

## Peer Review File

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### Reviewer A

This was a phase 1 single-arm study of autologous esophageal mucosa and polyglycolic acid transplantation with temporary stent implantation for prevention of stenosis after total esophageal ESD. This procedure is expected to be highly effective in preventing stenosis, with approximately 56% of patients not suffering from stenosis despite the circumferential and approximately 10 cm long esophageal ESD ulcers.

I read the manuscript with a great interest, but I have some comments listed below.

1. How was the length of ulcer measured? According to the resected lesion size or measured endoscopically after the resection?

**Reply 1:** We measured the length of ulcer endoscopically after the resection.

Changes in the text: Page 4, line 134 – 135.

2. The definition of stricture is defined as when a standard endoscope could not pass through at 2 weeks, 3 months, and 6 months' follow-up. Were there any cases in which endoscopic exam was performed for stenosis symptoms other than the prescribed timing?

**Reply 2:** When a patient has difficulties in eating, he will connect our doctors and came to the hospital. Actually there were 2 patients our doctors that they had stenosis symptoms and came to the hospital.

Changes in the text: Page 4, line 160 – 162.

3. Stent migration occurred in two cases, but did the stent ever fall into the stomach or lower? What measures can be taken to counteract this risk?

**Reply 3:** The stents fell into the stomach. We will pull the stent into their original location and ask the patient do not jump or do strenuous exercise when they are at home. One of the 2 patients experienced the stent migration twice so we remove his stent on the 5<sup>th</sup> week when the stent migration happened the second time.

Changes in the text: Page 5, line 187 – 188.

4. There was a case of stenosis which occurred before stent removal. Did the stenosis occurred in the area where the stent was placed?

**Reply 4:** No. The stenosis occurred in the anal side of the ulcer where had severe tissue proliferation.

Changes in the text: Page 5, line 202 – 204.

5. AEM was sutured on PGA, and the PGA was sutured to the stent. Was the regenerating mucosa injured during stent removal or were there any difficulties in removing the stent?

**Reply 5:** No. In our study, we found that the PGA sheet and absorbable line can be absorbed totally in 6 weeks. Even in the cases we have to remove the stents in 3 or 4 weeks, the PGA sheet and absorbable line were absorbed partly which were enough to let the mucosa separate

from the stent. So when we remove the stent, there were no difficulties in removing the stent.  
Changes in the text: Page 5, line 182 – 186.

6. There were some cases of SM invasion, but weren't any of these cases received additional surgery? This should be noted as it will preclude evaluation of the stenosis.

**Reply 6:** We advised all the cases of SM invasion to ask the radiotherapy doctor and thoracic surgeon for advice. 1 of the patients underwent additional surgery 9 months after ESD. When we wrote this article, the follow-up month of this patient was 11, we revised it to 9 in the revised manuscript. Besides, 1 case of SM invasion underwent radiotherapy 4 months after ESD, and he had no stenosis.

Changes in the text: Page 5, line 205 – 208.

### **Reviewer B**

1. Regarding the length of stent relative to the longitudinal length of ulcer, there were cases with same or longer length of stent to the ulcer length. Please discuss the desirable length of stent to the ulcer length.

**Reply 1:** We have modified our text as advised (see Page 6, line 229 - 236).

Changes in the text: Page 6, line 229 - 236

2. Line 247

The meaning of this sentence is difficult to understand. If the author considered that the PGA sheet plus esophageal stent method is not ineffective from the results of only 3 cases experienced by the authors, this sentence is undesirable because it may mislead the reader.

**Reply 2:** We have modified our text as advised (see Page 7, line 269-270)

Changes in the text: Page 7, line 269-270

3. Line 254

The author showed that lesions in the upper-middle esophagus have a higher risk of post-ESD strictures. Please discuss how to treat in such cases to prevent stenosis.

**Reply 3:** We have modified our text as advised (see Page 7, line 277-283).

Changes in the text: Page 7, line 277-283