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Original

Long-Term Outcomes of Colorectal Endoscopic Submucosal Dissection: Recurrence and Metachronous Cancer

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Background: Endoscopic submucosal dissection (ESD) is widely used to treat colorectal tumors, and long-term outcomes after ESD have increasingly been reported. Post-treatment endoscopic surveillance is essential for detecting local recurrence and metachronous cancer. However, although the incidence of metachronous cancer after ESD has been reported, the detailed clinicopathological characteristics remain unclear. To determine the incidence and clinicopathological characteristics of metachronous cancer, we evaluated long-term outcomes after colorectal ESD.

Methods: This retrospective study analyzed data on clinicopathological characteristics, procedural details, adverse events, and long-term outcomes for 486 patients (577 lesions) who underwent colorectal ESD between November 2005 and April 2017. Rates of local recurrence and metachronous cancer, and the clinicopathological characteristics of metachronous cancer, were investigated.

Results: The en bloc resection rate was 96.1%, and the curative resection rate was 93.5%. Delayed major bleeding occurred in 10 patients (1.7%). Additional colectomy with lymph node dissection was performed in 22 patients (3.3%). Local residual carcinoma was identified in four patients, and lymph node metastasis was observed in one patient with poorly differentiated adenocarcinoma. One patient with deep submucosal invasion and vascular invasion developed lung metastasis 31 months after ESD despite the absence of local residual carcinoma and lymph node metastasis. In addition, a patient with a rare 6-mm rectal neuroendocrine tumor developed liver metastasis 17 months after ESD. Local recurrence was observed in two lesions (0.4%) within 1 year after ESD, and both lesions were successfully treated by endoscopic resection. No recurrence was observed after complete and curative resection. During surveillance colonoscopy, 11 cases of metachronous cancer were detected. All were non-polypoid lesions and more than half were located in the right colon.

Conclusions: As was noted in previous studies, ESD for colorectal tumors yielded a high en bloc resection rate and favorable long-term outcomes, with a low incidence of local recurrence. Early surveillance colonoscopy is recommended after histologically incomplete resection to detect local recurrence. Long-term surveillance colonoscopy should focus on detecting metachronous cancer, particularly slightly elevated (type 0-IIa) lesions.

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Keywords: endoscopic submucosal dissection, colorectal cancer, long-term outcomes, metachronous cancer, surveillance colonoscopy

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Introduction

Endoscopic submucosal dissection (ESD) for colorectal tumors has been covered by the Japanese National Health Insurance system since April 2012. With advances in endoscopic techniques and instrumentation[1,2], ESD has become widely recognized as a standard minimally invasive treatment. Although long-term outcomes after colorectal ESD have been reported[3,4], few studies have included large patient cohorts[3,5].

The advantages of ESD include a high en bloc resection rate, the ability to resect large lesions with curative intent, and a low rate of local recurrence. A systematic review of mid-term clinical outcomes of colorectal ESD reported a local recurrence rate of approximately 1%[6]. Furthermore, a recent prospective multicenter cohort study in Japan reported a local recurrence rate of 0.5% after ESD for large colorectal epithelial neoplasms[5]. En bloc resection enables accurate histopathological assessment, allowing estimation of the risk of lymph node metastasis and appropriate selection of patients who require additional surgical treatment. According to the Japanese Society for Cancer of the Colon and Rectum (JSCCR), the incidence of lymph node metastasis was 1.4% when only the depth of submucosal invasion (>1,000 μm) did not meet the criteria for curative resection and no other risk factors for metastasis were present[7].

Even after curative resection by ESD, patients remain at risk of developing metachronous colorectal cancer; therefore, careful endoscopic surveillance after treatment is recommended. However, although several studies have reported the incidence of metachronous cancer after ESD[3–5], information on its clinicopathological characteristics is limited. Clarifying the morphological and other clinicopathological characteristics of metachronous cancers may help identify lesions that warrant close attention during surveillance colonoscopy, thereby facilitating earlier detection and appropriate endoscopic treatment. Therefore, this study evaluated the long-term outcomes of colorectal ESD, as well as the incidence and clinicopathological characteristics of metachronous cancer.

Materials and Methods

Participants

This retrospective observational study analyzed data from patients who underwent colorectal ESD at our institution between November 2005 and April 2017. The study was conducted in accordance with the principles of the Declaration of Helsinki and was approved by the Institutional Review Board of Tokyo Women's Medical University (approval number: 2022-0148). Because this was a retrospective study, study information was published on the institution website, and patients who opted out were excluded. Written informed consent was obtained from all patients before ESD.

