

July 22, 2014

Dear Editor,



Please find enclosed the edited manuscript in Word format (file name: 11806-Review.doc).

**Title: Clinical characteristics and management of gastric tube cancer with endoscopic submucosal dissection**

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

**ESPS Manuscript NO:** 11806

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

1 Format has been updated

2 Revision has been made according to the suggestions of the reviewer

(1) The topic is discussed in a little confusing manner.

**Answer:** We have revised discussion following as reviewer's comments.

(2) The English should be improved.

**Answer:** We have corrected grammatical mistakes and have asked an English native speaker to edit the manuscript.

(3) The clear-cut indications of ESD as treatment modality for GTC should be more clearly discussed.

**Answer:** We added the sentence 'According to the treatment guidelines for gastric cancer in Japan<sup>[11]</sup>, the indications for ESD in EGC tend to be mucosal cancer within 2 cm in size without ulcers. Furthermore, these guidelines have extended the indications for ESD in the following cases: (1) differentiated type, mucosal (M) cancer without ulcer, and larger than 2 cm; (2) differentiated type, M cancer with ulcer, and 3 cm or smaller; and (3) undifferentiated type, M cancer without ulcer, and 2 cm or smaller. The guidelines also state that an additional lymph node resection is not necessary when lymphovascular invasion is absent and when the tumor is not deeper than submucosal 1 (SM1; ~500  $\mu$ m). In the present study, we performed ESD for GTC following an extended indication for EGC, and the en bloc resection of all GTCs was successfully achieved using ESD.' in Discussion.

11. Association JGC. Japanese gastric cancer treatment guidelines 2010 (ver. 3). Gastric Cancer 2011; 14(2): 113-123

(4) Although the Authors concluded that only minor complications occurred, they should spend time to discuss the causes of high rate of anastomotic strictures (45%), food residue (36%), bleeding (45%), and finally in the postoperative phase, delayed bleeding (18%) and stenosis (9%).

**Answer:** We added the sentence 'Although anastomotic stenosis was observed at a high frequency (45.5%, 5/11) and the endoscopic extension was performed before the ESD, overtube insertion was impossible in most of those cases. Food residues were observed in 36.4% (4/11) of the cases and had to be fully removed before ESD. However, these complications were not associated with an extended resection time. Bleeding was observed in 45.5% of the patients during ESD. Intraoperative bleeding was more frequently observed in the gastric tube originating from the body of the stomach (71.4%, 5/7) than in those originating from the antrum (25%, 1/4). Emergency hemostasis was performed for postoperative bleeding in the gastric tube originating from the body in 2 cases (18.2%). Our results suggest that ESD for GTC originating from the body can be considered a high risk for intra- and postoperative bleeding. Stenosis after ESD was observed in only one case (9.1%) in the largest tumor size (68 mm) found in our study. Ono *et al.* have reported that resecting areas larger than three-quarters of the circumference of the esophageal lumen can be considered an important risk factor for postoperative stenosis in ESD of superficial esophageal cancer<sup>[26]</sup>. The risk factors for postoperative stenosis may be associated with the tumor size of the GTC. A greater accumulation of cases will be required to assess the complications of ESD for GTC in detail' in Discussion.

26. Ono S, et al. Predictors of postoperative stricture after esophageal endoscopic submucosal dissection for superficial squamous cell neoplasms. *Endoscopy* 2009; 41(8): 661-665

(5) The potential advantages of ESD over EMR should be discussed in more detail.

**Answer:** We added the sentence 'ESD has advantages over EMR in terms of the size and depth of the resected specimens and has been successfully applied for the en bloc resection of various cancers<sup>[22, 23]</sup>. Because the en bloc resection rate of ESD for GTC is reported to be 88%–95%, which is much higher than that of EMR (14.3%)<sup>[12,13,15]</sup>, ESD provides a more accurate histological assessment than EMR.' in Discussion.

12. Osumi W, et al. Endoscopic submucosal dissection allows less-invasive curative resection for gastric tube cancer after esophagectomy - a case series. *Endoscopy* 2009; 41(9): 777-780

13. Bamba T, et al. Surveillance and treatment for second primary cancer in the gastric tube after radical esophagectomy. *Surg Endosc* 2010; 24(6): 1310-1317

15. Nishide N, et al. Clinical outcomes of endoscopic submucosal dissection for early gastric cancer in remnant stomach or gastric tube. *Endoscopy* 2012; 44(6): 577-583

22. Fujishiro M, et al. Successful outcomes of a novel endoscopic treatment for GI tumors: endoscopic submucosal dissection with a mixture of high-molecular-weight hyaluronic acid, glycerin, and sugar. *Gastrointest Endosc* 2006; 63(2): 243-249

23. Onozato Y, et al. Endoscopic submucosal dissection for early gastric cancers and large flat adenomas. *Endoscopy* 2006; 38(10): 980-986

(6) The possibility that *Helicobacter pylori* (Hp) infection is a major cause of GTC after esophagectomy seems highly speculative.

**Answer:** We agree your comments. Nonaka et al. and we showed HP infection in most of GTC patients. However, previous studies have shown a lower prevalence of HP infection in GTC patients. Further studies, such as prospective assessment of mucosal status and HP infection after esophagectomy, will be required to clarify carcinogenetic factors in the gastric tube.

(7) The Reference list should be completed.

**Answer:** We have corrected the reference lists.

3 References and typesetting were corrected

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

Sincerely yours,

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