

## Long-term outcome comparison of endoscopic resection and surgery in early gastric cancer meeting the absolute indication for endoscopic resection CME

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**Background:** Endoscopic resection (ER) of early gastric cancer (EGC) meeting the absolute indication has excellent long-term outcomes.

**Objective:** To compare long-term outcomes of ER with those of surgery in patients with EGC who met the absolute indication for ER.

**Design:** Retrospective cohort study.

**Setting:** A specialized center for the treatment of cancer.

**Patients and Interventions:** We retrospectively reviewed data from patients who underwent gastrectomy or ER for EGC between 2002 and 2007. Gastric cancers were differentiated-type adenocarcinoma without ulceration confined to the mucosal layer and 2 cm or smaller in size.

**Main Outcome Measurements:** The primary outcome was overall survival (OS). Metachronous cancer rates and adverse event rates were compared. Kaplan-Meier plots and Cox proportional hazard regression analyses were applied for comparisons. Differences in baseline characteristics were adjusted by propensity score.

**Results:** Among 375 patients, 261 underwent ER and 114 underwent surgery. The median follow-up duration was 76.4 months. The 5-year OS rates did not significantly differ between the ER and surgery groups (95.7% vs 93.6%, respectively;  $P = .725$  by log-rank test). There were no gastric cancer-related deaths in either group. Metachronous gastric cancer developed more frequently in the ER group (6.1%, 16/261) than in the surgery group (0.9%, 1/114) ( $P = .024$ ). However, most patients (93.8%, 15/16) in the ER group were curatively treated with repeat ER. Adverse event rates were higher in the surgery group than those in the ER group (7.9% vs 2.7%,  $P = .028$ ).

**Limitations:** Retrospective, single-center study.

**Conclusions:** The OS rate after ER for mucosal gastric cancer that met the absolute indication was comparable to that achieved with surgery. Although metachronous cancers were more common after ER, they were usually treatable and did not affect survival. (Gastrointest Endosc 2015;81:333-41.)

*Abbreviations:* DFS, disease-free survival; DSS, disease-specific survival; EGC, early gastric cancer; ER, endoscopic resection; ESD, endoscopic submucosal dissection; OS, overall survival; RFS, recurrence-free survival; SD, standard deviation.

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Early gastric cancer (EGC) is defined as gastric cancer in which tumor invasion is limited to the mucosa or submucosa. Early diagnosis of gastric cancer has increased in South Korea due to screening programs and recent improvements in diagnostic techniques.<sup>1,2</sup> Gastrectomy with lymph node dissection is a standard treatment for gastric cancer, including EGC.<sup>3</sup> Long-term outcomes of gastrectomy are excellent, with 5-year overall survival (OS) rates of more than 92%.<sup>4,5</sup>

Endoscopic resection (ER), including EMR and endoscopic submucosal dissection (ESD), is widely accepted as a curative treatment for EGC without the risk of lymph node metastasis.<sup>6-8</sup> Currently, ER is considered a standard treatment for EGC that meets the absolute indication suggested in the Japanese gastric cancer treatment guidelines for ER.<sup>3</sup> The 5-year OS rates after ER are between 84% and 97%,<sup>6,9-11</sup> which is acceptable for standard treatment. Recent studies show that ER for EGC has long-term outcomes that are comparable to those of gastrectomy.<sup>12,13</sup> However, past studies had limitations, including significant differences in tumor characteristics for the ER and gastrectomy groups<sup>12</sup> and inclusion of tumors that did not meet the criteria for absolute indication.<sup>13</sup>

Thus, the aim of this study was to investigate whether long-term outcomes of ER are comparable to those of surgery for EGC that meets the criteria for absolute indication.

## METHODS

### Study population

This study was a retrospective cohort study of 665 patients who underwent gastrectomy or ER for EGC at the Center for Gastric Cancer in the National Cancer Center between January 2002 and December 2007. We included patients who met the following inclusion criteria: (1) 20 years of age and older, (2) newly diagnosed EGC without previous treatment, (3) histologically confirmed well- or moderately differentiated adenocarcinoma, (4) intramucosal tumor without ulceration and 2 cm or less in diameter, (5) received gastrectomy with lymph node dissection or ER with curative intent. Choice of treatment modality was usually decided after full consultation between the attending physician and the patient. Many patients chose surgery as opposed to EMR before April 2004 because ESD was not routinely covered by insurance during that time and because of the limitations in achieving en bloc resection with EMR. A detailed flow chart of this study is summarized in [Figure 1](#). This study was approved by the institutional review board of the National Cancer Center, Korea (NCCNCS-13-798).

### Data collection

Data related to baseline characteristics, endoscopic and pathological findings, and treatments were obtained

from our database of prospectively collected data based on medical records. Tumor stage was based on the sixth edition of the International Union Against Cancer/American Joint Committee on Cancer classification system.<sup>14</sup> The data related to treatments were ER methods, rate of complete resection, surgical method, extent of lymph node dissection, multiple tumors, and adverse events of each treatment. Early adverse events were defined as those that occurred within 30 days of treatment.

### ER and surgery

All of the patients included in this study underwent EGD and abdominal CT for clinical staging before treatment. EMR was performed until April 2004, and all ER methods were ESD after that time. Detailed ER methods were described previously.<sup>15,16</sup>

Patients treated by surgery underwent an open or laparoscopic gastrectomy with D1 +  $\beta$  or more lymph node dissection. A distal subtotal gastrectomy or total gastrectomy was performed depending on the tumor location. Reconstruction methods included gastroduodenostomy or gastrojejunostomy after distal gastrectomy and Roux-en-Y esophagojejunostomy after total gastrectomy. The extent of lymph node dissection was based on the recommendations of the Japanese Gastric Cancer Association.<sup>17</sup>

### Pathological evaluation

All resected specimens were flattened and fixed in 10% formalin for pathological evaluation. Specimens obtained from ER were sliced serially at 2-mm intervals,<sup>18,19</sup> embedded in paraffin blocks, and stained with hematoxylin and eosin. Resected surgical specimens were prepared for pathological evaluation in a similar manner except that serial sectioning was performed at 4-mm intervals. Although the Japanese guidelines recommended that the section intervals of surgically resected specimens be 5 to 7 mm, we made sections of our surgical specimens at 4-mm intervals to achieve a more accurate evaluation.<sup>19</sup> Histological subtypes were classified according to the World Health Organization classification of gastric cancer.<sup>20</sup> Histologically differentiated types included well- or moderately differentiated tubular adenocarcinoma and papillary adenocarcinoma. Undifferentiated types included poorly differentiated tubular adenocarcinoma, signet ring cell carcinoma, and mucinous adenocarcinoma.<sup>18</sup>

### Follow-up surveillance after treatment

EGD was performed 3 and 12 months after ER or surgery and then annually thereafter. In cases of ER, EGD was also performed at 6 months. Abdominal CT was performed annually. A biopsy of the ER scar tissue was performed at each EGD examination to evaluate the presence of local recurrence in patients who underwent ER.

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