# Predictors of incomplete resection and perforation associated with endoscopic submucosal dissection for colorectal tumors

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**Background and Objective:** Colorectal endoscopic submucosal dissection (ESD) is technically challenging. Our aim was to identify predictors of incomplete resection and perforation in colorectal ESD.

**Design:** Retrospective study.

**Setting:** Academic Japanese endoscopy unit.

**Patients and Main Outcome Measurements:** A total of 267 consecutive cases of colorectal tumors treated by ESD from May 2010 to February 2013 were analyzed. Predictors of incomplete resection and perforation, including lesion size, growth type, pathological diagnosis, use of hemostatic forceps, degree of fibrosis, history of biopsy, history of local endoscopic treatment, and endoscopic operability.

**Results:** The incomplete resection rate was 4.1%. The perforation rate was 5.6%. Univariate analysis identified severe fibrosis ($P = .032$), submucosal (SM) deep (>1000 μm) invasion ($P = .033$) and poor endoscopic operability ($P = .030$) as predictors of incomplete resection, and severe fibrosis ($P = .038$), postendoscopic treatment ($P = .016$), and poor endoscopic operability ($P = .012$) as predictors of perforation. Multivariate analysis identified poor endoscopic operability and SM deep invasion as independent predictors of incomplete resection, and poor endoscopic operability and severe fibrosis as independent predictors of perforation. There was no adjustment of $P$ values for multiple testing.

**Limitation:** A single-center study by a single colonoscopist. All statistical results should be taken as descriptive only.

**Conclusions:** Poor endoscopic operability and SM deep invasion were significant independent predictors of incomplete resections. Poor endoscopic operability and severe fibrosis were significant independent predictors of perforation. These features may provide helpful information when planning colorectal ESD. (Gastrointest Endosc 2014;79:427-35.)

With the development of various new tools and peripheral devices and the accumulation of experience and expertise in endoscopic submucosal dissection (ESD), colorectal ESD is gradually gaining widespread acceptance in Japan[1,2] and has been approved for health insurance coverage[3] since April 2012. According to a literature survey, colorectal ESD has been established as a procedure with reproducible safety and efficacy.[1] Technical difficulties associated with this procedure have been significantly reduced, and it is gaining popularity among experienced endoscopists.[4-9]

Colorectal ESD is more technically demanding than esophageal and gastric ESD because of the anatomic features of the large intestine, which is a long luminal organ with many folds and flexures that hinder the manipulation of the endoscope for some lesions, and an intestinal wall that is thin and easy to perforate. Moreover, operator skill can influence the outcomes, and the procedure has a learning curve that may hinder its widespread use by endoscopists. In fact, reports of the therapeutic outcomes of

*Abbreviations: CI, confidence interval; ESD, endoscopic submucosal dissection; OR, odds ratio; SM, submucosal.*

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**TABLE 1. Baseline characteristics of colorectal tumors (N = 267)**

| | |
|---|---|
| Age, y [range] | 66.4 (11.2) [22-91] |
| Sex, male/female, no. | 176/91 |
| Size of the tumor, mm [range] | 35.6 (18.6) [10-100] |
| Growth type of lesion, no. (%) | |
| LST-G/polypoid | 164 (61.4) |
| LST-NG | 103 (38.6) |
| Location of the tumors, no. (%) | |
| Cecum or ascending | 63 (23.6) |
| Transverse | 46 (17.2) |
| Descending | 5 (1.9) |
| Sigmoid | 44 (16.5) |
| Rectum | 109 (40.8) |

*LST-G*, Lateral spreading tumor granular type; *LST-NG*, lateral spreading tumor nongranular type.

**Take-home Message**

- The incomplete resection rate was 4.1% and the perforation rate was 5.6%. Poor endoscopic operability and submucosal deep invasion were independent significant predictors of incomplete resections. Also, fibrosis based on previous endoscopic treatment was significantly associated with perforation.
- Poor endoscopic operability and severe fibrosis were independent significant predictors of perforation.

ESD in the literature suggest that the procedure currently has higher perforation rates than EMR. The aim of this study was to clarify the predictors of incomplete resection and perforation in colorectal ESD.

