March 3, 2020

Subrata Ghosh, MD, PhD,
Andrzej S Tarnawski, MD, PhD,
Editor-in-Chief
World Jounal of Gastroenterology

Dear Dr. Subrata Ghosh, and Dr.Andrzej S Tarnawski;

Thank you for your careful consideration of our manuscript entitled "Clinicopathological features of early gastric cancers arising in *Helicobacter pylori* uninfected patients" (Manuscript NO: 54416). We thank you and the reviewers for your thoughtful suggestions and insights. The manuscript has benefited from these insightful suggestions. The following are our replies to the comments of the reviewers. We have incorporated all of the changes suggested by the reviewers into our revision, and we have provided a point-by-point response to these suggestions below.

We hope that you find this revised manuscript suitable for publication in *World Journal of Gastroenterology*. We look forward to hearing from you.

Sincerely,

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To Reviewer #1:

Thank you for your wonderful evaluation. Following the publication of this manuscript, we would like to design and conduct a multi-center prospective study to increase confidence in the ability of our findings to generalize to broader populations.

To Reviewer #2:

Answer #2-1:

We thank you for your pertinent comments. Following your suggestion, we have carefully proofread the document to eliminate all language and grammar errors.

Answer #2-2:

We thank you for very valuable comments. We chose not to perform NBI classification owing to the difficulty that system has in classifying HpUIGCs. For example, in fundic gland type adenocarcinoma, the demarcation line is not clear because the tumor is covered with non-neoplastic foveolar epithelium. Because the surface microstructure pattern is not irregular, the NBI classification scheme for differentiated type adenocarcinoma, which includes features like a fine network pattern or intralobular loop pattern, could not be identified. In addition, pure signet-ring cell carcinoma does not exhibit a typical corkscrew pattern because tumor cells do not completely replace the mucosa and often exist only in the proliferative zone. These cases do not fall into any of the established NBI classifications. We believed this to be an important finding and incorporated this into the discussion section of our manuscript.

Answer #2-3:

We thank you for your pertinent comments. There was one patient that had a tumor that invaded into the SM2 and they received additional surgical treatment as per guidelines. Proximal gastrectomy was selected, and no lymph node metastasis was observed in the resected specimen. We added this content to the discussion section. There were no specific NBI findings in this case, and the tumor morphology was indistinguishable from the SMT in other fundic gland type adenocarcinoma.

Answer #2-4:

We thank you for the valuable comment. We added the long-term outcomes for all HpUIGC cases, including the signet-ring cases, to the results section and elaborated on this in the discussion section. With a median observation period of 30 months, neither gastric cancer mortality nor death from any other disease was observed, and endoscopic follow-up did not show any metachronous occurrence.