Second-look endoscopy is not associated with better clinical outcomes after gastric endoscopic submucosal dissection: a prospective, randomized, clinical trial analyzed on an as-treated basis

Ho Yoel Ryu, MD,[*,1] Jae Woo Kim, MD,[*,1] Hyun-Soo Kim, MD,[1] Hong Jun Park, MD,[1] Hyo Keun Jeon, MD,[1] So Yeon Park, MD,[1] Bo Ra Kim, MD,[1] Cui Cui Lang, MD,[2] Sung Ho Won, PhD[3]

Wonju, Republic of Korea

Background: The efficacy of routine second-look endoscopy (SLE) to detect or prevent bleeding after gastric endoscopic submucosal dissection (ESD) has not yet been validated.

Objective: The aim of this study was to determine whether SLE affects clinical outcomes including bleeding and morbidity after gastric ESD.

Design: A prospective, randomized, controlled study with consecutive data analyzed on an as-treated basis.

Setting: A single, tertiary-care referral center.

Patients: A total of 182 patients.

Intervention: Gastric ESD and SLE.

Main Outcome Measurements: Incidence of and risk factors related to bleeding after ESD and outcomes by univariate or multivariate analysis.

Results: Among 182 patients enrolled, 74 and 81 patients were assigned to the SLE and no-SLE groups, respectively. Two groups were observed closely for 4 weeks. Bleeding occurred after ESD in 21 patients (13.5%). Hemoglobin loss (≥2.0 g/dL) was observed in 20 patients, and melena developed in 1 patient after ESD. However, only 1 patient needed a transfusion. Twelve patients (16.2%) in the SLE group and 9 in the no-SLE group (11.1%) experienced bleeding after ESD. The frequency of bleeding after ESD was not significantly different between the 2 groups ($P = .66$). There were no risk factors related to bleeding after ESD.

Limitations: Single-center analysis.

Conclusion: SLE is not routinely necessary because it does not affect clinical outcomes, including bleeding and morbidity after ESD. (Clinical trial registration number: KCT0000146.) (Gastrointest Endosc 2013;78:285-94.)

Endoscopic submucosal dissection (ESD) has been recognized as an optimal treatment for gastric epithelial neoplasia.[1,2] Although gastric ESD is an outstanding treatment method, bleeding after ESD is a main concern affecting the safety, effectiveness, and outcome of the procedure. Previous studies reported that the bleeding rate was approximately 5% after gastric ESD.[1,3-5] A second-look endoscopy (SLE) is routinely performed the day after gastric ESD to

Abbreviations: APC, argon plasma coagulation; aPTT, activated partial thromboplastin time; ESD, endoscopic submucosal dissection; PT, prothrombin time; SLE, second-look endoscopy.

DISCLOSURE: *This research was supported by the Basic Science Research Program through the National Research Foundation of Korea funded by the Ministry of Education, Science and Technology (2012-0004734) and Chong Kun Dang Pharmaceutical Corporation. No other financial relationships relevant to this publication were disclosed.*

*Drs Ryu and J.W. Kim contributed equally to this article.

0016-5107/$36.00
http://dx.doi.org/10.1016/j.gie.2013.02.008

Received September 5, 2012. Accepted February 4, 2013.

Current affiliations: Department of Internal Medicine, Yonsei University Wonju College of Medicine, Wonju, Korea (1), Department of Gastroenterology, Liaocheng People's Hospital, Liaocheng, China (2), Department of Applied Statistics, Chung-Ang University, Seoul, Republic of Korea (3).

Reprint requests: Hyun-Soo Kim, MD, Digestive Disease Center, Department of Internal Medicine, Yonsei University Wonju College of Medicine, 162, Ilsan-dong, Wonju, Korea 220-701.

If you would like to chat with an author of this article, you may contact Dr Kim at hyskim@yonsei.ac.kr.

detect and prevent bleeding after ESD. However, use of routine SLE in patients without any signs of bleeding has not yet been validated with regard to clinical outcomes.

In 2010, Osamu et al[6] reported that an SLE after gastric ESD may contribute little to the prevention of delayed bleeding. However, interpretation of the results was limited because that study was a retrospective analysis. The present study was a prospective, randomized, controlled trial analyzed on an as-treated basis performed to determine whether SLE affects clinical outcomes, including bleeding and morbidity after gastric ESD.

