Format for ANSWERING REVIEWERS

September 07, 2013

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 4181-review.doc).

Title: Investigation of relationships among gastroesophageal reflux disease subtypes with NBI magnifying endoscopy

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Name of Journal: *World Journal of Gastroenterology*

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The manuscript has been improved according to the suggestions of reviewers:
1 Format has been updated

2 Revision has been made according to the suggestions of the reviewer

(1) We've had GERD, NERD, RE and BE definition in the Materials and Methods section. And our NBI diagnostic criteria compare with the Montreal Definition, an evidence-based global consensus definition.

(2) As the reviewer said, if we could really 'define' GERD with NBI magnifying endoscopy, it's really exciting. However, the conclusion needs to be made from more multi-center studies with a larger sample size, what we are doing now.

(3) We designed the study under several concerns, one of which is that some of the healthy control may be 'silent GERD'. If this happened, then the pH monitoring should be done. However, during our study, none of our healthy control was 'silent GERD', so we didn't do 24 hr pH monitoring. Moreover, we selected our subjects with the RDQ. And if the subjects had PPIs history 4 weeks prior to the study, they would be excluded.

(4) The wide use of NBI magnifying endoscopy is truly one limitation for such studies. However, the future is promising with economic development and rapid progress of medical standard.

(5) We are a dedicated research group to study GERD, and we've done this for more than 20 years. Many patients are properly registered and go to the clinic regularly. In the meanwhile, we collected newly discovered GERD patients in the Clinic. Then they would fulfill the RDQ. Some of them were included and some were excluded. Eventually, we got the disease group. A total of 157 patients were screened, of whom 145 were eligible for inclusion (40 NERD, 54 RE and 51 BE). To keep the balance among groups, we selected 40 RE and 40 BE patients randomly. Altogether, we had 120 (66 male, 54 female) patients and 40 healthy controls (16 male, 24 female) included in the final analysis. Among these 120 GERD patients, there were 40 NERD, 40 RE and 40 BE patients, respectively.

(6) It's better to explain the acronym 'IPCLs' on its first appearance, so we modified the manuscript.

(7) It's more vivid to name erosive reflux esophagitis (ERE). However, we use the Montreal Definition as our criteria. So we used reflux esophagitis (RE).

(8) Theoretically, BE could present any esophageal lesion related to GERD. Most critically, we should observe intestinal metaplastic epithelium confirmed by histopathological examination. And we did the histopathological examination to define BE no matter whether they have macro lesions or not. Moreover, we have another article about BE which will be published soon.

(9) The Los Angeles Classification includes patients with different intensity of erosive esophagitis. All

RE patients probably had evident esophageal erosions. We only found 60% of the RE patients with microerosions. There are some reasons. First, it's may be one limitation that the subjects number is not quite large enough, we need to do more with a larger number of patients. Second, some microerosions may develop to erosion. And this is the exact results, and we just show it. Maybe we could answer your question better after we finish the whole study with a larger population.

(10) The explanation of Table 2 should be more detailed, and we've done that.

(11) According to our results, GERD patients have larger numbers of IPCLs/field compared to healthy controls. However, there was no significant difference in the presence of prolonged, dilated, and tortuous IPCLs in the distal esophagus between the 2 groups.

(12) GERD has been considered as resulted from long-period gastroesophageal reflux that causes troublesome symptoms and/or complications. In addition, the micro changes include increment of IPCLs and microerosion, which could truly represent the regurgitation-induced damage from our results and the articles we cited.

(13) A practical diagnostic test needs not only to provide an accurate diagnosis, but also support specific and efficacious treatment to improve patients outcomes. If GERD patients were reevaluated after the therapy of standard PPIs, it may provide the basis of treatment and the results may be better cogent. This is also part of our next study.

(14) The limitations such as the use of such facility and magnification are included in the Discussion.

3 References and typesetting were corrected

Thank you again for publishing our manuscript in the *World Journal of Gastroenterology*.

Sincerely yours,

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