Diagnosis

Preoperative diagnosis was performed using magnifying endoscopy with dye-spraying pit-pattern analysis[8], the Japan Narrow Band Imaging Expert Team classification using narrow-band imaging[9], and endoscopic ultrasonography to evaluate invasion depth[10].

Indications for ESD were consistent with the colorectal ESD/EMR guidelines[11]. These included laterally spreading tumor-nongranular type lesions unsuitable for en bloc EMR, lesions with a Vi-type pit pattern, tumors with suspected limited T1 submucosal invasion, and large depressed or protruding lesions suspected to be carcinoma. Intramucosal tumors with submucosal fibrosis and localized tumors associated with chronic inflammatory diseases such as ulcerative colitis were also included. Neuroendocrine tumors (NETs) measuring <10 mm that were localized and confined to the submucosa were included when curative endoscopic resection was considered feasible[12].

ESD Procedure and Histopathological Evaluation

Initially, ESD was performed using a needle-type knife (FlushKnife BT; Fujifilm Corporation, Tokyo, Japan). After 2012, scissor-type knives such as the ClutchCutter (Fujifilm Corporation, Tokyo, Japan) and SB Knife Jr (Sumitomo Bakelite Corporation, Tokyo, Japan) were used. Histopathological evaluation followed the General Rules for Clinical and Pathological Studies on Cancer of the Colon, Rectum and Anus (7th edition)[13] and the Japanese Classification of Colorectal Carcinoma (8th edition)[14]. Histological complete resection was defined as negative horizontal and vertical margins. Curative resection was defined as histological complete resection without pathological risk factors for lymph node metastasis.

Additional Surgical Treatment

Indications for additional surgery for pT1 (submucosal) colorectal cancer were consistent with the Japanese guidelines for colorectal cancer treatment[15,16]. Additional surgical resection was strongly recommended for positive vertical margins and was considered when pathological risk factors for lymph node metastasis were present, including submucosal invasion depth ≥1,000 μm, vascular

invasion, poorly differentiated adenocarcinoma, signet ring cell carcinoma or mucinous carcinoma, and budding grade 2/3 at the deepest invasive front.

Surveillance Colonoscopy

Patients with histologically complete resection were advised to undergo surveillance colonoscopy at 1 year after ESD. When piecemeal resection was performed or margins were uncertain because of coagulation artifacts, surveillance colonoscopy was recommended within 6 months. Thereafter, colonoscopy was recommended every 1–2 years.

In the present study, we analyzed patients who underwent ESD for colorectal cancer or adenoma to evaluate metachronous cancers detected ≥1 year after ESD. Patients with other benign lesions or neuroendocrine tumors were excluded. Metachronous colorectal cancer was defined as a newly detected colorectal cancer identified ≥1 year after the initial ESD.

In accordance with the JSCCR guidelines, post-ESD surveillance was recommended for up to 5 years, particularly in patients with colorectal cancer[15,16]. In addition, patients who underwent additional surgery after non-curative resection were followed with postoperative surveillance for both local recurrence and distant metastasis, including periodic colonoscopy, CT and other imaging studies, and tumor marker measurements. Patients who declined additional surgery were also followed according to the same postoperative surveillance protocol. The surveillance intervals and duration were determined at the discretion of the attending physician. Follow-up data were obtained from medical records or, when possible, through direct contact with referring physicians.

Variables

Clinicopathological characteristics evaluated included age, sex, tumor location, tumor size, morphology (Paris classification), histology, procedure time, en bloc resection rate, histological complete resection rate, curative resection rate, and adverse events. Delayed bleeding requiring endoscopic hemostasis was defined as major bleeding. Long-term outcomes, including local recurrence and metachronous cancer, were also assessed.

Statistical Analysis

Statistical analysis was performed using JMP Pro (version 17.0; SAS Institute, Cary, NC). Continuous variables are presented as the median with interquartile range (IQR). Categorical variables were compared using Pearson's chi-square test or Fisher's exact test, and continuous variables using the Mann–Whitney U test. A P value of <0.05 was considered to indicate statistical significance.

