need clarification. We added a new table (Table 1) and changed the relevant explanations in the Methods and Results sections to ensure better understanding.

3. It is not entirely clear what the confidence intervals mean when the authors give the percentage of patients with one or another endoscopic pattern.

Reply: In our study, the accuracy of proportion of changes of each pattern was estimated using the proportion and its 95% confidence interval. The 95% confidence interval was described to indicate the degree of accuracy (variation) in the proportions of patterns.

4. The formulated conclusion does not follow in any way from the stated results. Moreover, the statement that changing AMPs from Spotty pattern to Cracked pattern may help endoscopists easily and precisely evaluate H. pylori-related gastritis status is not entirely justified due to the low of specificity of the method (41,8%).

Reply: Thank you for this valuable comment. To address this issue, we added a new figure (Figure 5) to describe the relationship between the Spotty and Cracked patterns.

Results.

1. The authors provide data on significant age differences in patients with different types of AMPs. In this regard, a reasonable question arises: are the observed changes in the AMPs due to infection or does age also play a role in their development?

Reply: We considered that the infection duration plays a role in the changes in AMPs. Older patients tended to experience longer infection periods.

2. It is also necessary to clarify in the results why the number of patients (101 patients) who underwent ET does not match the total number of patients with different GM patterns (76 patients with the Spotty pattern, 90 patients with the Cracked pattern, and 70 patients with the Mottled pattern).

Reply: In our study, multiple patterns commonly coexisted in many patients, with some patients having all three patterns. Therefore, we evaluated whether each of the three patterns appeared/increased or disappeared/decreased after *H. pylori* eradication, rather than simply examining the presence or absence of each pattern.

Of the 101 patients, 38 showed all three patterns (Spotty, Cracked, and Mottled), 59 had two patterns (Spotty and Cracked, 28; Spotty and Mottled, 7; and Cracked and Mottled, 24), and four presented with only one pattern (Spotty, 3; Cracked, 0; and Mottled, 1) either before or after eradication. For example, a patient showed only the Spotty pattern before eradication. However, after eradication, the Spotty pattern disappeared and the Cracked pattern appeared. The two patterns were considered as “present” before or after eradication. Further explanations have been added to the Results section of the revised manuscript.

3. It is necessary to provide a table or figure that reflects the specific number of patients with different AMPs and how they changed during ET, and not the total percentage of their appearance or disappearance. From this table it should be clear that out of 101 patients, N patients had such and such a AMPs before

eradication. Of these N patients after eradication, so many had a Spotty pattern, so many had a Cracked pattern, etc.

Reply: As per your valuable suggestion, we have added a new figure (Figure 5) to describe how the Spotty patterns were changed to Cracked patterns after the eradication. These pattern changes reflect important shifts before and after the eradication.

4. Considering that the title of the manuscript is "Atrophic mucosal patterns change after *Helicobacter pylori* eradication: evaluation using blue laser imaging in patients with atrophic gastritis", it is necessary to consider separately and in more detail the group of patients who received ET, preferably indicating the morphological changes that were observed before and after ET.

Reply: Thank you for your valuable suggestion. We plan to consider this issue in a future study.

5. It is desirable to compare the data on the identified AMPs with morphological changes in the gastric mucosa, as well as their comparison with the Kyoto Classification of Gastritis.

Reply: The comparison between our findings and the Kyoto Classification is an issue that we would like to address in our studies in the near future.

Discussion.

1. The statement about the simple diagnosis of H. Pylory status is not entirely correct, due to the fact that the method is characterized by insufficient sensitivity (41.8%), which follows from a previously published work (Nishikawa Y, et al. 2018). Also confusing is the percentage of inconsistency in the conclusions between the three experts (Nishikawa Y, et al. 2018), which indicates the subjectivity of this assessment..

Reply: In our previous study, we examined and determined the mucosal patterns of each patient. In this study, we evaluated the changing patterns

before and after the eradication in each patient because two or three different patterns were often observed in each patient.

