Incidence of gastric cancer after endoscopic resection of gastric adenoma CME

Seung Bae Yoon, MD, Jae Myung Park, MD, PhD, Chul-Hyun Lim, MD, PhD, Jin Soo Kim, MD, PhD, Yu Kyung Cho, MD, PhD, Bo-In Lee, MD, PhD, In Seok Lee, MD, PhD, Sang Woo Kim, MD, PhD, Myung-Gyu Choi, MD, PhD

Seoul, South Korea

Background and Aims: The annual incidence of metachronous cancer after endoscopic resection (ER) of early gastric cancer (EGC) is approximately 3%. However, the incidence of gastric cancer after ER of a gastric adenoma is not known. The aim of this study was to determine whether the incidence of gastric cancer after ER of a gastric adenoma was different compared with that of metachronous cancer after ER of EGC.

Methods: We retrospectively analyzed data from patients who underwent ER for gastric neoplasia from January 2005 to August 2013. Enrolled patients were divided into 2 groups: patients with low-grade dysplasia were included in the adenoma group and patients with high-grade dysplasia or invasive neoplasia were included in the EGC group. The main outcome was the incidence of gastric cancer after ER.

Results: At a median follow-up of 28 months, gastric cancer newly developed in 13 adenoma patients (3.6%) and in 30 EGC patients (5.1%). The incidence rate of gastric cancer after ER was 14.4 cases per 1000 person-years in adenoma patients and 18.4 cases per 1000 person-years in EGC patients ($P = .309$ by the log-rank test). The hazard ratio of metachronous neoplasia in adenoma patients compared with EGC patients was 0.97 (95% confidence interval, 0.62–1.53). Metachronous tumors with invasion beyond the muscularis mucosa were more frequent in adenoma patients than in EGC patients (7/35 [20.0%] vs 3/63 [4.8%], $P = .017$).

Conclusion: The incidence of gastric cancer after ER for gastric adenoma was not significantly different from that of EGC. If further prospective studies confirm these findings, careful endoscopic surveillance with the same level of intensity should be considered for both gastric adenoma and EGC patients after ER. (Gastrointest Endosc 2016;83:1176-83.)

Endoscopic resection (ER), including EMR and endoscopic submucosal dissection (ESD), is widely performed as a curative treatment for early gastric cancer (EGC). However, metachronous cancer after successful ER has emerged as a major problem. In previous studies, the cumulative incidence of metachronous cancer generally increased linearly, and the mean annual incidence rates were approximately 3%.[1-3] Patients who have undergone ER for EGC have such a high incidence of secondary cancer because this treatment leaves most of the gastric mucosa containing a large amount of abnormal mucosa affected by atrophic gastritis or intestinal metaplasia. Although *Helicobacter pylori* eradication reduces the occurrence of metachronous cancer, it does not completely eliminate the risk of recurrence.[4] Therefore, careful surveillance with endoscopic evaluation is important for patients who have undergone ER of gastric cancer.

Abbreviations: CI, confidence interval; EGC, early gastric cancer; ER, endoscopic resection; ESD, endoscopic submucosal dissection; HR, hazard ratio.

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Current affiliations: Division of Gastroenterology, Department of Internal Medicine, College of Medicine, The Catholic University of Korea, Seoul, South Korea.

Reprint requests: Jae Myung Park, MD, PhD, Division of Gastroenterology, Department of Internal Medicine, College of Medicine, The Catholic University of Korea, 222 Banpo-daero, Seocho-gu, Seoul, 137-701 South Korea.

Gastric adenomas are usually endoscopically resected because they can become malignant lesions.[5-8] In addition, some cases initially reported as noninvasive adenomas by endoscopic biopsy can be upgraded to invasive carcinoma after total resection (range 4%-30%).[9-11] For these reasons, adenoma is currently actively treated by ER; however, the incidence of gastric cancer after ER of gastric adenoma has not been well studied.

We hypothesized that the incidence of gastric cancer after ER might differ between gastric adenoma and EGC patients because an adenoma is a less-invasive form than gastric cancer by histological classification. If that is true, the endoscopic surveillance interval in adenoma patients can be extended compared with that in cancer patients. The aim of this study was to determine whether the incidence of gastric cancer after ER of gastric adenoma was different compared with the incidence of metachronous cancer after ER of EGC.