## PATIENTS AND METHODS

### Patients

Since May 2010, cases of colorectal ESD were prospectively registered in a multicenter listing in Japan, which included our hospital, as those requiring highly advanced medical treatment. A total of 267 consecutive colorectal tumors (adenoma/early carcinoma) treated by ESD at Hiroshima University Hospital in Hiroshima, Japan, from May 2010 to February 2013 were included in the analysis (Table 1). All patients had been informed about the risks and benefits of ESD and provided written informed consent for the procedure, which has been covered under health insurance since April 2012 in Japan. This study protocol was approved by the Institutional Review Board of Hiroshima University Hospital. In this study period, we had no patients who refused ESD. Age and coagulopathy are not limited for inclusion to this study.

The ESD procedures were performed by an endoscopic specialist (S.T.) who has performed about 550 colorectal ESD procedures from November 2002 to February 2013.

The indications for colorectal ESD at our center were based on the Criteria of Indications for Colorectal ESD proposed by the Colorectal ESD Standardization Implementation Working Group,[10,11] which specifically states that colorectal ESD is indicated for lesions requiring endoscopic en bloc excision that cannot be easily performed by using the snare technique, such as laterally spreading tumor nongranular type, especially the pseudodepressed type, tumors with a type V(I) pit pattern, shallow (submucosal [SM] $\leq$1000 μm) invasive SM carcinomas, large depressed tumors, and large elevated lesions that are probably malignant (ie, large nodular lesions such as the laterally spreading tumor granular type). Other lesions, such as intramucosal tumors accompanied by SM fibrosis, including those that occur as a result of chronic inflammation such as ulcerative colitis and local residual early carcinoma after endoscopic excision are also included in the indications. We included all cases that satisfied our inclusion criteria.

### ESD procedure

The patients were sedated with intravenous diazepam 0.1 mg/kg, and cardiorespiratory function was monitored. We used a single endoscope attached to a transparent tip hood with carbon dioxide insufflation. We use a GIF-Q260J (Olympus, Tokyo, Japan), which is a gastroscope, for sigmoid colon or rectal lesions, and a PCF-Q260AZI (Olympus) for lesions from the descending colon and cecum. We usually use a standard tip hood (Olympus). A bell-shaped, small-caliber tip, transparent tip hood (ST hood; FTS, Omiya, Japan) was used in cases of severe fibrosis to make it easier to enter the SM layer. Hyaluronic acid-indigo carmine mixed with glycerol was injected to the SM layer using a 21-gauge injection needle. We mixed half and half 0.4% sodium hyaluronate (Muco Up; Johnson & Johnson, New Brunswick, NJ) and 10% glycerin solution, and added a small amount of indigo carmine (indigo carmine/Muco Up + glycerin: 0.2 mL/20 mL). Because the margin of colorectal tumors can be observed clearly, marking was not required. We never marked the borders of a lesion. A circumferential incision was made in the mucosa around the lesion. Because dissection of the entire circumference of the lesion causes the injection solution to flow from the lesion and results in poor observation of the SM layer, a partial dissection is performed first and then further local dissection is performed after the lesion is adequately located. The tissue was dissected along the SM layer with the DualKnife (Olympus), an SB knife Jr (Sumitomo Bakelite, Tokyo, Japan), or a HookKnife