2. Also, the statement that “the Mattled pattern represents the terminal stage of infection” is not confirmed by anything. Moreover, it is not clear what the authors mean by terminal stage of infection. Thus, the manuscript requires serious revision and changes.

Reply: We agree with your valuable suggestion. We have deleted this description from the manuscript.

Responses to Reviewer #2:

Reviewer #2:

Scientific Quality: Grade C (Good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Accept (General priority)

Specific Comments to Authors: The authors this manuscript used new innovative visual endoscopy method to ensure the accurate evaluation of H. pylori infection.

This is image-enhanced endoscopy method (IEE) using blue laser imaging (BLI). They declare to study atrophic mucosal patterns (AMP). The study does not contain mucosal atrophic morphological correlations with visual endoscopic assessment of atrophic mucosal patterns (AMP).

The method studied by the authors needs to be compared with morphological histological standards within the visual scale of the Sydney system or the Updated Kimura-Takemoto classification of atrophic gastritis.

Reply: Thank you for your valuable comment. We will carry out our future studies from this viewpoint.

At the same time, the study is very interesting. This manuscript proposes a promising screening method for the diagnosis of Helicobacter pylori eradication. The article is very well illustrated.

A necessary condition for publication: the word "Atrophic" should be removed from the title and text of the manuscript and AMP will be replaced by MP. The manuscript is recommended for publication after this condition is met.

Reply: As per your comment, we deleted the term "atrophic" from the title and main text, and replaced "AMP" with "MP" throughout the manuscript text.

Round 2

Reviewer#03270609: I am completely satisfied with the answers of the authors and the corrected version of the manuscript. There are several comments that the authors need to consider and, at their discretion, make appropriate adjustments if necessary: 1. Considering that three patients with indeterminate patterns were excluded from the study, it may be more correct to indicate that 768 patients were included in the study rather than 771. 2. If I understand correctly, there were 236 patients infected with *H. pylori*, not 235 (76 patients with the Spotty pattern, 90 patients with the Cracked pattern, and 70 patients with the Mottled pattern). Please check this information and make corrections if necessary. 3. It may be desirable in the abstract to clarify that out of 771 (or 768?) patients with atrophic gastritis, 236 (or 235?) were infected with *Helicobacter pylori*. 4. Check table 1 accordingly. It is desirable that the number of patients in the text of the manuscript match the data in table 1.

Reply: 1. Considering that three patients with indeterminate patterns were excluded from the study, it may be more correct to indicate that 768 patients were included in the study rather than 771. Reply: Thank you for this valuable comment. As your advice, the indicated case number in the Abstract and Methods was revised from 771 cases to 768 cases. 2. If I understand correctly, there were 236 patients infected with *H. pylori*, not 235 (76 patients with the Spotty pattern, 90 patients with the Cracked pattern, and 70 patients with the Mottled pattern). Please check this information and make corrections if necessary. Reply: There were 325 patients infected with *H. pylori* not 236(or 235) patients. The manuscript contains the exact number. In our study, multiple patterns commonly coexisted in many patients. Of the 101 patients, a Spotty pattern was detected in 76 patients and not detected in 25 patients before or after *H. pylori* eradication. Similarly, Of the 101 patients, a Cracked pattern was detected in 90 patients and not detected in 11 patients before or after *H. pylori* eradication. A Mottled pattern was detected in 70 patients and not detected in 31 patients before or after *H. pylori* eradication. Of course, all 101 cases were infected with *H. pylori*. 3. It may be desirable in the abstract to clarify that out of 771 (or 768?) patients with atrophic gastritis, 236 (or 235?) were infected with *Helicobacter pylori*. Reply: A description of 325 people infected with *H. pylori*

was added to the abstract. 4. Check table 1 accordingly. It is desirable that the number of patients in the text of the manuscript match the data in table 1.

Reply: We checked table 1. The number of patients in the text of the manuscript match the data in table 1.