Routine Mucosal Closure with a Detachable Snare and Clips after Endoscopic Submucosal Dissection for Gastric Epithelial Neoplasms: A Randomized Controlled Trial

Bo-In Lee*, Byung-Wook Kim*, Hyung-Keun Kim†, Hwang Choi*, Jeong-Seon Ji*, Sun-Mee Hwang*, Young-Seok Cho†, Hiun-Suk Chae† and Kyu-Yong Choi‡

*Division of Gastroenterology, Department of Internal Medicine, Incheon St. Mary’s Hospital, The Catholic University of Korea College of Medicine, Incheon, † Division of Gastroenterology, Department of Internal Medicine, Uijeongbu St. Mary’s Hospital, The Catholic University of Korea College of Medicine, Uijeongbu, and ‡ Division of Gastroenterology, Department of Internal Medicine, Seoul St. Mary’s Hospital, The Catholic University of Korea College of Medicine, Seoul, Korea

Background/Aims: The aim of this study was to determine whether the routine closure of mucosal defects after endoscopic submucosal dissection (ESD) can enhance mucosal healing and reduce ESD-associated bleeding. Methods: Patients with gastric epithelial neoplasias and no obvious submucosal invasion were prospectively enrolled. Mucosal defects were left untreated in the control group. In the study group, mucosal closure was attempted with a 2-channel endoscope, a detachable snare, and clips. All participants received a second-look endoscopy the day after ESD, and coagulation therapy was administered to patients with visible vessels and active bleeding points. Results: Fifty-two patients were enrolled in the study, and 26 patients were assigned to each group. Complete mucosal defect closure occurred in 16 patients (61%) in the study group; incomplete closure occurred in 8 patients (31%) in the study group, and failed closure occurred in 2 patients (8%). Coagulation therapy at the second-look endoscopy was performed more often in the control group than in the study group (31% vs 4%, p=0.024). There were no significant differences in the incidence of immediate or delayed bleeding or in the two-week decrease in hemoglobin between the groups. The prevalence of open ulcers after 8 weeks was significantly lower in the study group than in the control group (18% vs 43%, p=0.012). Conclusions: Routine mucosal closure after ESD supports earlier healing of artificial ulcers. A larger-scale trial is necessary to determine whether mucosal closure can reduce ESD-associated bleeding. (Gut Liver 2011;5:454-459)
MATERIALS AND METHODS

1. Study subjects

This randomized controlled trial was carried out at Incheon St. Mary’s Hospital, The Catholic University of Korea in Incheon, Korea between January 2008 and August 2009. The protocol was approved by the Institutional Review Board. Eligible patients had gastric epithelial neoplasias (noninvasive low grade dysplasia, noninvasive high grade dysplasia, or invasive neoplasia without obvious submucosal invasion). The depth of invasion was estimated primarily by gross findings. Endoscopic ultrasonography (EUS) was performed when the depth of invasion could not be assessed by gross findings only. All biopsy specimens from the body and antrum were stained using the Warthin–Starry method to identify Helicobacter pylori infection at the preoperative endoscopy.

Patients were excluded from the study if they had received anticoagulant, or had a coagulation disorders, end-stage renal disease, severe cardiopulmonary disorder, or undifferentiated cancer. Patients were also excluded if they were scheduled to receive ESD for multiple gastric lesions or a locally recurrent lesion after a previous EMR or ESD. Patients were also excluded if a clip was applied to control profuse bleeding or to close an obvious or impending perforation during the procedure. Patients with neoplasia at the cardia, fundus, or upper one third of corpus were not included because mucosal closure with a detachable snare and clips often cannot be performed at those locations.

Patients were excluded from the study if they had received antiplatelet agents, including aspirin, were stopped one week before ESD and were then withdrawn for three weeks under the supervision of the cardiologist or neurologist.

2. ESD

All ESD procedures were performed by one physician (B.W. Kim). During the procedure, patients were under conscious sedation with midazolam (0.05 mg/kg) and pethidine (50 mg); additional doses were given according to the physician’s instructions.

A conventional gastroscope (GIF-Q240X; Olympus, Tokyo, Japan) fitted with a transparent distal attachment (D-201-11304; Olympus) was used for the ESD procedures. The margin of the tumor was determined by gross findings and indigocarmine chromoscopy. Circumferential markings were generated with argon plasma coagulation, effect 2 (ARCO 3000; Söring GmbH, Quickborn, Germany), 0.5 cm from the margin of the tumor. After a mixture of 0.9% normal saline and 0.005% epinephrine was injected into the submucosal layer, a precut was made outside the marking with a hook knife (KD-620LR; Olympus) and an Endocut-I current (effect 1, duration 3, interval 3; VIO300D; ERBE Elektromedizin GmbH, Tübingen, Germany). Submucosal dissection was performed mainly with a hook knife and a forced coagulation current (effect 2, 40 W). A coagrasper (FD-410LR; Olympus) and a soft coagulation current (effect 7, 80 W) was primarily used to control bleeding.

ESD was performed as extensively as possible for complete removal of the lesion. When extreme difficulty was encountered during the submucosal dissection for any reason (e.g., severe fibrosis or profuse bleeding), snaring with an Endocut-Q current was allowed for the final excision.

The size of the resected specimen/mucosal defect was measured with a 3-cm flexible linear probe, and the area was estimated using the formula to calculate the area of an ellipse ($\pi \times \text{major axis} \times \text{minor axis}$).

3. Mucosal closure

Patients were randomly assigned to either a study group or a control group; attempts were made to close mucosal defects in the study group, and these defects were left untreated in the

Fig. 1. Mucosal closure with a detachable snare and clips after endoscopic submucosal dissection. (A) A mucosal defect remains after ESD. (B) A detachable snare is deployed on the mucosal defect through a working channel, and a rotating clip-fixing device with a long clip is inserted through the other working channel. (C) The wire of the detachable snare is placed between both legs of the clip. (D) The clip is applied to the edge of the mucosal defect. (E) Another clip is applied to the opposite side of the mucosal defect in the same manner. (F) The snare is squeezed gently, and the mucosal defect is approximated. (G) Additional clips are applied to close the defect. (H) The defect is closed completely.