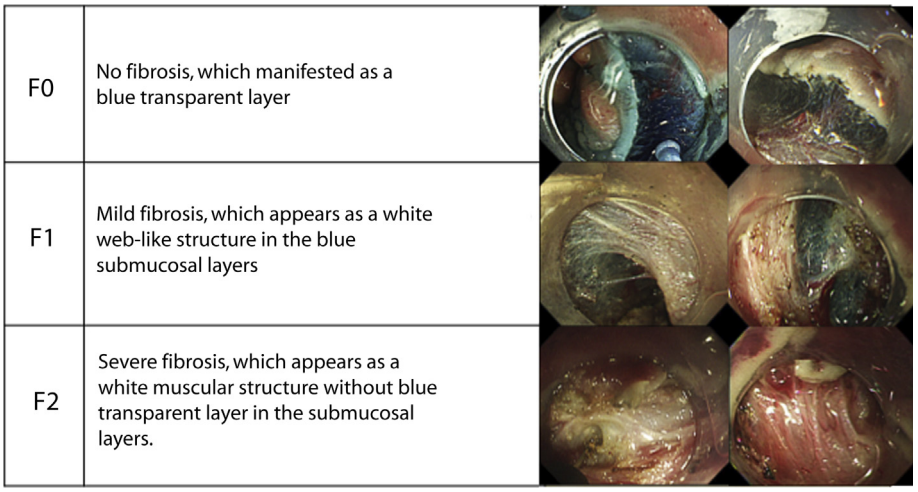


**Figure 1.** Degree of fibrosis of the submucosal layers in colorectal tumors. Degree of fibrosis of the submucosal layers was classified into the following 3 grades according to the appearance of the layers during the submucosal injection of a mixture of sodium hyaluronate and indigo carmine: F0, no fibrosis, which manifested as a blue transparent layer; F1, mild fibrosis, which appears as a white weblike structure in the blue submucosal layers; and F2, severe fibrosis, which appears as a white muscular structure without blue transparent layer in the submucosal layers.[12]

**TABLE 2. Overall outcome of colorectal tumors (N = 267)**

| | |
|---|---|
| En bloc resection, no. (%) | 256/267 (95.9%) |
| Perforation, no. (%) | 15/267 (5.6) |
| Time of procedure, min [range] | 79.6 (55.5) [10-340] |
| Pathological diagnosis, no. (%) | |
| Adenoma | 115 (43.1) |
| Mucosal carcinoma | 91 (34.1) |
| Submucosal carcinoma | |
| Scanty (SM $\leq$1000 μm) invasion | 30 (11.2) |
| Deep (SM $\geq$1000 μm) invasion | 31 (11.6) |

*SM*, Submucosal.

(Olympus) depending on the situation. A DualKnife is a basic knife used for ESD procedures. If possible, we complete ESD with DualKnife alone. However, if the approach direction was positioned perpendicularly against the lesion, or if a rich vascular bed was found during SM dissection, the DualKnife was exchanged for an SB knife Jr or HookKnife. Basically we completed the ESD with 1 or 2 knives. Endoscopic hemostasis was achieved with hemostatic forceps (Coagrasper; Olympus) and the high-frequency generator was an ESG-100 (Olympus). The setting used was the pulse cut slow mode (25 W) for mucosal incision and forced coagulation mode (25 W) for SM dissection. With an SB knife Jr, we used the pulse cut fast mode setting (30 W) and soft coagulation (40 W). Further, we used a single overtube (Olympus) in 3 cases at the hepatic flexure.

We continued the procedure until the resection was accomplished.

## Endoscopic and histopathological evaluations

Analysis of predictors of incomplete resection and perforation included the lesion size, growth pattern (lateral spreading tumor granular type/polypoid or lateral spreading tumor nongranular type), pathological diagnosis and depth of invasion (adenoma: SM shallow invasion or SM deep invasion), use of hemostatic forceps (low frequency or high frequency), degree of fibrosis, history of biopsy, history of local endoscopic treatment, and endoscopic operability. Complete resection is defined as histopathological complete en bloc resection with a negative tumor margin.

Endoscopically, the degree of SM fibrosis was classified as follows based on the findings obtained by using injection of indigo carmine solution under the SM layer (Fig. 1), as reported previously: no fibrosis (F0) (the layer appeared blue and transparent), mild fibrosis (F1) (the layer appeared as a white weblike structure in the blue SM layer), and F2, severe fibrosis (the layer appeared as a white muscle-like structure without a blue transparent component) as described previously.[12] Low frequency of bleeding during ESD was defined as no visible bleeding during the procedure or minor bleeding that stopped spontaneously or was easily controlled by a few applications of coagulation. High frequency of bleeding during ESD was defined as bleeding that required repeated coagulation by hemostatic forceps (>10 times). Poor endoscopic operability was characterized as paradoxical movement of the endoscope, poor control for adhesion,

