

Dear Editor-in-Chief,

I would like to thank you for your response and for giving us the opportunity to improve and resubmit my manuscript titled “Endoscopic submucosal dissection for early gastric cancer: It is time to consider the quality of its outcomes” for consideration for publication in *World Journal of Gastroenterology*.

I am hereby resubmitting a revised manuscript conforming to all the reviewers’ comments. In particular, I have addressed all the comments in a point-by-point manner, and the revisions are indicated in red font in the revised paper. I hope that the revised manuscript is now suitable for publication in your journal.

Thank you for your consideration. I look forward to hearing from you.

Sincerely,

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Reply to Reviewer #1's Comments

I thank the reviewer for the constructive critique for improving the manuscript. I have made every effort to address the issues raised and have responded to all the comments. These revisions are indicated in red font in the revised manuscript. Please find below a detailed point-by-point response to the reviewer's comments. I hope that my revisions meet the reviewer's expectations.

1. I am glad to see this excellent manuscript. This article is innovative and can somewhat guide the next direction of clinical research. This manuscript deals with the quality indicators of ESD of EGCs. But the identification of these indicators in the final table still seems to be not rigorous enough and needs to be supported by more studies or references. Moreover, the two indicators regarding the ESD complications section, post-ESD bleeding and perforation, are not presented in the article and seem to appear directly in the table. Also, some of the references in this paper are not from the last 5 years and I hope they can be modified as appropriate.
- I agree with the reviewer that the suggested indicators in Table 1 seem insufficiently rigorous and need to be supported by more studies in the future. I have added a brief description of post-ESD bleeding and perforation to the manuscript and updated the references.

According to a recent meta-analysis, *en bloc*, complete, and curative resection rates in Eastern studies were 95% (95% confidence interval [CI], 94%–96%), 89% (95% CI, 88%–91%), and 82% (95% CI, 81%–84%), respectively[21]. EGC cases in which ESD is performed beyond the current ESD indications, considering patient factors such as comorbidities, life expectancy, and the ability to tolerate surgery, should be excluded from this calculation. Furthermore, the main adverse events of ESD, such as post-ESD bleeding and perforation, should be considered when evaluating the quality of ESD outcomes. The overall rates of delayed bleeding and perforation are reported to be 2.6–8.5% and 2.3–3.9%, respectively[22-24]. Based on previous reports, I suggest quality indicators for the outcomes of ESD for EGC in Table 1.

Reply to Reviewer #2's Comments

I would like to thank the reviewer for the constructive critique to improve the manuscript. We have made every effort to address the issues raised and to respond to all comments. The revisions are indicated in red font in the revised manuscript. Please find below a detailed, point-by-point response to the reviewer's comments. I hope that my revisions meet the reviewer's expectations.

1. As reference 5, authors introduced the Korean clinical guideline for gastric cancer. Is criteria for indication of gastric cancer for ESD similar over the world?

- The indications of ESD for gastric cancer in the Korean clinical guidelines are similar to those resented in the Japanese clinical guidelines. Considering the limited experience with the procedure in Western countries, this indication of ESD for early gastric cancer is currently accepted in most countries. Therefore, I have added a reference to the Japanese clinical guidelines for gastric cancer.

7. Japanese Gastric Cancer Association. Japanese Gastric Cancer Treatment Guidelines 2021 (6th edition). *Gastric Cancer* 2023; **26**: 1-25 [PMID: 36342574 DOI: 10.1007/s10120-022-01331-8]

2. Not all patients achieve curative resection after ESD of EGC, which is a critical problem. Authors should mention about risk factor of patients with problem for gastric ESD.

- I have added the following sentence.

The main risk factors for non-curative resection are as follows: tumor location in the upper body, large tumor size (≥ 2 cm), presence of an ulcer, presence of undifferentiated-type component tumor, submucosal invasion, and an inexperienced endoscopist[9-11].

3. Authors mentioned NBI. How about IEE, such as LCI, BLI and TXI, for detection and evaluation for gastric cancer?

- Other IEEs such as LCI, BLI, and TXI are also useful for detecting and delineating the horizontal extent of EGC. However, most studies, including my previous studies, have reported the usefulness of IEE using NBI. Therefore, I have included a representative IEE using the NBI, in this editorial.
4. Please mention about *H. pylori* infection status for detection and evaluation of gastric cancer? Is it better to eradicate *H. pylori* infection before ESD?
- A recent study in China (Dig Dis. 2023 Oct 13. doi: 10.1159/000534332) reported that *H. pylori* eradication before ESD was beneficial for precise delineation of lesions and reduction of the risk of positive horizontal resection margins. However, previous studies in Japanese have shown that *H. pylori* eradication before ESD obscures the horizontal margins of EGC. Based on my personal experience, *H. pylori* eradication before ESD tends to obscure the horizontal margins of EGC, which is similar to the results of Japanese studies. Therefore, I believe that it is too early to recommend *H. pylori* eradication before ESD at the present editorial.
5. Compared with surgical gastrectomy, ESD is a minimal invasive procedure with additional advantages such as preserving the entire stomach and maintaining of the patient's quality of life. I agree. However, authors should explain adverse events of ESD.
- I have added the following sentences briefly because this manuscript is an editorial article and not a review article.

Furthermore, the main adverse events of ESD, such as post-ESD bleeding and perforation, should be considered when evaluating the quality of ESD outcomes. The overall rates of delayed bleeding and perforation are reported to be 2.6–8.5% and 2.3–3.9%, respectively[22-24].

6. Please add references in each quality indication of Table 1.

- I have added the content and references showing this in the main text as follows:

According to a recent meta-analysis, *en bloc*, complete, and curative resection rates in Eastern studies were 95% (95% confidence interval [CI], 94%–96%), 89% (95% CI, 88%–91%), and 82% (95% CI, 81%–84%), respectively[21]. EGC cases in which ESD is performed beyond the current ESD indications, considering patient factors such as comorbidities, life expectancy, and the ability to tolerate surgery, should be excluded from this calculation. Furthermore, the main adverse events of ESD, such as post-ESD bleeding and perforation, should be considered when evaluating the quality of ESD outcomes. The overall rates of delayed bleeding and perforation are reported to be 2.6–8.5% and 2.3–3.9%, respectively[22-24]. Based on previous reports, I suggest quality indicators for the outcomes of ESD for EGC in Table 1.