



# Should we perform surveillance endoscopy after endoscopic submucosal dissection of premalignant gastric adenoma?

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## Metachronous gastric cancer (MGC) after curative endoscopic resection (ER) of early gastric cancer (EGC)

Endoscopic submucosal dissection (ESD) is an advanced endoscopic technique that allows curative resection of EGC. Several studies reported excellent short- and long-term outcomes in patients undergoing curative resection (1,2). In addition, ER of EGC, as opposed to surgical resection, allows preservation of stomach and in turn provides a better quality of life (3). However, development of MGC following curative ER is one of the major issues of gastric ESD. Our retrospective study found that the 5-year, 7-year and 10-year cumulative incidence of MGC were 9.5%, 13.1% and 22.7%, respectively. Furthermore, some patients who lost to follow up were found to have advanced gastric cancer and died of gastric cancer (4). Currently, no standardized recommendations are available for endoscopic surveillance after curative resection of EGC. However, continuous annual or biannual surveillance endoscopies may be reasonable. Regular surveillance is required for early detection of MGCs and thus less invasive treatment option can be curative (4-7).

## Surveillance endoscopy after ER of gastric adenoma with low grade dysplasia

Gastric adenoma with low grade dysplasia is classified as category 3 in the Vienna classification and known to

transform into malignant lesions (8-11). Approximately 4% to 30% of gastric lesions initially diagnosed as adenomas by endoscopic biopsy are upgraded to gastric cancer after ER (12,13). For these reasons, gastric adenomas are actively resected mainly by ESD in Korea. However, optimal surveillance protocol after ER of gastric adenoma is unknown. The risk of gastric cancer after curative ER has not been well studied.

Given this background, Yoon *et al.* conducted a retrospective study to investigate the incidence of gastric cancer after ER in patients undergoing ESD of gastric adenoma and EGC (14). This study also compared the incidence of MGC between the adenoma group and the EGC group. The follow-up period after ER in this study ranged from 1.0 to 8.9 years (median, 2.3 years). In this study, the incidence of gastric cancer after ER for gastric adenoma was similar to that of EGC: 14.4 cases per 1,000 person-years in adenoma patients and 18.4 cases per 1,000 person-years in EGC patients ( $P=0.309$  by log-rank test). In addition, the lesion characteristics of newly developed gastric neoplasias (adenoma and MGC) were also similar between the two groups.

This study gave us two important messages. First, patients with gastric adenomas without high grade dysplasia or cancer have an increased risk of MGC. Therefore surveillance endoscopy is necessary after ER of gastric adenoma in order to detect MGC at early stage when endoscopic therapy is feasible. The primary purpose of ER

of premalignant gastric adenoma with low grade atypia was cancer prevention similar to the concept of endoscopic removal of colorectal adenomatous polyp to prevent colon cancer (15). In addition, en bloc specimens obtained by ESD facilitate precise histological assessment which could have been understaged at tissue biopsy. This study showed that the risk of development of gastric cancer remained after the endoscopic removal of the index lesions and the cumulative incidence of MGC in the adenoma group was very high. It can be reasonably explained by field cancerization theory and the fact that some gastric adenomas with low-grade dysplasia coexist with gastric cancer.

Second, this study suggested that surveillance endoscopy should be continued indefinitely. The incidence of MGC increased overtime after ESD of gastric adenoma with low grade dysplasia and more aggressive second lesion can develop after ESD of index gastric adenoma even after 5-year follow-up period. It should be noted that 7 patients with gastric adenoma at index endoscopy developed submucosal invasive gastric cancer at long term follow-up. Of these, only one patient fully complied with the surveillance endoscopic schedule, whereas the other irregularly followed their surveillance schedule (14).

The median follow-up period after ER of the adenoma group was shorter than that of the EGC group. The reason for this is unclear. Possibly, both endoscopists and patients may underestimate importance of surveillance endoscopy after ER of gastric adenoma because of its lesser invasiveness. Thus, it is essential to recognize the risk of cancer development in other part of the stomach and adhere to surveillance protocol.

### The next issues to be resolved

Both of gastric low grade dysplasia and gastric cancer occur on the similar background, i.e., chronic atrophic gastritis due to the infection of *Helicobacter Pylori* (*H. Pylori*). The International Agency for Research on Cancer (IARC), a subsidiary of the World Health Organization (WHO), categorized *H. pylori* as a group 1 carcinogen for gastric cancer (16). A multicenter prospective randomized control trial by Fukase *et al.* showed that *H. pylori* eradication could play a preventative role to reduce the occurrence of MGC in patients who have undergone ER (17). This strategy should be considered for gastric cancer prevention in patients with gastric adenoma following ER, although, further prospective studies are warranted to investigate the clinical impact of *H. Pylori* eradication in this setting.