**TABLE 3. Summary of cases with incomplete resection**

| Case | Size, mm | Growth type | Location | Pathology depth | Histological type of deepest invasive site | Reason for incomplete resection |
|---|---|---|---|---|---|---|
| 1 | 60 | LST-G | R | M | – | Piecemeal mucosal resection because of bleeding |
| 2 | 30 | LST-NG | C | SM 1800 μm | por | Tumor cut end positive at the submucosal deepest margin |
| 3 | 30 | LST-G | A | Adenoma | – | Piecemeal mucosal resection because of poor operability |
| 4 | 50 | LST-G | T | SM 4500 μm | por | Tumor cut end positive at the submucosal deepest margin |
| 5 | 80 | LST-G | A | SM 2000 μm | tub | Tumor cut end positive at the submucosal deepest margin |
| 6 | 20 | LST-NG | A | Adenoma | – | Piecemeal mucosal resection because of fibrosis |
| 7 | 40 | LST-G | S | Adenoma | – | Piecemeal mucosal resection because of poor operability |
| 8 | 20 | LST-NG | R | Adenoma | – | Piecemeal mucosal resection because of fibrosis |
| 9 | 25 | LST-NG | S | Adenoma | – | Piecemeal mucosal resection because of poor operability |
| 10 | 20 | LST-NG | S | SM 3000 μm | por | Tumor cut end positive at the submucosal deepest margin |
| 11 | 25 | LST-NG | A | SM 3500 μm | muc | Tumor cut end positive at the submucosal deepest margin |

*LST-G*, Lateral spreading tumor granular type; *R*, rectum; *M*, intramucosal carcinoma; *LST-NG*, lateral spreading tumor nongranular type; *C*, cecum; *SM*, submucosal invasive carcinoma; *por*, poorly differentiated adenocarcinoma; *A*, ascending colon; *T*, transverse colon; *tub*, tubular adenocarcinoma; *S*, sigmoid colon; *R*, rectum; *muc*, mucinous adenocarcinoma; –, not available.

and lesion motion with heart beat or breathing. Poor endoscopic operability was further analyzed according to age, sex, history of abdominal operation, location (colon or rectum), the presence of the lesion on a fold, the presence of the lesion on a flexure, and the presence of a perpendicular approach to the muscular layer.

### Statistical analysis

Values are reported as mean (standard deviation). The Fisher exact test was used for comparison of categorical variables. Multivariate logistic regression analysis was performed to examine the effects of independent variables adjusted for the effects of all others. The method of selecting a variable is the stepwise method, and the Akaike Information Criterion used to determine the variable when the Akaike Information Criterion was the minimal. Analyses were performed with JMP Statistical software version 9.02 (SAS Institute, Cary, NC. $P$ values $<.05$ were considered statistically significant. There was no adjustment of nominal $P$ values to correct for multiple testing of outcome data arising from individual patients because the main focus of this research is exploratory in nature.

## RESULTS

### Overall outcome of ESD

The overall en bloc resection rate was 95.9% (256/267) (Table 2). There were 11 cases of incomplete resection. Three lesions were accompanied by severe fibrosis at the SM layer because of a previous EMR or ESD. Five lesions were tumor-cut end positive at the deepest SM margin because of SM deep invasion with poorly differentiated or mucinous carcinoma (Fig. 3), and 6 lesions were finally excised by piecemeal mucosal resection by using a snare instead of ESD because of poor endoscopic operability, fibrosis, or severe bleeding during ESD (Table 3). The perforation rate was 5.6% (15/267). One patient with perforation required emergent surgery because of peritonitis. This perforation was located on scar of intestinal tuberculosis. We performed clipping to close the perforation hole; however, complete closure was not possible, most likely because the severe fibrosis caused by tuberculosis was so hard that clipping was insufficient. The other 14 were successfully treated nonsurgically with endoscopic clipping, fasting, and intravenous antibiotic infusion.

