

## Format for ANSWERING REVIEWERS

May 5, 2015

Dear Editor,



Enclosed please find the edited manuscript in Word format (file name: 17555-review.doc).

**Title:** Conservative reconstruction using stents as salvage therapy for disruption of esophago-gastric anastomosis

**Author:** Taro Oshikiri, Yoshinobu Yamamoto, Ikuya Miki, Masahiro Tsuda, Tetsu Nakamura, Yasuhiro Fujino, Masahiro Tominaga, and Yoshihiro Kakeji

**Name of Journal:** *World Journal of Gastroenterology*

**ESPS Manuscript NO:** 17555

The manuscript has been improved according to the suggestions of the reviewers as follows:

1 The format has been updated.

2 The revisions were made according to the suggestions of the reviewer.

### Reviewer 00071054

This manuscript includes some useful information; however, the following remarks should be discussed.

1. Please describe the detailed methods of cervical anastomosis performed in this patients, for example, hand-sewn or stapled anastomosis; end-to-end, end-to-side, or side-to-side fashion.

→The phrase “**by end-to-end stapling**” was inserted for clarification.

2. I could not understand the rationale that the authors considered this case as gastric conduit necrosis. In Figure 2, it seemed complete anastomotic dehiscence due to technical failure because the stump of gastric conduit was too healthy, rarely seen in the conduit necrosis. I think that it was difficult to distinguish between conduit necrosis and anastomotic dehiscence because gastrointestinal endoscopy on POD 21 or thereafter were too late to evaluate the status of the anastomosis.

→As you noted, gastric conduit necrosis typically occurs rapidly, resulting in an observable critical change in the clinical condition; thus, gastrointestinal endoscopy is performed immediately, revealing typical necrotic lesions of the gastric conduit. The clinical course of our patient was quite rare. Namely, gastric conduit necrosis occurred quite slowly and thus, saliva drained entirely via the neck, and the patient's general condition remained stable. As a result, the performing of gastrointestinal endoscopy and the diagnosis of gastric conduit necrosis were delayed. With regard to the technical failure of anastomosis, we added the CT findings on postoperative day (POD) 6, which showed continuity of the anastomosis and no evidence of malformation of the staple line, indicating that the anastomotic dehiscence was not caused by technical failure. The stump of the gastric conduit was healthy because the ischemic area was extremely localized at the top of the gastric conduit and necrosed, with complete drainage via the neck tube. In conclusion, we diagnosed gastric conduit necrosis comprehensively by a chronological change in the CT findings, the nature of the drainage, including pus, and

gastrointestinal endoscopy. We added the following information to the Discussion section:

“In our patient, we diagnosed gastric conduit necrosis comprehensively by a chronological change in the CT findings, the nature of the drainage, including pus, and gastrointestinal endoscopy. The CT findings on POD 6 showed continuity of the anastomosis and no evidence of malformation of the staple line; thus, anastomotic dehiscence was not caused by technical failure. Gastrointestinal endoscopy on POD 21 showed disruption of the anastomosis, but the stump of the residual gastric conduit was quite healthy without necrosis, which may have been because the ischemic area was extremely localized at the top of the gastric conduit and completely isolated, with drainage via a neck tube.”

3. The authors considered that the anastomotic leakage developed on POD 10. Are there any signs of the leakage before POD 10? When do patients usually resume oral intake after esophagectomy in the authors' hospital?

→There were signs of leakage on POD 6. CT was performed at this time, indicating no anastomotic dehiscence or malformation of the staple lines. Therefore, we diagnosed this patient with regular anastomotic leakage without gastric conduit necrosis and performed conservative management. We modified the sentences and included the CT imaging results and findings as follows:

“On postoperative day (POD) 6, the white blood cell (WBC) count and C-reactive protein (CRP) level were elevated at 11,600/ $\mu$ l and 9.4 mg/dl, respectively. The neck drainage tube was dirty, with signs of anastomotic leakage. Computed tomography (CT) performed at this time showed continuity of the anastomosis, with no fluid or air surrounding it (Fig. 1a, arrows).”

4. This manuscript should be checked by the native English speaker.

→Our manuscript was corrected again by a native English speaker.

## Reviewer 3254380

This article is a case report about the conservative management of gastric tube necrosis as a complication of esophagectomy. The authors describe a 61-year-old man who underwent minimally invasive esophagectomy complicated by slowly progressive gastric conduit necrosis associated with complete neck drainage and stable overall condition. The patient's anastomotic leakage was treated by inserting a covered self-expanding metal stent (SEMS) into the esophagus. Due to the high morbidity and mortality after esophagectomies, especially after gastric conduit necrosis, it is crucial to find the adequate treatment, either operative or conservative treatment to handle the complications. This is a report of successful conservative management of gastric conduit necrosis. Treating an anastomotic leakage by a SEMS is a novel and innovative therapeutic strategy. The quality of the manuscripts presentation and readability is fair. The main and short titles accurately reflect the major topic of the content of the study. The abstract provides a clear delineation between the research backgrounds, objectives, materials and methods, results and conclusion.

Materials and methods are not sufficiently described.

1. How long was the gastric conduit necrosis?

→We added the following phrase:

“which was 2 cm in length at the top of the conduit”

2. When did the necrosis appear?

→Anastomotic leakage was diagnosed on POD 6, and pus was found in the drainage tube in the neck on

POD 15. Necrosis then appeared on POD 15. We added the following sentence:

“On POD 15, a small amount of pus was found in the drainage tube in the neck.”

