ORIGINAL ARTICLE

Efficacy and safety of endoscopic submucosal dissection for gastric neoplasms in patients with compensated liver cirrhosis: a propensity score–matched case-control study

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Background and Aims: The clinical outcomes of endoscopic submucosal dissection (ESD) for gastric neoplasms in liver cirrhosis patients have not been adequately reported, leading to clinician concerns about adverse events, including bleeding and the deterioration of liver function. We compared the efficacy and safety of ESD between cirrhosis and noncirrhosis patients.

Methods: Between January 2005 and December 2014, 158 cirrhosis patients underwent ESD for gastric neoplasms at a tertiary medical institution. Their clinical outcomes were compared with those of a propensity score–matched control group (158 patients) selected from noncirrhosis patients, using age, sex, histology, tumor location, and lesion size as variables.

Results: En bloc resection (96.8%), curative resection (89.9%), and adverse event (bleeding [10.1%] and perforation [1.9%]) rates in the cirrhosis group did not differ significantly from those in the noncirrhosis group. The median procedure time (25.0 vs 23.0 minutes) was also comparable between the groups. In a survival analysis cirrhosis patients exhibited a significantly higher mortality risk than noncirrhosis patients (hazard ratio [HR], 3.52; 95% confidence interval [CI], 1.35-9.23; $P = .01$). Cirrhosis patients without hepatocellular carcinoma (HCC) showed no statistically significant difference in mortality compared with the noncirrhosis group (HR, 2.14; 95% CI, .72-6.39; $P = .171$). Three of 153 patients (2%) exhibited a deterioration of prognosis from Child-Pugh class A to B.

Conclusions: In compensated cirrhosis patients, especially those without HCC, ESD for gastric epithelial neoplasms can be performed with safety and efficacy comparable with that in noncirrhosis patients, without deterioration in liver function. (Gastrointest Endosc 2018;■:1-9.)

Endoscopic submucosal dissection (ESD) is more convenient and less invasive than surgery for gastric adenoma and early gastric cancer. Furthermore, ESD allows a faster return to work in properly selected cases without the risk of lymph node metastasis. The operative mortality rate after gastrectomy is not low, at 2% to 3%,[1] making endoscopic treatment a more desirable treatment option.

Although the prevalence of liver cirrhosis due to hepatitis B is decreasing in Korea, it was ranked as the eighth leading cause of death in 2014 and remains a major concern.[2] The relationship between cirrhosis and gastric cancer has been examined in a few studies. A nationwide cohort study conducted in Denmark observed a disproportionate number of gastric cancer cases among

Abbreviations: CI, confidence interval; ESD, endoscopic submucosal dissection; HCC, hepatocellular carcinoma; HR, hazard ratio.

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cirrhosis patients (standardized incidence ratio, 1.9; 40/1447 cancers).[3] In addition, in a systematic review researchers reported a 2.6-fold higher prevalence of gastric cancer among cirrhosis patients compared with the general population.[4] Given the high prevalence of gastric cancer in cirrhosis patients, it is essential to determine whether ESD can be safely performed without high adverse event rates in this patient group; however, to date, only few studies have investigated whether this is the case. In a Japanese study the en bloc resection rate for gastric cancer in cirrhosis patients was 88.9% and the en bloc resection rate with free lateral/basal margins (R0 resection) 77.8%.[5] A study in Korea reported en bloc and R0 resection rates as 82.6% and 91.3%, respectively.[6] However, these studies had small sample sizes, including only several tens of patients. Furthermore, to the best of our knowledge no study has evaluated the changes in liver function before and after ESD.

In the present study we compared the clinical outcomes of ESD for gastric neoplasms between cirrhosis and noncirrhosis patients. In addition, we analyzed the Child-Pugh classification status before and after ESD in cirrhosis patients.

METHODS

Subjects

From January 2005 to December 2014, 42,823 patients were diagnosed with liver cirrhosis according to the International Statistical Classification of Diseases and Related Health Problems, 10th Revision diagnosis code at Asan Medical Center, Seoul, Korea. Of these, 385 patients (.9%) underwent endoscopic treatment for superficial gastric neoplasms. Patients were excluded from the present study if they met any of the following criteria: no imaging study was available showing cirrhotic features (n = 84), the patient underwent EMR (n = 63), laboratory data for calculating the Child-Pugh score were lacking (n = 43), the patient underwent liver transplantation (n = 29), the pathologic examination showed only gastritis (n = 7), and the patient underwent ESD for a subepithelial tumor (n = 1). After exclusion, 158 patients were enrolled in the case group, and their data were retrospectively analyzed.

The diagnosis of liver cirrhosis was based on imaging findings, clinical data with laboratory investigations, and medical history that implied portal hypertension (eg, the presence of esophageal or gastric varices). The liver function of the enrolled patients was assessed according to the Child-Pugh classification. To provide a comparison for the therapeutic efficacy and safety of ESD, 158 propensity score–matched patients without cirrhosis were designated as the control group (Fig. 1). This study was approved by the institutional review board of the Asan Medical Center (2017-0649; date of registration, June 5, 2017).

Endoscopic procedure

All ESDs were performed by experienced GI endoscopists using a single-channel endoscope (GIF-H260; Olympus, Tokyo, Japan). The patients were sedated using intravenous midazolam (.05 mg/kg) and pethidine (50 mg), and their cardiorespiratory functions were continually monitored throughout the procedure. The typical ESD procedure sequence involved marking, mucosal incision, and submucosal dissection with simultaneous hemostasis. After placing several marker dots outside the lesion, saline solution containing epinephrine and indigo carmine was injected into the submucosal layer with a 21-gauge needle. A circumferential incision was made in the mucosa with a needle-knife (MTW Endoskopie, Wesel, Germany) or an insulation-tipped knife (Olympus), which was then used to directly dissect the submucosal layer until the lesion was completely removed. If bleeding was observed, endoscopic hemostasis was achieved with hemoclips, hemostatic forceps (FD-410LR; Olympus), or argon plasma coagulation. After the completion of the endoscopic resection, all nonbleeding visible vessels were coagulated. The ESD procedure was identical for both the cirrhosis and noncirrhosis groups, and the final decision to perform ESD was made by the practicing endoscopist (after discussion with the hepatologist for the cirrhosis group patients).

Follow-up schedule

The day after the ESD procedure the complete blood cell count was measured and chest radiographs assessed. Second-look endoscopy was performed on the second day after the procedure to assess for postprocedural ulcers. If there was no evidence of bleeding or perforation, oral feeding was initiated. A proton pump inhibitor was administered intravenously from the morning of the day of the procedure to the end of the nil per os period, followed by oral proton pump inhibitor therapy for 4 to 8 weeks. Endoscopy follow-up was performed at 3, 6, and 12 months after ESD. Abdominal CT scans were performed every 6 months for the first year and annually thereafter to detect any extragastric recurrence.

Definitions

Macroscopic types were classified according to the Japanese classification of gastric carcinoma: type I (protruded), type IIa (superficial elevated), type IIb (flat), type IIc (superficial depressed), and type III (excavated).[7] Types I and IIa were classified as elevated and types IIb, IIc, and III as flat-depressed.

The absolute indication for ESD was differentiated histology with a diameter ≤2 cm but without ulcerative findings. The expanded indications were differentiated histology without ulceration but with a diameter >2 cm, differentiated histology with ulceration and a diameter ≤3 cm, and undifferentiated histology without ulceration and with a diameter ≤2 cm.[8] Patients were