**TABLE 4. Univariate analysis of risk factors for incomplete resection**

| | Complete resections (n = 256) | Incomplete resections (n = 11) | P value |
|---|---|---|---|
| Size, mm | 36.4 (17.9) | 39.4 (20.4) | .670 |
| Growth type, no. (%) | | | .871 |
| LST-G/polypoid | 158 (96.3) | 6 (3.7) | |
| LST-NG | 98 (95.2) | 5 (4.8) | |
| Pathological diagnosis, no. (%) | | | .033 |
| Adenoma/ M/SM-s | 229 (97.0) | 7 (3.0) | |
| SM-d | 27 (87.1) | 4 (12.9) | |
| Use of hemostatic forceps, no. (%) | | | .166 |
| Low frequency | 179 (97.8) | 5 (2.2) | |
| High frequency | 77 (89.6) | 6 (10.5) | |
| Degree of fibrosis, no. (%) | | | .032 |
| F0/F1 | 164 (98.2) | 3 (1.8) | |
| F2 | 92 (92.0) | 8 (8.0) | |
| History of biopsy, no. (%) | | | 1.000 |
| No | 234 (95.5) | 10 (4.5) | |
| Yes | 22 (95.7%) | 1 ( 4.3%) | |
| History of previous local endoscopic treatment, no. (%) | | | .050 |
| No | 239 (96.8) | 8 (3.2) | |
| Yes | 17 (85.0) | 3 (15.0) | |
| Endoscopic operability, no. (%) | | | .030 |
| Good/normal | 144 (98.6) | 2 (1.4) | |
| Poor | 112 (95.6) | 9 (4.4) | |

*LST-G*, Lateral spreading tumor granular type; *LST-NG*, Lateral spreading tumor nongranular type; *M*, intramucosal invasion; *SM-s*, submucosal shallow invasion (SM ≤1000 μm); *SM-d*, submucosal deep invasion (SM >1000 μm); *F0*, no fibrosis; *F1*, mild fibrosis; *F2*, severe fibrosis.

## Risk factors for incomplete resections

Severe fibrosis (F2), SM deep invasion, and poor endoscopic operability were significantly associated with a higher frequency of incomplete resections ($P = .032$, $P = .033$, and $P = .030$, respectively), whereas tumor size, growth type, location, and pathological diagnosis and depth of invasion, use of hemostatic forceps, and history of biopsy were not (Table 4).

**TABLE 5. Multivariate analysis of risk factors for incomplete resection**

| Variable | OR (95% CI) | P value |
|---|---|---|
| Poor endoscopic operability | 5.84 (1.18-28.8) | .030 |
| SM deep invasion (SM ≥1000 μm) | 4.96 (1.26-19.6) | .022 |
| Degree of fibrosis F2 (severe) | 3.73 (0.93-14.9) | .062 |

*OR*, Odds ratio; *CI*, confidence interval; *SM*, submucosal; *F2*, severe fibrosis.

On multivariate logistic regression analysis, poor endoscopic operability (odds ratio [OR] 5.84; 95% confidence interval [CI], 1.18-28.8) and SM deep invasion (OR 4.96; 95% CI, 1.26-19.6) were significant factors for predicting incomplete resections during the colorectal ESD procedure (Table 5).

## Risk factors for perforation

Severe fibrosis, postendoscopic treatment, and poor endoscopic operability were significantly associated with perforation ($P = .038$, $P = .016$, and $P = .012$, respectively), but we did not detect an association among a higher frequency of perforation and tumor size, growth type, location, pathological diagnosis and depth of invasion, use of hemostatic forceps, and history of biopsy (Table 6).

On multivariate logistic regression analysis, poor endoscopic operability (odds ratio 4.58; 95% CI, 1.24-16.9) and severe fibrosis (OR 4.41; 95% CI, 1.35-14.5) were significant factors for predicting perforation during colorectal ESD procedures (Table 7).

The percentage of incomplete resection and perforation is shown in Figure 2. The ratio of incomplete resections (7.9%) in cases with either poor endoscopic operability or SM deep invasion were significantly higher than that (0.0%) in cases without both factors (Fig. 2, left; $P = .0009$). The ratio of perforation (8.3%) in cases with either poor endoscopic operability or severe fibrosis (F2) were significantly higher than that (1.0%) in cases without both of these factors (Fig. 2, right; $P = .0118$).

Furthermore, we analyzed the causes of poor endoscopic operability supplementally. We verified that location in colon ($P < .001$) and the presence of lesions on a flexure ($P < .001$) were significantly associated with poor endoscopic operability; however, our analysis did not indicate an association with age, sex, history of abdominal operation, the presence of a lesion on a fold, and the presence of a perpendicular approach to the muscular layer with poor endoscopic operability (Table 8).

