Prediction model and risk score for perforation in patients undergoing colorectal endoscopic submucosal dissection

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Background and Aims: Perforation is the adverse event of greatest concern during colorectal endoscopic submucosal dissection (ESD). Accurate risk prediction of perforation may enable prevention strategies and selection of the most efficient therapeutic option. This study aimed to develop and validate a risk prediction model for ESD-induced perforation.

Methods: A multicenter cross-sectional study was performed on 2046 patients who underwent colorectal ESD at 9 Korean ESD Study Group–affiliated hospitals. The enrolled patients were randomly divided into either a derivation set or a validation set. In the derivation set, a prediction score was constructed to assess the risk of perforation using preoperative and procedural-related predictors selected via logistic regression. Discrimination and calibration of the prediction model was assessed using the validation set.

Results: An ESD-induced perforation occurred in 135 patients (6.6%). In the derivation set, multivariate logistic regression identified endoscopist experience (≥50 ESDs: odds ratio [OR] = 0.59; 95% confidence interval [CI], 0.35-1.00), tumor size (+1-cm increments: OR = 1.39; 95% CI, 1.19-1.62), colonic location (OR = 2.20; 95% CI, 1.24-3.89), and submucosal fibrosis (OR = 2.00; 95% CI, 1.04-3.87) as predictive factors (C-statistic = 0.678; 95% CI, 0.617-0.739). In the validation set, the model showed good discrimination (C-statistic = 0.675; 95% CI, 0.615-0.735) and calibration (P = .635). When a simplified weighted scoring system based on the OR was used, risk of perforation ranged from 4.1% (95% CI, 2.8%-5.9%) in the low-risk group (score ≤4) to 11.6% (95% CI, 8.5%-15.6%) in the high-risk group (score >4).

Conclusions: This study developed and internally validated a score consisting of simple clinical factors to estimate the risk of colorectal ESD-induced perforation. This score can be used to identify patients at high risk before colorectal ESD. (Gastrointest Endosc 2016;84:98-108.)

Endoscopic submucosal dissection (ESD) is an innovative endoscopic technique for removing superficial gastrointestinal neoplasms. Perforation is the most concerning adverse event during colorectal ESD. The perforation rate during colorectal ESD has been reported to be as high as 1.4% to 20.4%[1-5] because of the anatomy of the large intestine,

Abbreviations: AUC, area under the curve; CI, confidence interval; ESD, endoscopic submucosal dissection; LST, laterally spreading tumor; LST-G, laterally spreading tumor, granular type; LST-NG, laterally spreading tumor, nongranular type; OR, odds ratio; ROC, receiver operating characteristic; SD, standard deviation; SE, standard error.

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with its narrow lumen, thin walls, tortuous structure, and redundancy.[6-8] Furthermore, peritonitis caused by colonic perforation can be more severe than that caused by gastric perforation because of secondary contamination by colonic bacteria and feces.[6-8] The risk of perforation during ESD is still higher than that during EMR.[9] Therefore, research has sought to identify the risk factors of perforation. Several predictors have been elucidated, including submucosal fibrosis, tumor size, nongranular laterally spreading tumors (LSTs), and endoscopist experience.[4,10-13]

However, the actual risk of perforation based on these predictive factors has not yet been stratified. Risk prediction models have not yet been proposed to guide appropriate planning strategies for ESD. In this study, we performed cross-sectional analysis using data from a Korean nationwide multicenter colorectal ESD registry to clarify the predictors of ESD-induced perforation. We also derived a risk prediction model based on readily available clinical findings that can be used to predict the likelihood of ESD-induced perforations. In the future, risk prediction models for ESD-induced perforation can be used to stratify patients at high risk before undergoing a procedure.

METHODS

The Korean nationwide multicenter colorectal ESD registry includes 2666 consecutive colorectal ESDs performed in 2621 patients between November 2004 and December 2013 at 9 Korean ESD Study Group–affiliated hospitals (Asan Medical Center, Hallym University Medical Center, Presbyterian Medical Center, Samsung Medical Center, Kyungpook National University Medical Center, Keimyung University Dongsan Medical Center, Seoul St. Mary's Hospital, Ewha Woman's University Medical Center, and Incheon St. Mary's Hospital). All the endoscopic findings and medical records were reviewed thoroughly and were evaluated from the original endoscopic database system. Registry data included demographics (age, sex, comorbidities, and use of antithrombic agents), endoscopic tumor findings (size, location, and macroscopic shape), ESD-related factors (endoscopist experience in performing ESD, ESD type, number of knives used, and submucosal fibrosis), histologic findings, outcome, adverse events, and prognosis.

We performed a cross-sectional analysis of patients who underwent colorectal ESD for superficial colorectal neoplasms at 9 Korean ESD Study Group–affiliated hospitals. Patients who met any of the following criteria were excluded: ESD for removal of carcinoid tumor, submucosal tumor, or nonneoplastic lesion; synchronous lesions requiring 2 or more ESD sessions; or incomplete endoscopic or pathologic findings. The institutional review board of Samsung Medical Center (Seoul, Korea) approved this study.

ESD procedure

In brief, the typical sequence of ESD procedures was as follows. Before ESD, the operator estimated the tumor location and size and then determined whether ESD was applicable. When deep submucosal invasive cancer was suspected on the basis of endoscopic gross morphologic findings, Kudo's pit pattern, or a nonlifting sign, surgery was recommended instead of ESD. Written informed consent was obtained from all patients. Each ESD was performed using a standard single accessory channel endoscope with the patient under conscious sedation. After the tumor outlines had been delineated using indigo carmine dye spraying or narrow-band imaging, a mixture of normal saline solution, hypertonic saline solution, glycerin, and/or sodium hyaluronate with a small amount of indigo carmine was injected into the submucosal space using a 21- or 23-gauge needle. The injection was repeated a few times until the target mucosa was sufficiently elevated. After the tumor had been lifted, electrosurgical instruments, such as flex, hook, dual, insulated tip (IT), and IT-nano knives, were used for mucosal incision and submucosal dissection. Submucosal fibrosis was defined as a partial nonlifting sign, white web, or muscle-like structure in the submucosal layer. Direct dissection of the submucosal layer was performed with one of the specified knives until complete removal was achieved (ESD throughout) or until the tumor could be removed using a snare (ESD snaring). After ESD, preventive endoscopic hemostasis and clipping was performed for any oozing, exposed vessels, or injured muscle layers.

Histopathologic evaluation of ESD specimens

Resected ESD specimens were retrieved using forceps or nets, were placed on a Styrofoam surface, and were stretched to their approximate lengths in the living body. The full thickness (mucosa, submucosa, and muscularis mucosae) of each specimen was then pinned (using rust-proof pins) to identify the horizontal margin. After macroscopic observation, ESD specimens were cut parallel to the closest margin direction. Lesions were step sectioned at 1-mm or 2-mm intervals and then examined. The depth of submucosal invasion was considered the distance from the deeper edge of the muscularis mucosae to the deepest invasive portion. When muscularis mucosae could not be identified, the depth of submucosal invasion was considered the distance between the tumor surface and the deepest invasive portion. All colorectal tumors were histologically evaluated and classified according to the World Health Organization system.[14]

En bloc resection was defined as tumor resection in 1 piece without fragmentation.[11] Curative resection was defined as the absence of tumor cells at the resection margins of the specimen and endoscopic en bloc resection. For curative resection of carcinoma, the following criteria were additionally fulfilled: well or