Results

Clinicopathological Characteristics

A total of 486 patients (577 lesions) underwent ESD for colorectal tumors. The cohort included 310 men and 176 women, with a median age of 69 (IQR, 62–75) years. Lesion locations were as follows: right colon, 331 lesions (87 in the cecum, 111 in the ascending colon, 133 in the transverse colon); left colon, 150 lesions (31 in the descending colon, 119 in the sigmoid colon); and rectum, 96 lesions. The median tumor diameter was 22 (IQR, 18–30) mm, with a maximum of 120 mm. Among these, the median cancer diameter was 24 (IQR, 20–36) mm. Morphologically, 212 lesions were polypoid, 365 lesions were non-polypoid (slightly elevated: 0-IIa, 345 lesions, slightly depressed; 0-IIc, 10 lesions, submucosal tumor-like, 10 lesions). The final pathological results of the completed ESD cases were 379 adenoma cases (66.4%); six cases of other benign lesions; 136 Tis (intramucosal cancer) cases; 14 T1a (carcinoma with superficial [<1,000 μm] submucosal invasion) cases; 28 T1b (carcinoma with deep [≥ 1,000 μm] submucosal invasion) cases; and eight NET cases (**Table 1**).

ESD Treatment Outcomes

The overall completion rate for ESD was 99.0% (571/577). Incomplete resections occurred in six patients, including one with severe fibrosis from prior intestinal tuberculosis, three with T1b lesions, and two with T2 (muscularis propria-invasive cancer) lesions. The en bloc resection rate was 96.1%, and the median procedure time was 38 (IQR, 23–61) minutes. Histological complete resection was achieved in 93.9% of patients, and the CR rate was 93.5%. Two histological complete resection cases were classified as non-CRs because of the presence of deep submucosal invasion.

Adverse events occurred in 64 cases (11.1%), including delayed major bleeding in 10 patients (1.7%). Minor bleeding was noted in 18 cases (3.1%). Mild muscularis propria incision was observed in 21 cases (3.6%), retroperitoneal emphysema in 5 cases (0.9%), and small perforations in 3 cases (0.5%), all of which were managed conservatively with endoscopic clipping. No delayed perforations were reported (**Table 2**). Surgical treatments were not required in any patient.

Table 1 Baseline clinicopathological characteristics of patients

Variable	Total (%)
Number of patients	486
Age (years), median (IQR)	69 (61–75)
Gender, male/female	310/176
Number of lesions	577
Location	
Right colon	331 (57.4)
Left colon	150 (26.0)
Rectum	96 (16.6)
Morphology	
Polypoid	212 (36.7)
Slightly elevated (0-IIa)	345 (59.8)
Slightly depressed (0-IIc)	10 (1.7)
Submucosal tumor	10 (1.7)
Size (mm), median (IQR)	22 (18–30)
Histology (resected lesions by ESD)	571
Adenoma	379 (66.4)
Other benign lesions	6 (0.1)
Carcinoma	178 (31.2)
Tis	136 (23.6)
T1a	14 (2.4)
T1b	28 (4.9)
NET	8 (1.4)

ESD, endoscopic submucosal dissection; Tis, intramucosal cancer; T1a, carcinoma with superficial (<1,000 μm) submucosal invasion; T1b, carcinoma with deep (≥1,000 μm) submucosal invasion; NET, neuroendocrine tumor.

Table 2 ESD treatment outcomes

Variable	Total (%)
Number of cases of complete ESD	571 (99.0)
Procedure time (min), median (IQR)	38 (23–61)
Resection status	
En bloc	549 (96.1)
Piecemeal	22 (0.4)
Histological complete resection	
Complete	536 (93.9)
Incomplete	35 (6.1)
Endoscopic curability	
Curative resection	534 (93.5)
Non-curative resection	37 (6.4)
Adverse event	64 (11.1)
Postoperative bleeding	28 (4.9)
Major bleeding	10 (1.7)
Minor bleeding	18 (3.1)
Decrease in blood pressure	1 (0.2)
Abdominal pain	6 (1.0)
Muscularis propria incision	21 (3.6)
Retroperitoneum emphysema	5 (0.9)
Perforation	3 (0.5)

ESD, endoscopic submucosal dissection.

