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Dear Dr Cui

We would like to submit our original manuscript entitled “**Severity of gastric mucosal atrophy affects healing speed of artificial ulcer after endoscopic submucosal dissection: retrospective study**” (Number: 37992) for publication in the ‘Original Article’ of your journal. We wish to thank you for your helpful comments. We have attempted to address yours comments and made the appropriate changes according to those comments.

We believe that this letter will be of a great interest to the readers of your Journal. All authors have read the manuscript and conflict of interest statement and approved their submission for publication.

We thank you for your consideration and prompt handling of our manuscript and look forward to hearing from you.

Sincerely yours,  
*Mitsushige Sugimoto*

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## Our responses to comments raised by the Reviewer 1

### 1. Exclusion criteria must be mentioned in the methods section.

#### **Response:**

In this study, exclusion criteria were patients with advanced-stage gastric cancer, patients who refuse follow-up endoscopy at both 4 and 8 weeks after ESD treatment and patients with lack of informed consent. In general, it is important to show exclusion criteria. According to your suggestion, we added exclusion criteria in revised version.

### 2. Anemia is an important factor that effects the wound-healing, and anemia can be reveal after occult bleeding of gastric cancer. Transfusion status of the patients must be cleared.

#### **Response:**

Thank you for your comments. As your comments, severity of anemia is expected to affect the healing speed of ulcer after ESD. In this study, two patients (1.5%) experienced delayed bleeding with tarry stool after ESD treatment, and only one patient received transfusion treatment. In addition, no patient of hemoglobin 10 g/dl was observed at point before ESD treatment.

As your comments, we added explanation of transfusion status of the patients in revised paper.

### 3. Oxygenation is another factor on wound-healing, so respiration status of the patients must be mentioned if possible (e.g arterial blood gases)

#### **Response:**

As your comments, oxygenation also influences the healing speed of ulcer after ESD. However, there was no patient with hypoxemia in this study.

According to your suggestion, we added this information in revised version.

### 4. Minerals (eg. Zn) and vitamins (eg. vit C) may effect the results. Please cite this issues in the discussion section.

#### **Response:**

According to your suggestion, minerals and vitamins may affect the healing speed of ulcer after ESD. Unfortunately, we have no data of minerals and vitamins in this study.

With agreement to your suggestion, we discussed association with ulcer healing and minerals or vitamins with any references in the Discussion section of revised version.

### 5. Hematologic and coagulation parameters must be mentioned in the text.

#### **Response:**

Thank you for your comments. In this study, the prevalence of patients received anti-coagulants was 16.7%. No cases with hematologically abnormal coagulation ability were observed. In addition, although intake of aspirin/NSAIDs affects the healing speed of ulcer after ESD, intake of

aspirin/NSAIDs did not increase incidence of gastric bleeding after ESD. As your comments, we mentioned about hematologic and coagulation parameters in revised version.

## Our responses to comments raised by the Reviewer 2

1. Please add the detailed exclusion criteria in the article.

**Response:**

In this study, exclusion criteria were patients with advanced-stage gastric cancer, patients who refuse follow-up endoscopy at both 4 and 8 weeks after ESD treatment and patients with lack of informed consent. According to your suggestion, we added exclusion criteria in the Methods section of the revised version.

2. As we all know, there are many types of PPI, why did the authors choose only the two kinds of PPI, lansoprazole and vonoprazan, to analyze the association between acid inhibitory drugs and the healing of post-ESD ulcers. Please give a reasonable explanation.

**Response:**

Thank for your comments. As your questions, there are many types of acid inhibitory drugs (four kinds of PPIs and vonoprazan) in Japan. In our hospital, we have two kinds of clinical pathways scheduled to use lansoprazole or vonoprazan after ESD treatment for gastric tumors. Therefore, we analyzed the healing speed of ulcer after ESD by use of only the two kinds of acid inhibitory drugs, lansoprazole and vonoprazan. We added this explanation in revised version.

3. Of the many possible related factors, the authors concluded that the severity of gastric atrophy was a possible factor to affect the healing speed of ESD-induced ulcer, therefore, it might be better if the authors could elaborate on the potential mechanism in discussion section.

**Response:**

As your comments, we concluded that the severity of gastric atrophy was one of possible factor to affect the healing speed of ESD-induced ulcer. According to your suggestion, we added our hypothesis for the potential mechanism in discussion section of the revised version.

4. There are some spelling mistakes in the text, and the abbreviations of words in their first appearance should state their original words, please check and correct carefully.

**Response:**

Thank you for your comments. We carefully checked spelling mistakes throughout text.

## **Our responses to comments raised by the Reviewer 3 and 4**