MATERIALS AND METHODS

Patients

We retrospectively analyzed patients who underwent ER for gastric neoplasia between January 2005 and August 2013 at Seoul St. Mary's Hospital, Seoul, Korea. The histologic criteria of gastric neoplasia were defined as categories 3, 4, and 5 of the Vienna classification.[12] We divided the patients into 2 groups: patients with low-grade dysplasia (Category 3 in the Vienna classification) were included in the adenoma group and those with high-grade dysplasia (Category 4) and invasive neoplasia (Category 5) were in the EGC group. Patients with EGC and synchronous adenoma were included in the EGC group. We collected data from electronic patient files including demographic characteristics, histology, treatment modality, and results, *H pylori* status, endoscopic atrophy, and the incidence of metachronous neoplasia. This study was approved by the institutional review board of Seoul St. Mary's Hospital.

ER and follow-up

Either EMR or ESD was used for resection of gastric neoplasia. Indigo carmine solution was sprayed onto the gastric mucosa, and lesion marking and circumferential incision were performed. A snare was used in EMR, and a hook knife (Olympus Medical Systems Co Ltd, Tokyo, Japan) was used in ESD. Simultaneous electronic coagulation was used during ER. All ER procedures were performed by expert endoscopists with more than 5 years of experience.

All patients after ER of gastric neoplasia were scheduled to be examined with endoscopy at 2, 6, and 12 months and annually thereafter. At follow-up examination, all suspicious mucosal lesions were evaluated histologically on endoscopic biopsy specimens. Surveillance endoscopy was performed by the same experienced endoscopist who had performed ER. Metachronous neoplasia was defined as a new tumorous lesion developing at least 1 year after ER.

Determination of endoscopic atrophy and *H pylori* status

The extent of gastric atrophy was determined by endoscopic findings and categorized as closed or open type based on the Kimura–Takemoto classification.[13] *H pylori* infection was diagnosed based on either positive results on a rapid urease test (CLO test; Ballard Medical Products, Draper, Utah) or histological examination by Warthin–Starry silver staining at the time of ER of gastric neoplasia. The first-line eradication regimen was proton pump inhibitor (30 mg lansoprazole or 20 mg rabeprazole), 1 g amoxicillin, and 500 mg clarithromycin, all twice daily for 7 days. If first-line eradication failed, a second-line regimen was administered for 14 days that consisted of 4 drugs: proton pump inhibitor twice daily, 250 mg metronidazole 3 times daily, 500 mg tetracycline 4 times daily, and 240 mg bismuth 4 times daily. The first- and second-line eradication treatment was performed based on the physician's recommendation and patient's decision. A ^{13}C-urea breath test (Helifinder; Medichems, Seoul, South Korea) was used to confirm successful eradication at least 4 weeks after completion of treatment. The patients were divided into 4 categories based on the *H pylori* infection status and eradication results: (1) a persistent group who did not undergo *H pylori* eradication or in whom it failed, (2) an eradicated group who underwent successful *H pylori* eradication, (3) a negative group without *H pylori* infection at the time of ER, and (4) uninvestigated group who underwent neither a rapid urease test nor histological examination at the time of ER.

Outcome measurements

The primary outcome was the development of gastric cancer in adenoma and EGC patients after ER. The secondary outcome was the development of gastric neoplasia including gastric cancer and adenoma in both groups. Metachronous gastric neoplasia was defined as a secondary gastric neoplastic lesion that was detected more than 1 year after ER. The patients were censored at the time of their last surveillance endoscopy, and the follow-up period was calculated as the interval from the initial ER to the last endoscopic examination.

Statistical analysis

Continuous data are presented as mean ± SD or median (interquartile range), and categorical data as number and percent. Comparison of baseline characteristics and metachronous lesions between the adenoma and carcinoma groups was performed by using a 2-sample independent *t* test or the Mann–Whitney *U* test for numerical variables, and a χ^2 test or the Fisher exact test for nominal variables. The cumulative incidence of gastric cancer and neoplasia