Long-Term Outcomes after ESD

Additional colectomy was performed in 22 of the 29 patients (5.1%) with T1 cancers who had risk factors for lymph node metastasis. The remaining seven patients did not undergo surgery, because of their advanced age or other underlying disease. Residual carcinoma was found in four colectomy specimens, and another patient had lymph node metastasis with mucin formation and poorly differentiated adenocarcinoma in the deepest part of the specimen. During the long-term course, lung metastasis recurred after 31 months in one case. The patient had a type 0-IIa+IIc 14-mm lesion in the ascending colon, with a moderate differentiated adenocarcinoma submucosal layer of 1,500 μm, and was positive for vascular invasion, necessitating an additional colectomy, and resulting in no residual cancer and no lymph node metastasis. Despite undergoing pneumonectomy for metastatic lung tumors, the patient ultimately died of the primary disease 63 months after ESD.

Additionally, a patient with a rare 6-mm rectal NET developed liver metastasis 17 months after resection. Retrospective pathological review confirmed lymphatic invasion via positive immunostaining (**Figure 1**).

Local Recurrence

The local recurrence rate was 0.4% (2 of 571 lesions). Recurrence was significantly associated with histological incomplete resection (P = 0.004), non-CR (P = 0.004), and presence of adverse events (P = 0.012). No recurrence occurred in cases of complete resection or CR (**Table 3**).

The characteristics of the two patients with local recurrence after ESD are presented in **Table 4**. Both cases occurred within 1 year after the initial ESD. The first case of Tis was a 70-mm type 0-IIa in which the splenic flexure of the transverse colon was severely curved and difficult to treat. Although en bloc resection was performed, the presence of cancer invasion in the horizontal margins was unclear. Therefore, the first surveillance colonoscopy was conducted 3 months later, and a 4-mm type 0-IIa lesion was detected near the scar. The small locally recurrent lesion was excised by hot biopsy. The second case involved a 35-mm type 0-Is (sessile) adenoma in the cecum with severe white fibrosis, which required piecemeal resection. At the first surveillance colonoscopy, performed 7 months later, a locally recurrent 11-mm type 0-Is lesion was identified and subsequently resected by EMR. Both recurrent lesions were successfully removed by endoscopic resection without requiring additional surgery.

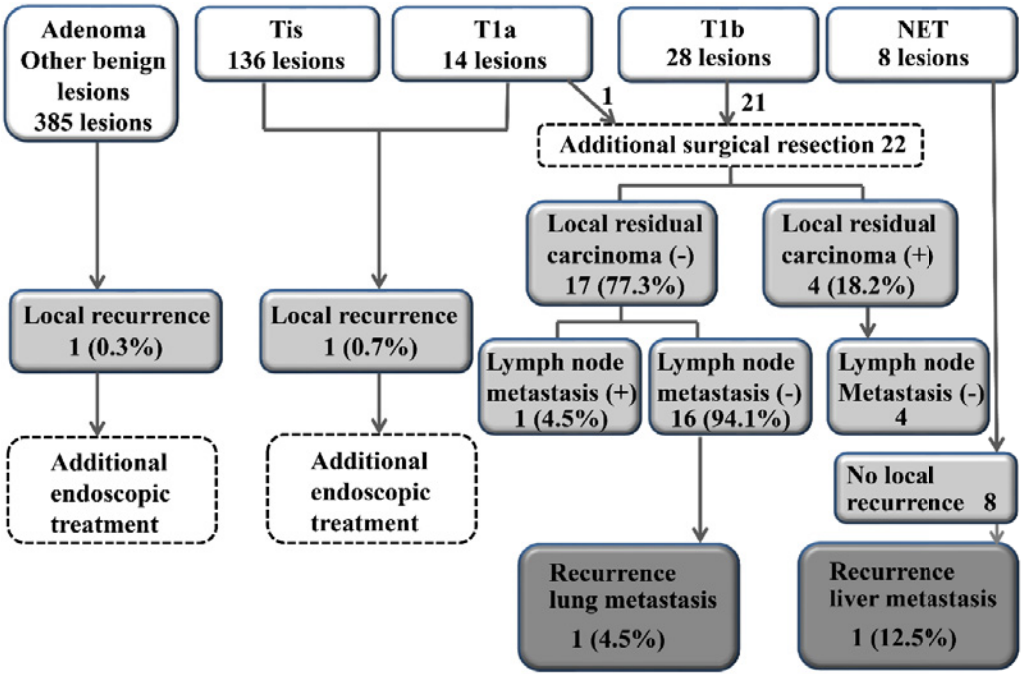

Figure 1 Pathological diagnosis and additional treatment
Tis, intramucosal cancer; T1a, carcinoma with superficial (<1,000 μm) submucosal invasion; T1b, carcinoma with deep (≥1,000 μm) submucosal invasion; NET, neuroendocrine tumor.

