

Format for ANSWERING REVIEWERS



December 21, 2014

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 15008-review.doc).

Title: Optimal management of biopsy-proven low-grade gastric dysplasia

Author: Jung-Wook Kim & Jae Young Jang

Name of Journal: *World Journal of Gastrointestinal Endoscopy*

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I am really appreciative of Editor's and reviewers' thoughtful and constructive comments. We have revised the manuscript that includes additional explanations as recommended by Editor and the reviewers. I hope that my endeavor to address these issues is satisfactory to both Editor and the reviewers. Again, on behalf of our authors, thank you.

Reviewer Comments:

Reviewer #1: Dysplasia in the gastrointestinal tract is considered a carcinoma precursor and a marker of high cancer risk for the site where it is found. So there is no guideline for low-grade dysplasia (LGD). Though some past issues discussed treatments of LGD, their results were controversial. In this manuscript, you presented certainly appropriate treatment for LGD. Though those findings were very interesting, I have several concerns.

Q1. I suggest that you add concrete data regarding complications for both resection types in the MANAGEMENT part. You described that "intra-operative bleeding, perforation risk, and operation time were significantly greater for ESD", however I would like to ask you to explain specifically how much higher the risk was for each type of complication.

Answers: Thank you for your important suggestion. As you recommended, we additionally have cited two meta-analyses. We have added some sentences in the MANAGEMENT section as follows.

"One meta-analysis^[46] showed that procedure-related bleeding (OR 2.2, 95% CI 1.58-30.7) and perforation rates (OR 4.09, 95% CI 2.47-6.80) during ESD were much higher compared with those for EMR. However, these were not statistically significant in another meta-analysis including 12 studies^[45]. Both studies^[45,46] showed that ESD was more time-consuming."

45 Park YM, Cho E, Kang HY, Kim JM. The effectiveness and safety of endoscopic submucosal dissection compared with endoscopic mucosal resection for early gastric cancer: a systematic review and metaanalysis. *Surg Endosc* 2011; **25**: 2666-2677 [PMID: 21424201 DOI: 10.1007/s00464-011-1627-z]

46 Cao Y, Liao C, Tan A, Gao Y, Mo Z, Gao F. Meta-analysis of endoscopic submucosal dissection versus endoscopic mucosal resection for tumors of the gastrointestinal tract.

Q2. Does the position of the adenoma in the stomach change your tactics? Please add this aspect to your DISCUSSION part.

Answers: We agree with your comments. As you know, the location of the tumor is one of the predictor of success of en bloc resection. Therefore, we may fail to perform the ESD for gastric LGD. In these cases, we can try another treatment option such as ablation therapy. We have added some sentences in the MANAGEMENT section as follows.

“Miyamoto et al.^[50] reported that tumor size and location of the lesion are important factors that affect the success rate of en bloc resection. Because not all lesions can be resected en bloc for technical difficulty, another treatment option such as ablation therapy should be considered for the treatment of LGDs^[51].”

50 Miyamoto S, Muto M, Hamamoto Y, Boku N, Ohtsu A, Baba S, Yoshida M, Ohkuwa M, Hosokawa K, Tajiri H, Yoshida S. A new technique for endoscopic mucosal resection with an insulated-tip electrosurgical knife improves the completeness of resection of intramucosal gastric neoplasms. *Gastrointest Endosc* 2002; **55**: 576-581 [PMID: 11923778]

51 Jung SJ, Cho SJ, Choi IJ, Kook MC, Kim CG, Lee JY, Park SR, Lee JH, Ryu KW, Kim YW. Argon plasma coagulation is safe and effective for treating smaller gastric lesions with low-grade dysplasia: a comparison with endoscopic submucosal dissection. *Surg Endosc* 2013; **27**: 1211-1218 [PMID: 23076459 DOI: 10.1007/s00464-012-2577-9]

Reviewer #2: The topic is of major interest considering the prognosis of gastric cancer.

Q1. In figure 1 should be inserted for extended low-grade dysplasia (LGD)

Answers: Thank you for your careful comment. As you recommended, we have inserted “extend low-grade dysplasia” in Figure 1 as follows.

“Figure 1 A lesion with a histologic upgraded from extended low-grade dysplasia (LGD) to adenocarcinoma following endoscopic submucosal dissection (ESD).”

Q: 2. I would add only that large clinical trials are needed to assess the long-term prognosis of patients with gastric LGD.

Answers: As you commented, we have removed a small study (24. Park et al. *Eur J Gastroenterol Hepatol* 2008;20:966-970) in NATURAL HISTORY section as follows. Furthermore, we have removed table 2. Thank you again.

~~“Furthermore, a retrospective study from Korea^[24] analyzed the follow-up results of 26 LGDs and 1 HGD for a mean of 58 months. The authors found that eight (29.6%) adenomas of progressive dysplasia, three (11.5%) LGDs and one (100%) HGD progressed to invasive carcinoma irrespective of the clinical, morphological and histological characteristics (Table 2). Considering the high rate of progression to cancer, this study suggested that gastric LGD, as well as HGD, should be treated vigorously by therapeutic endoscopy before malignant transformation^[24].”~~

Thank you again.

Sincerely yours,

Jae Young Jang, MD, PhD

Division of Gastroenterology, Department of Internal Medicine, College of Medicine, Kyung Hee University, 1 Hoegi-dong Dongdaemun-gu, Seoul, 130-702, South Korea.

Email: jjjang@khu.ac.kr

Telephone: +82-2-958-8200 Fax: +82-2-968-1848