3. What would be, according to authors the limit of the SEMS treatment (length of the necrosis, appearance of the necrosis: early vs. late)?

→We added the following sentences:

“By contrast, a patient with early onset gastric conduit ischemia that occurs within POD 5 may not be suitable for stent therapy because the progression will likely be acute and critical. To diagnose conduit necrosis immediately, rapid execution of gastrointestinal endoscopy should be recommended if there are any signs of anastomotic leakage. Considering the abovementioned criteria, the distance between the two ends of the anastomosis or the circumference of the leakage may not be the limit for stent therapy.”

4. Are there any other conservative options? What about the endo-sponge therapy?

What would be the surgical approach?

The results do not provide sufficient experimental evidence. There is a need of a retrospective or a prospective analysis to evaluate the SEMS in the conservative management of anastomotic leakage after esophagectomy in comparison to the end-sponge therapy.

In the discussion, the author gives us a view on the patient's therapy and why they used the SEMS. Nevertheless, there is no discussion about other conservative therapeutic possibilities, like endoluminal vacuum therapy. Moreover it lacks the comparison to the surgical approach. The reference is appropriate, relevant and up to date.

→We added the following sentences to the Discussion section and added reference [14] as follows:

“Dawson et al. have reported surgical management with removal of a conduit following gastric conduit necrosis. In their patients, reconstruction with the jejunum or left colon was performed with 0% mortality and 57% morbidity. These procedures can provide good clinical and functional outcomes, but they require a specialized multidisciplinary approach and are associated with a high morbidity rate <sup>[5]</sup>.” “Recently, a new approach for the treatment of anastomotic leakage following esophageal resection has been reported involving the combination of vacuum-assisted therapy with covered SEMS [14]. In this approach, an Endo-sponge (Braun BBD Aesculap GmbH, Tuttlingen, Germany) is placed into the esophageal lumen and pushed into the cavity, which is overstented with a partially covered SEMS. The suction tube of the sponge is retrieved through the nose and connected to a continuous negative pressure of 75 to 100 mm Hg within 18 hours in a stepwise manner, and the pressure is increased when secretion production is diminished [14]. In our patient, the paraesophageal cavity was too large to enclose the sponge tightly. Additionally, he experienced complete drainage by the percutaneous drain and thus, simple SEMS therapy was selected. In the case of leakage in a patient with a small paraesophageal cavity without a percutaneous drainage tube, endoluminal vacuum therapy with an Endo-sponge is an ideal and excellent therapy.”

**14 Gubler C, Schneider PM, Bauerfeind P. Complex anastomotic leaks following esophageal resections: the new stent over sponge (SOS) approach. *Dis Esophagus* 2013;26:598-602 [PMID: 23199232 DOI: 10.1111/dote.12005]**

Stomach and colon are often used to reconstruct the esophagus and gastric transplant is the first choice. The transplant necrosis is a fatal early complication which is associated with high rate mortality. The major cause of delayed conduit necrosis is the venous stasis which leads to ischemia. The esophageal stent placement is frequently used in thoracic anastomosis leakage because leak is more fatal. This case report described a proximal localized necrosis of the gastric transplant (tip) after esophageal reconstruction for carcinoma that was managed conservatively with stent placement. The authors reported that this is the first successful use of stent in such situation. But I have noted the following concerns.

1. Reformulate the main and running title: to accurately reflect the major topic of work

→ We revised the title as follows:

Main title: Conservative reconstruction using stents as salvage therapy for ~~gastric conduit necrosis~~ **disruption of esophago-gastric anastomosis** after esophagectomy.

Running title: Stent placement for ~~gastric conduit necrosis~~ **disruption of anastomosis**.

2. The manuscript's presentation (form and text) needs to be reconsidered. More details are needed in the clinic presentation of the case.

→ We added detailed information on the clinical presentation, including CT figures with findings and the state of the anastomosis.

3. Are there any perioperative technical problems such as: venous stasis of transplant, anastomotic tension which leads to leak and retraction of the anastomotic ends?

→ We added the following sentence:

**"There was no evidence of anastomotic tension or venous stasis of the gastric conduit."**

4. Esophago-gastric anastomotic site: cervical or mediastinal (behind manubrium).

→ We added the following sentence:

**"The esophago-gastric anastomotic site was ultimately determined to be located in the mediastinum (behind the manubrium)."**

5. Detail more the discussion: early diagnosis of conduit necrosis, criteria for conservative management, anastomotic conditions to use stent (distance between the two ends, circumference of leakage)

→ We added the following sentence to the Discussion section:

**"By contrast, a patient with early onset gastric conduit ischemia that occurs within POD 5 may not be suitable for stent therapy because the progression will likely be acute and critical. To diagnose conduit necrosis immediately, rapid execution of gastrointestinal endoscopy should be recommended if there are any signs of anastomotic leakage. Considering the abovementioned criteria, the distance between the two ends of the anastomosis or the circumference of the leakage may not be the limit for stent therapy."**

6. Reformulate the conclusion

→ We revised the Conclusion as follows:

**"In conclusion, the case highlights the diagnosis and evaluation of ~~gastric conduit necrosis~~ **esophago-gastric conduit anastomosis disruption** and demonstrates that a conservative approach with no surgery may result in a successful outcome."**

3 References and typesetting were corrected

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

Sincerely yours,

A handwritten signature in cursive script, reading "Taro Oshikiri".

Taro Oshikiri

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