Metachronous Cancer

We analyzed a cohort of 470 patients who underwent endoscopic submucosal dissection (ESD) for treatment of cancer or adenoma. Of these, 273 patients (58.1%; 108 treated for cancer, 165 for adenoma) underwent follow-up colonoscopy after ESD. Among them, surveillance colonoscopy was performed in 223 patients (81 with cancer, 142 with adenoma) after a minimum of 1 year. The median follow-up duration was 47 (IQR, 27–70) months. Metachronous cancers were evaluated in patients who underwent surveillance colonoscopy at ≥1 year after the procedure. The clinicopathological features of metachronous cancers are shown in **Table 5**. Eleven cases of metachronous cancer (4.9%) were identified: eight in patients with initial adenomas (5.6%) and three in patients with initial cancers (3.7%).

Six metachronous cancers (54.5%) were located in the right colon. All lesions were non-polypoid (0-IIa, 10 lesions; 0-IIc, 1 lesion). Tumor size was significantly smaller in metachronous cancers than in initially treated tumors (median 20 [IQR, 10–20] mm vs. median 24 [IQR 20–36] mm; P = 0.002). Histologically, six were Tis, four were T1a, and one was T1b. The median time to detection of metachronous cancer after the initial ESD was 42 (IQR, 19–71) months, with a maximum of 89 months.

Eight patients (72.7%) underwent endoscopic treatment (seven treated by ESD and one by EMR); one patient required additional surgical resection. EMR was conducted for a 6-mm type 0-IIa lesion. This patient had positive vertical margins because of deep tumor invasion of the submucosa and vascular invasion. Three cases underwent colectomy from the outset. In one case, the lesion was located on scar tissue secondary to ulcerative colitis; in the other, it was situated over a diverticulum in the sigmoid colon. In both cases, ESD was viewed as technically demanding. Another case involved a type 0-IIc lesion, in which deep submucosal (SM) invasion was suspected.

Discussion

In the present study, colorectal ESD achieved a high en bloc resection rate, low local recurrence rate, and favorable long-term outcomes, consistent with previous reports[3–6].

A Japanese multicenter study of colorectal ESD examined 816 cases in the JSCCR "Colorectal Endoscopic Resection Standardization" Project and reported an en bloc resection rate of 94.5%, a perforation rate of 1.6%, and a delayed bleeding rate of 2.2%[17]. The respective values in the present study were 96.1%, 0.5%, and 1.7%, indicating favorable short-term outcomes with comparable or better safety and efficacy[18].

According to the Japanese guidelines for the Treatment of Colorectal Cancer (2014 and 2016)[15,16], additional colec-

Table 3 Clinicopathological features of local recurrent lesions

Variable	Local recurrent lesions (%)	P value
Number of lesions	2	
Age (years)		
<65	0/195 (0.0)	0.550
≥65	2/376 (6.5)	
Gender		
Male	0/367 (0.0)	0.127
Female	2/204 (1.0)	
Tumor location		
Right colon	2/326 (0.6)	0.509
Left colon and rectum	0/245 (0.0)	
Morphology		
Polypoid	1/208 (0.5)	1.000
Non-polypoid	1/363 (0.3)	
Tumor size (mm)		
<30	0/400 (0.0)	0.089
≥30	2/171 (1.2)	
Histology of initial lesion		
Adenoma	1/379 (0.3)	0.527
Carcinoma	1/186 (0.5)	
Resection status		
En bloc	1/549 (0.2)	0.076
Piecemeal	1/22 (4.5)	
Histological status		
Complete resection	0/536 (0.0)	0.004
Incomplete resection	2/35 (5.7)	
Curability		
Curative resection	0/534 (0.0)	0.004
Non–curative resection	2/37 (5.4)	
Adverse event		
+	2/64 (3.1)	0.012
–	0/507 (0.0)	

tomy with lymph node dissection is recommended for patients with pathological risk factors for lymph node metastasis. In the present study, 22 patients underwent additional colectomy with lymph node dissection. Local residual carcinoma was detected in 4 patients (18.2%) and lymph node metastasis in 1 patient (4.8%). The patient with lymph node metastasis had poorly differentiated adenocarcinoma, which is a known risk factor for lymph node metastasis according to the guidelines. These findings support the validity of the current guideline-based criteria for recommending additional surgical treatment after endoscopic resection.