**TABLE 6. Univariate analysis of risk factors for perforations**

| | Perforations (−) (n = 252) | Perforations (+) (n = 15) | *P* value |
|---|---|---|---|
| Size, mm | 36.5 ± 1.24 | 36.2 ± 4.98 | .940 |
| Growth type, no. (%) | | | .139 |
| LST-G/polypoid | 158 (96.3) | 6 (3.7) | |
| LST-NG | 72 (91.3) | 9 (8.7) | |
| Pathological diagnosis, no. (%) | | | .052 |
| Adenoma/M/SM-s | 225 (95.3) | 11 (4.7) | |
| SM-d | 27 (87.1) | 4 (12.9) | |
| Use of hemostatic forceps, no. (%) | | | 1.000 |
| Low frequency | 174 (94.6) | 10 (5.4) | |
| High frequency | 78 (94.0) | 5 (6.0) | |
| Degree of fibrosis, no. (%) | | | .038 |
| F0/F1 | 163 (97.6) | 4 (2.4) | |
| F2 | 89 (89.0) | 11 (11.0) | |
| History of biopsy, no. (%) | | | 1.000 |
| No | 230 (94.3) | 14 (5.7) | |
| Yes | 22 (95.7) | 1 (4.7) | |
| History of local endoscopic treatment, no. (%) | | | .016 |
| No | 236 (95.6) | 11 (4.4) | |
| Yes | 16 (80.0) | 4 (20.0) | |
| Endoscopic operability, no. (%) | | | .012 |
| Good/normal | 143 (98.0) | 3 (2.0) | |
| Poor | 109 (90.1) | 12 (9.9) | |

*LST-G*, Lateral spreading tumor granular type; *LST-NG*, Lateral spreading tumor nongranular type; *M*, intramucosal invasion; *SM-s*, submucosal shallow invasion (SM ≤1000 μm); *SM-d*, submucosal deep invasion (SM >1000 μm); *F0*, no fibrosis; *F1*, mild fibrosis; *F2*, severe fibrosis.

**TABLE 7. Multivariate analysis of risk factors for perforations**

| Variable | OR (95% CI) | *P* value |
|---|---|---|
| Poor endoscopic operability | 4.58 (1.24-16.9) | .022 |
| Degree of fibrosis: F2 | 4.41 (1.35-14.5) | .014 |

*OR*, Odds ratio; *CI*, confidence interval.

## DISCUSSION

Perforation is one of the most critical adverse events of ESD, particularly in colorectal cases. The anatomic characteristics of the colon and rectum present unique challenges, and it may be more difficult to perform ESD successfully and safely on colorectal lesions than on gastric lesions. However, with the increasing refinement of ESD and the improvement in the associated instruments and peripheral devices, both of which have enhanced the safety and clinical simplicity of ESD, the technique is being used more commonly for colorectal lesions.[1,13]

In this study, the overall en bloc resection rate and perforation rate were 95.9% and 5.6%, respectively. In previous reports from single-center studies, combined complete en bloc resection rates were 76.9% (range 58%-95.6%, 1385/1801),[12-29] and the combined perforation rate was 5.4% (range 1.3%-20.4%, 180/3339).[12-29] A summary of outcomes of colorectal ESD reported from previous multicenter studies included data from the early period of colorectal ESD to the more recent period without consideration for the learning curve, and complete en bloc resection rates were 62.4% to 83.8% with perforation rates of 3.3% to 14.0%.[11,13,30-34] Our study did not include data from the early period, and it was thought, therefore, that the en bloc resection rate was higher and the perforation rate was relatively low.

Until now, there have been no reports regarding the association between poor endoscopic operability and outcome of colorectal ESD. The current analysis showed that poor endoscopic operability could be a significant independent predictor of incomplete resection and perforation. Location in the colon and the presence of the lesion on a flexure were both significant predictors of poor endoscopic operability. Thus, when operators encounter these factors in ESD, it should be expected that the procedure will be more challenging, and this information can be useful in the selection of the device and operator and in maximizing operator vigilance.

In this study, there were 5 lesions with SM deep invasion that showed tumor-cut end positivity at the SM deepest invasive margin. All 5 of these lesions had poorly differentiated or mucinous carcinoma (unfavorable histology) at the SM deepest invasive margins, suggesting that unfavorable carcinoma cells at the SM deepest invasive margin may not be recognized during ESD because these types of cancer cells often invade diffusely without expansive growth.