Take-home Message

- Given that complete hemostatic coagulation for visible vessels during endoscopic submucosal dissection (ESD) is assured, a routine second-look endoscopy after gastric ESD is not necessary.
- Routine second-look endoscopy is likely to increase unnecessary hemostatic procedures for non-bleeding visible vessels and the economic burden in a substantial number of patients.

PATIENTS AND METHODS

A total of 182 patients with a diagnosis of gastric epithelial neoplasia were consecutively treated with ESD in our hospital from March 2011 to March 2012. ESD was principally indicated for early gastric cancer or gastric adenoma. Among them, 27 patients were excluded because perforation developed in 2 patients, immediate bleeding in 3 patients, surgery for incomplete resection or patients' preferences in 12 patients, and a change of therapeutic plan from ESD to EMR with a ligation device in 8 patients. In addition, 2 patients were excluded because 1 patient was unable to tolerate the procedure, and 1 was lost to follow-up. Therefore, a total of 155 patients were closely observed for 4 weeks. Before ESD, they were randomly assigned to 1 of 2 groups by an envelope method by the research assistant in a third room. The endoscopists and the patients were blinded during ESD. After ESD, randomization was opened to plan SLE. SLE was performed the day after ESD in the SLE group, whereas the no-SLE group was followed without a routine SLE. Finally, 74 (47.7%) patients were included in the SLE group. A flowchart outlining patient enrollment in this study is shown in Figure 1.

Preparation before ESD

All patients provided written informed consent before treatment. This study was approved by the Institutional Review Board for Human Research Yonsei University Wonju College of Medicine. The Institutional Review Board approval number was CR310035, and the approval date was February 16, 2011. The trial was also registered in the Clinical Research Information Service on March 8, 2011. The Clinical Research Information Service approval number was KCT0000146. We evaluated patients' medical histories including the presence of hypertension, diabetes, ischemic heart disease, cerebrovascular disease, chronic kidney disease, liver cirrhosis, chronic pulmonary disease, previous ulcer history, peripheral vascular disease, dementia, connective tissue disease, any tumors, hematologic malignancy, and AIDS before ESD. Patients with chronic pulmonary disease underwent a pulmonary function test. A complete blood count, blood chemistry, prothrombin time (PT), international normalized ratio, and activated partial thromboplastin time (aPTT) analyses in addition to chest radiography and electrocardiogram were performed in all patients. Patients taking aspirin stopped it at least 3 days before ESD. We recommended that patients taking warfarin stop taking it at least 3 to 4 days before the procedure, and we confirmed that the international normalized ratios of these patients were below 1.5. Similarly, we recommended that patients on an aspirin-plus-antiplatelet medication such as clopidogrel or cilostazol stop these drugs at least 7 days before the procedure.

ESD procedure

ESD was performed with the patients under conscious sedation by using midazolam (4-8 mg), pethidine (25-50 mg) or propofol (20-80 mg) by 3 endoscopists. Before ESD, chromoendoscopy with indigo carmine spraying, narrow-band imaging or a combination were performed in addition to standard white light endoscopy in order to clarify lesion margins and classify morphology according to the Paris classification.[7] After circumferential marking with argon plasma coagulation (APC), a mixture of epinephrine hydrogen chloride and 0.9% saline solution (1:7) was injected below the lesion to lift it and create a submucosal fluid cushion. Next, circumferential cutting of the muscularis mucosa was performed, followed by submucosal dissection beneath the lesion in order to detach it from the stomach wall. The hook knife (KD-620LR; Olympus, Tokyo, Japan) was selected as the main electrosurgical knife, and other knives such as the insulation-tipped (IT) knife-2 (KD-611L; Olympus) and dual knife (KD-650L; Olympus) were used instead of or in addition to the hook knife according to the endoscopist's preference. During ESD, mild bleeding was coagulated by using a knife, and moderate or severe bleeding was managed by using APC or hemostatic clips (HX-610-135; Olympus), according to the endoscopist's preference. We coagulated nonbleeding visible vessels in the ulcer bed as completely as possible by using APC or hemostatic clips immediately after ESD.[5] After ESD, we recorded the severity of vascularity, the degree of fibrosis, the size of the specimen after resection, the location of the lesion, the endoscopist's skill level, whether or not the lesion was removed by en block or piecemeal resection, the number of hemostatic clips