A comparison of a group that underwent surgery at the outset for pT1 (submucosal) cancer with a group that underwent surgery after endoscopic treatment found no difference in lymph node metastasis or recurrence rate[19]. Furthermore, ESD is first performed to achieve an excisional biopsy, even if the SM invasion depth is T1b (> 1,000 μm); the need for additional colectomy is then determined after histological examination of the resected specimens. These findings underscore the importance of accurate histopathological assessment after ESD to determine the need for further treatment[20]. Therefore, en bloc resection of the lesion is important and specimens must be handled with care.

One notable case in our study involved lung metastasis 31 months after ESD of a type 0-IIa+IIc 14-mm moderately differentiated adenocarcinoma with deep submucosal invasion and vascular invasion. No residual local carcinoma and no lymph node metastasis were detected at the time of an additional colectomy. In the abovementioned multicenter study, only large (≥20 mm) lesions in patients undergoing ESD were examined[5]; however, this case suggests that distant metastasis can occur even when lesions are small and that detailed pathological diagnosis after complete en bloc resection by ESD is also important for small early invasive cancers. Additionally, the Guidelines for the Treatment of Colorectal Cancer suggest that it is necessary to consider both local recurrence and distant metastatic recurrence and to conduct surveillance, including image diagnosis such as CT and serum tumor markers, for approximately 5 years after surgery[21].

A patient with a rare case of a 6-mm rectal NET developed liver metastasis 17 months after ESD. Although small (<10 mm) rectal NETs confined to the submucosa are generally considered suitable for endoscopic treatment because of their limited metastatic potential[12,22–24], small (<10 mm) rectal NETs with metastasis, lymphatic invasion, and venous invasion are strongly associated with metastasis[23].

Pathological diagnosis of recent endoscopically resected specimens has shown a high positive rate for vascular invasion when immunostaining and special staining such as D2-40 and Elastica van Gieson were used. Metastatic recurrence is also observed rarely in these cases[25]. However, many issues lack a consensus. Because current guidelines do not include specific surveillance recommendations for colorectal NETs, results from a colorectal NET multicenter prospective case registry follow-up study may help establish clearer follow-up protocols in the future[22].

Regarding the clinical course, local recurrence was observed in only two cases, corresponding to a local recurrence rate of 0.4%. This outcome was not inferior to the 1.4% local recurrence rate reported in the above-

Table 4 Clinicopathological characteristics of local recurrences

	Case 1	Case 2
Age (years)	75	69
Gender	Female	Female
Initial lesion		
Location	Transverse colon	Cecum
Morphology	0-IIa	0-Is
Size (mm)	70	35
Histology	Tis carcinoma	Adenoma
Resection status	En bloc	Piecemeal
Horizontal margin	Unclear	Unclear
Vertical margin	Negative	Unclear
Local recurrent lesion		
Morphology	0-IIa	0-Is
Size (mm)	4	11
Histology	Tis carcinoma	Adenoma
Interval from ESD to local recurrence (months)	3	7
Treatment	Hot Biopsy	EMR

Tis, intramucosal carcinoma; ESD, endoscopic submucosal dissection; EMR, endoscopic mucosal resection; IIa, slightly elevated; Is, sessile.

Table 5 Clinicopathological features of metachronous cancers

Variable	Total (%)
Initial lesion	
Carcinoma (n=81)	3 (3.7)
Adenoma (n=142)	8 (5.6)
Total (n=223)	11 (4.9)
Metachronous cancers	
Location	
Right colon	6 (54.5)
Left colon	3 (27.3)
Rectum	2 (18.2)
Morphology	
Polypoid	0 (0.0)
Slightly elevated (0-IIa)	10 (90.9)
Slightly depressed (0-IIc)	1 (9.1)
Size (mm), median (IQR)	20 (10–20)
Histology	
Tis	6 (54.5)
T1a	4 (36.4)
T1b	1 (9.1)
Time to metachronous cancers from ESD (month), median (IQR)	42 (19–71)
Treatment	
ESD	7 (63.6)
EMR + Colectomy	1 (9.1)
Colectomy	3 (27.3)

Tis, intramucosal cancer; T1a, carcinoma with superficial (<1,000 μm) submucosal invasion; T1b, carcinoma with deep (≥1,000 μm) submucosal invasion; ESD, endoscopic submucosal dissection; EMR, endoscopic mucosal resection.

mentioned project study. Additionally, a 2022 multicenter joint study of long-term outcomes after ESD reported a local recurrence rate of 0.5%[5], a similarly encouraging outcome. The CR rate in our study was 93.5%, indicating that ESD is an effective local treatment for appropriately selected colorectal tumors. In particular, our findings con-

firm the utility and safety of ESD when performed in high-volume centers.