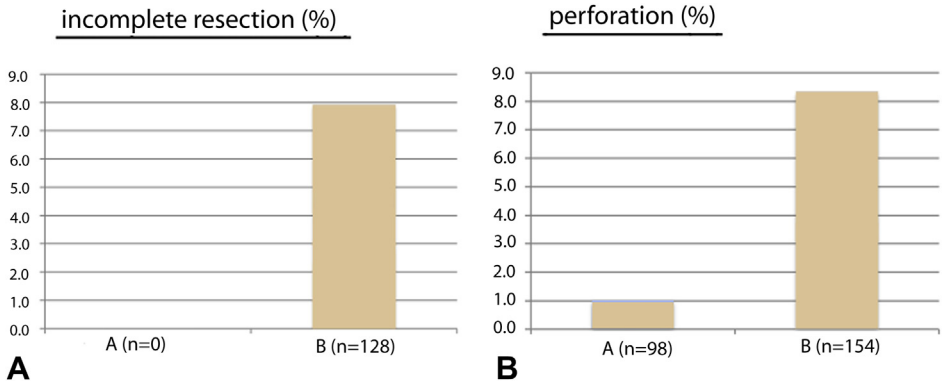


**Figure 2.** The prevalence (%) of incomplete resections and perforation. **A,** Cases with either poor endoscopic operability or submucosal deep invasion. **B,** Cases without both poor endoscopic operability and submucosal deep invasion.

**TABLE 8. Univariate analysis of factors for poor endoscopic operability**

| Factor | Good/ normal (n = 146) | Poor (n = 121) | *P* value |
|---|---|---|---|
| Age, y | 64.9 (0.92) | 68.3 (1.00) | .054 |
| Sex, no. (%) | | | .648 |
| Male | 98 (53.7) | 78 (46.3) | |
| Female | 48 (52.0) | 43 (48.0) | |
| History of abdominal operation, no. (%) | | | .145 |
| Yes | 31 (46.3) | 36 (53.7) | |
| No | 115 (57.5) | 85 (42.5) | |
| Location, no. (%) | | | <.001 |
| Colon | 54 (34.2) | 104 (65.8) | |
| Rectum | 92 (84.4) | 17 (15.6) | |
| Lesion on a fold, no. (%) | | | .146 |
| Yes | 41 (47.7) | 45 (52.3) | |
| No | 105 (58.0) | 76 (42.0) | |
| Lesion on a flexure, no. (%) | | | <.001 |
| No | 11 (17.5) | 52 (82.5) | |
| Yes | 135 (66.2) | 69 (33.8) | |
| Perpendicular approach to the muscular layer, no. (%) | | | .297 |
| No | 19 (64.3) | 10 (35.7) | |
| Yes | 127 (53.4) | 111 (48.7) | |

We reported previously that risk factors for tumor-cut end positive at the deepest SM margin after ESD are severe SM fibrosis, unfavorable histology at the SM deepest invasive margin, and SM deep invasion. If a lesion is diagnosed as SM invasion by conventional and magnifying colonoscopy, we recommend additional EUS because an EUS-based assessment of invasion depth helps the operator to determine whether the lesion will be amenable to complete resection by ESD. However, even with EUS, it may be difficult to detect the diffuse spread of tumor cells at the SM deepest invasive margin.

Previous clinical studies focusing on the factors predicting perforation risk during colorectal ESD have shown that large lesions, fibrosis, tumor location, and operator experience are potential risk factors for perforation during ESD,[16,28,32,35,36] although another report on perforations indicated that there were no significant differences in terms of tumor location.[37] Isomoto et al[18] found that right-sided colon tumors and fibrosis had significant associations with incomplete resection and that perforation was associated with large tumor size (>30 mm) and the presence of fibrosis. These authors also reported that when the contributing factors for each element were combined, the risks of incomplete resection and perforation increased substantially. We previously[12] reported that in cases involving lesions with severe fibrosis, the rate of complete en bloc resection was low and the perforation rate was high, even when ESD was performed by a single experienced operator. However, it was impossible to know the presence and extent of fibrosis before the colorectal ESD.[12] Saito et al[32] reported that less experience performing ESDs (<50 cases) was an independent risk factor for adverse events.

