Clinical impact of endoscopic clip closure of perforations during endoscopic submucosal dissection for colorectal tumors

Hiroyuki Takamaru, MD, PhD, Yutaka Saito, MD, PhD, Masayoshi Yamada, MD, PhD, Eriko S. Tsuruki, MD, Yuzuru Kinjo, MD, Yosuke Otake, MD, Taku Sakamoto, MD, Takeshi Nakajima, MD, PhD, Takahisa Matsuda, MD, PhD

Tokyo, Japan

Background and Aims: Despite advances in endoscopic submucosal dissection (ESD), perforation can still occur. The purpose of this study is to determine the clinical course and effectiveness of endoscopic closure in addition to the clinicopathologic features related to perforation.

Methods: A total of 935 lesions in 900 consecutive patients between February 1998 and February 2013 underwent ESD for colorectal tumors at our institution. We studied the clinical course and histologic features of perforation through a matched case-control study that included 24 patients with intraprocedural perforation and 240 matched patients without perforation as a control group. Endoscopic closure by using through-the-scope endoclips was attempted in all cases of intraprocedural perforations immediately after perforation was recognized during the procedure.

Results: Perforation occurred in 25 cases (2.7%), including 24 intraprocedural perforation and 1 delayed perforation. All but 1 patient with intraprocedural perforation was conservatively managed by endoscopic closure. One patient with unsuccessful endoscopic closure required emergency surgery. Analysis of clinical courses revealed statistically significant differences ($P < .01$) between the patients with perforation and the case-controlled, non-perforation patients in total procedure time, white blood cell count, and level of serum C-reactive protein on the day after the procedure, admission period, and fasting period. Both location ($P = .027$) and submucosal fibrosis ($P = .04$) of the lesion were significantly associated with perforation. Multivariate analysis revealed that fibrosis was a significant risk factor associated with perforation (odds ratio 2.86; 95% confidence interval, 1.03-7.90).

Conclusions: Endoscopic closure allows effective nonsurgical management in cases of intraprocedural perforation during ESD. (Gastrointest Endosc 2016;84:494-502.)

Endoscopic submucosal dissection (ESD) now plays an important role in the minimally invasive treatment of colorectal tumors, because it allows for en bloc resection and more accurate histologic staging.[1-4] EMR and piecemeal EMR are other treatment options, although the risk of recurrence and difficulty with accurate histologic evaluation must be considered.[5-9]

Furthermore, recurrence may make repeat endoscopic treatment difficult because of fibrosis.[10] Laparoscopy-assisted colorectal surgery (LACS) and transanal resection also are treatment options, but LACS is more invasive, and transanal resection has reportedly higher recurrence rates than ESD.[11] Therefore, ESD is now frequently performed by various institutions and has been recently introduced in several Asian, European, and South American countries and the United States.[12]

Perforation is generally considered the most serious adverse effect of colorectal ESD; however, the rate of perforation has been decreasing because of improvements in technique with more experience and the development of new equipment. Perforation still occurs in 1.4% to 14.0% of colorectal ESD cases,[4,6,13,14] making it critically important to understand the clinical course and determine the most effective management strategies. Until now, there

Abbreviations: CO_2, carbon dioxide; ESD, endoscopic submucosal dissection; LACS, laparoscopy-assisted colorectal surgery; LST, lateral spreading tumor; WBC, white blood cell.

DISCLOSURE: *All authors disclosed no financial relationships relevant to this publication.*

0016-5107/$36.00
http://dx.doi.org/10.1016/j.gie.2016.01.014

Received May 30, 2015. Accepted January 7, 2016.

Current affiliations: Endoscopy Division, National Cancer Center Hospital, Tokyo, Japan.

Reprint requests: Yutaka Saito, MD, PhD, National Cancer Center Hospital, Endoscopy Division, 5-1-1 Tsukiji Chuo-ku, Tokyo 104-0045, Japan.