In this study, histological incomplete resection, non-curative resection, and adverse events were significant risk factors for local recurrence. The abovementioned multicenter study also found that piecemeal resection and positive surgical margins were significant risk factors for local recurrence[5]. Both of the present cases of recurrence within 1 year were successfully treated with additional endoscopic procedures. Therefore, surveillance colonoscopy to detect and treat local recurrence soon after ESD is important after histological incomplete resection or piecemeal resection. Local recurrence is usually confirmed 3–6 months after endoscopic treatment[26], and the Guidelines for Colorectal ESD/EMR (2nd edition) of the Japan Gastroenterological Endoscopy Society recommend a colonoscopy after 6 months in cases of piecemeal resection or if the tumor margin after resection is unclear[7].

The number of ESD cases is increasing, and there are more opportunities for surveillance colonoscopy. Therefore, we attempted to clarify the salient characteristics of metachronous cancers. Many patients were referred for ESD treatment from other facilities, and only 273 patients (58.1%) were confirmed to have surveillance colonoscopy after ESD. This suggest a need for collaboration between hospitals and clinics so that surveillance can be implemented more reliably. The 2020 Colonoscopy Screening and Surveillance Guidelines of the Japan Gastroenterological Endoscopy Society propose surveillance intervals based on risk stratification[27]. Most lesions suitable for ESD were Tis, T1, or adenoma ≥20 mm, and surveillance colonoscopy after 1 year is recommended.

Metachronous cancer was detected in 4.9% of patients who underwent surveillance colonoscopy ≥1 year after ESD, despite low follow-up rates. The median time to detection was 42 months, with about half identified ≥5 years after ESD. This highlights the importance of sustained long-term follow-up. A 2022 multicenter joint study of long-term outcomes after ESD reported an incidence of metachronous invasive cancers of 1.0%, and the median (IQR) follow-up period after ESD was 26.8 (23.4–43.6) months[5]. Furthermore, the incidence of ≥6-mm metachronous tumors after ESD was 18.9% (38/201 cases) over 6.4 years, of which 4.0% (8/201 cases) were cancers[4], highlighting the importance of surveillance colonoscopy for discovery of metachronous cancers.

A cohort study in Japan reported that the cumulative detection rate of metachronous tumors was higher for lesions detected during post-surgery surveillance than for local recurrent lesions (8% vs. 0.7%), and colonoscopy in the first year after surgery was essential for detection of local recurrent lesions[28]. However, subsequent surveillance endoscopy should focus on detection of metachronous tumors[28]. All metachronous cancers in this study were non-polypoid lesions, and more than half were located in the right colon. These findings suggest that metachronous cancers after colorectal ESD often appear as subtle lesions that may be easily overlooked. Therefore, meticulous endoscopic observation, particularly in the right colon, is crucial for detecting superficial lesions such as type 0-IIa lesions during surveillance colonoscopy. Image-enhanced endoscopy has also been reported to improve detection of easily overlooked polyps, suggesting its usefulness in detecting lesions[29].

This study had some limitations. First, it was a single-center retrospective study. Second, surveillance colonoscopy was not performed in all eligible patients, largely because of the patterns of referral from other institutions. Improving collaboration between hospitals and outpatient clinics may increase the rate and consistency of long-term follow-up.

In conclusion, colorectal ESD achieved a high en bloc resection rate and favorable long-term outcomes, including a low rate of local recurrence. Early surveillance colonoscopy is particularly important after histologically incomplete resection because of the increased risk of local recurrence. Notably, the incidence of metachronous cancer exceeded that of local recurrence, underscoring the importance of continued endoscopic surveillance beyond the first year. Careful endoscopic inspection is particularly important for slightly elevated (type 0-IIa) lesions, which accounted for most metachronous tumors.

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