Our study had the limitation of being a single-center study examining results from a single colonoscopist. Expertise is also reflected by a low rate of incomplete resection. Thus, the results may not apply to those experts with less experience. We would like to call attention to the studies of Western endoscopists in which the en bloc resection has been as low as 70%.[29] We anticipate that several other

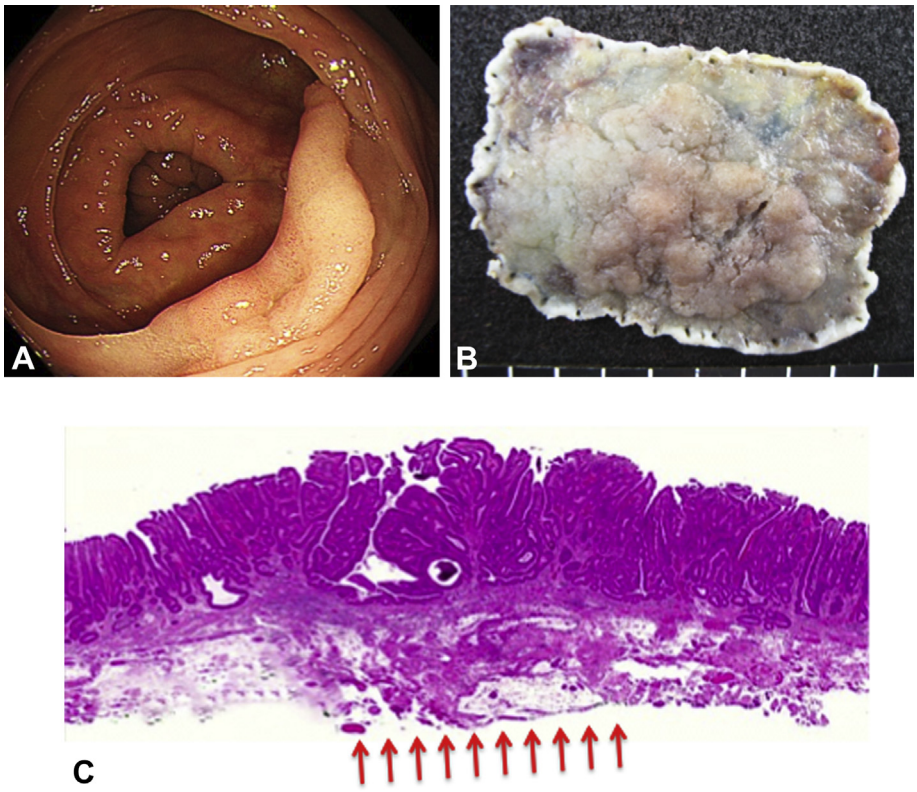


**Figure 3.** A positive vertical tumor margin after endoscopic mucosal dissection for submucosal colorectal carcinoma, Paris classification 0–IIa, ascending colon, 25 mm in diameter. **A,** Standard colonoscopic view. **B,** ESD specimen. **C,** Pathological examination revealed tubular adenocarcinoma with mucinous component. Submucosal invasion depth was 3500 μm, and vertically cut end of the tumor (mucinous component: *arrows*) was positive.

factors (including operator skill) do play a role during ESDs performed by beginners and less-experienced endoscopists. On the other hand, the highest standards of excellence and expertise should be established. Thus, the study is strong for having analyzed only 1 endoscopist. Nevertheless, other studies involving trainees at ESD centers should be performed in the near future. Because the main focus of this research is exploratory in nature, meant to highlight any potential relationships, there was no adjustment of nominal *P* values to correct for multiple testing of outcome data arising from individual patients. Thus, there may be instances of overstating significance, which necessarily leaves open the possibility of overfitting in the main results. Hence, these results should be taken as descriptive only, suggesting potential relationships to future researchers.

In conclusion, poor endoscopic operability was a significant independent predictor of incomplete resection and perforation during colorectal ESD, and location in the colon and the presence of a lesion on a flexure were significant predictors of poor endoscopic operability. SM deep invasion and severe fibrosis were significant independent predictors of perforation. These results will be helpful when considering appropriate approaches before performing colorectal ESD.

## ACKNOWLEDGMENTS

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