TABLE 1. Summary of comparison of clinical courses and short-term outcomes between perforation and age/sex matched control group

	Perforation (n = 24)	Control (n = 240)	*P* value
Age, median (range)	70 (48-81)	70 (47-82)	.98
Sex, male/female	10/14	100/140	1.00
Resected size, median, (range), mm	33.5 (15-70)	35 (12-110)	.69
Procedure time*, median, (range), min	120 (25-420)	87.5 (15-480)	< .01
WBC count at POD 1, median, (range), /mm^3	9400 (5100-20,900)	6700 (3400-17,900)	< .01
CRP level at POD 1, median, (range), mg/dL	1.3 (0.1-6.88)	0.37 (0.02-7.95)	< .01
Fold change of WBC count, median, (range)	1.6 (0.9-3.1)	1.2 (0.5-2.9)	< .01
Fold change of serum CRP level, median, (range)	7.3 (0.6-152)	4.0 (0.2-159)	.14
Maximum body temperature, median, °C	37.4	36.9	.15
Proportion of abdominal findings	33%	9%	.02
Admission period, mean (± SD), d	8.0 (± 0.3)	5.3 (± 0.1)	< .01
Fasting period, mean (± SD), d	4.5 (± 0.2)	2.3 (± 0.1)	< .01
Curative resection rate, %	83.3	84.3	.90

WBC, White blood cell; *POD*, postoperative day; *CRP*, C-reactive protein.
*Including the time of management for perforation.

has been a lack of large-scale data describing the clinical course of perforation during colorectal ESD, with only small case reports on which to base management. The aim of this study is to investigate the clinical course and the histologic factors relating to perforation during colorectal ESD.

METHODS

Patients

From February 1998 to February 2013, 900 consecutive patients with 935 colorectal lesions underwent ESD at the National Cancer Center Hospital, Tokyo, Japan. Data from these procedures were entered into a prospective database. Age, sex, macroscopic type, tumor size, resected size of the specimen, location of the lesion, procedure time, presence of fibrosis (described in database as negative or positive), endoscopic clipping, histologic diagnosis, depth of invasion, and presence of intraprocedural perforation were entered into the database prospectively (Table 1). If delayed perforation or delayed bleeding occurred, these were added prospectively to the database. To compare with the perforation group, a control group of patients without perforation matched for age and sex were randomly selected from the database. The number of control cases was determined based on an approximate perforation rate of 10%, according to previous reports.[14,15] Perforation occurred in 25 of the 935 lesions (2.7%). One of these perforations was delayed, requiring emergency surgery; thus, 24 of the 25 perforations were included in the final analysis. A total of 240 lesions without perforation were selected randomly as controls (Fig. 1). In order to specifically investigate intraprocedural colorectal perforation, the case of delayed perforation was not included in this analysis. This study was approved by the internal review board in our institution, and informed written consent was obtained from all patients for each specific colonoscopic treatment.

Indication for ESD

All ESD cases were discussed, and the indication was confirmed in a multidisciplinary endoscopy conference before the procedure. Indications for colorectal ESD have been reported previously.[1,4,16] Briefly, we defined the indications for ESD as nongranular type lateral spreading tumors (LSTs) >20 mm; granular type lateral spreading tumors (nodular-mixed type) >30 mm, large villous tumors, recurrent lesions, and residual mucosal lesions with nonlifting sign, without invasive pit patterns.[1,8,17,18]

Clinical pathway for ESD

All patients were treated according to the "clinical pathway." As we reported previously,[19] the clinical pathway has been established as the following: patients are admitted for a total of 5 days. All patients are admitted the day before the procedure (day 1), ESD is performed on day 2, and blood tests are done on day 3. According to the clinical pathway, blood examination including white blood cell (WBC) count and serum C-reactive protein level was performed for all patients. This laboratory data, as well as body temperature during hospital stay, physical findings such as abdominal pain, fasting period, and length of hospital stay, were retrospectively obtained from the patient's medical records. Prophylactic antibiotic (cefmetazole 1.0 g, intravenously) was given once a day before the procedure.[19]