A prospective study showed that the accumulation of methylation could be an epigenetic cancer risk prediction of MGC after *H. pylori* eradication (18). The results of this study provided convincing data to stratify the risk factors for MGC including *H. pylori* eradication (19). The same risk stratification may be applied to patients with gastric adenoma.

Careful and regular surveillance endoscopy is strongly recommended for patients undergoing ER of gastric adenoma with low grade atypia as well as gastric cancer. Large prospective studies are warranted to identify the high risk group of cancer development and determine the optimal surveillance interval.

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## References

- Oda I, Oyama T, Abe S, et al. Preliminary results of multicenter questionnaire study on long-term outcomes of curative endoscopic submucosal dissection for early gastric cancer. *Dig Endosc* 2014;26:214-9.
- Suzuki H, Oda I, Abe S, et al. High rate of 5-year survival among patients with early gastric cancer undergoing curative endoscopic submucosal dissection. *Gastric Cancer* 2016;19:198-205.
- Choi JH, Kim ES, Lee YJ, et al. Comparison of quality of Life and worry of cancer recurrence between endoscopic and surgical treatment for early gastric cancer. *Gastrointest Endosc* 2015;82:299-307.
- Abe S, Oda I, Suzuki H, et al. Long-term surveillance and treatment outcomes of metachronous gastric cancer occurring after curative endoscopic submucosal dissection. *Endoscopy* 2015;47:1113-8.
- Hahn KY, Park JC, Kim EH, et al. Incidence and impact of scheduled endoscopic surveillance on recurrence after curative endoscopic resection for early gastric cancer. *Gastrointest Endosc* 2016;84:628-638.e1.
- Kato M, Nishida T, Yamamoto K, et al. Scheduled endoscopic surveillance controls secondary cancer after curative endoscopic resection for early gastric cancer: a multicentre retrospective cohort study by Osaka University ESD study group. *Gut* 2013;62:1425-32.
- Min BH, Kim ER, Kim KM, et al. Surveillance strategy based on the incidence and patterns of recurrence after curative endoscopic submucosal dissection for early gastric cancer. *Endoscopy* 2015;47:784-93.
- Rugge M, Cassaro M, Di Mario F, et al. The long term outcome of gastric non-invasive neoplasia. *Gut* 2003;52:1111-6.
- Lee SY. Gastric adenoma with Low-Grade dysplasia: two countries, two outcomes. *Dig Dis Sci* 2014;59:235-7.
- Kato M, Nishida T, Tsutsui S, et al. Endoscopic submucosal dissection as a treatment for gastric noninvasive neoplasia: a multicenter study by Osaka University ESD Study Group. *J Gastroenterol* 2011;46:325-31.
- de Vries AC, Van Grieken NC, Looman CW, et al. Gastric cancer risk in patients with premalignant gastric lesions: A nationwide cohort study in the Netherlands. *Gastroenterology* 2008;134:945-52.
- Choi CW, Kang DH, Kim HW, et al. Endoscopic submucosal dissection as a treatment for gastric adenomatous polyps: predictive factors for early gastric cancer. *Scand J Gastroenterol* 2012;47:1218-25.
- Kim YJ, Park JC, Kim JH, et al. Histologic diagnosis based on forceps biopsy is not adequate for determining endoscopic treatment of gastric adenomatous lesions. *Endoscopy* 2010;42:620-6.
- Yoon SB, Park JM, Lim CH, et al. Incidence of gastric cancer after endoscopic resection of gastric adenoma. *Gastrointest Endosc* 2016;83:1176-83.
- Matsuda T, Chiu HM, Sano Y, et al. Surveillance colonoscopy after endoscopic treatment for colorectal neoplasia: From the standpoint of the Asia-Pacific region. *Dig Endosc* 2016;28:342-7.
- Schistosomes, liver flukes and *Helicobacter pylori*. IARC Working Group on the Evaluation of Carcinogenic Risks to Humans. Lyon, 7-14 June 1994. IARC Monogr Eval Carcinog Risks Hum 1994;61:1-241.
- Fukase K, Kato M, Kikuchi S, et al. Effect of eradication of *Helicobacter pylori* on incidence of metachronous gastric carcinoma after endoscopic resection of early gastric cancer: an open-label, randomised controlled trial. *Lancet* 2008;372:392-7.
- Asada K, Nakajima T, Shimazu T, et al. Demonstration of the usefulness of epigenetic cancer risk prediction by a multicentre prospective cohort study. *Gut* 2015;64:388-96.
- Maeda M, Nakajima T, Oda I, et al. High impact of methylation accumulation on metachronous gastric cancer: 5-year follow-up of a multicentre prospective cohort study. *Gut* 2016. [Epub ahead of print].

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