Surg Endosc (2010) 24:1941–1947
DOI 10.1007/s00464-010-0883-7

Endoscopic submucosal dissection with a combination of small-caliber-tip transparent hood and flex knife for large superficial colorectal neoplasias including ileocecal lesions

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Received: 26 August 2009 / Accepted: 3 January 2010 / Published online: 29 January 2010

Abstract
Background Large superficial neoplasias of the ileocecal region pose an increased degree of complexity for endoscopic resection. This study aimed to evaluate the safety and efficacy of endoscopic submucosal dissection (ESD) for large superficial colorectal neoplasias including ileocecal lesions.
Methods A total of 33 superficial colorectal neoplasias, including eight neoplasias in the ileocecal region, were treated with ESD from December 2005 to April 2009. Therapeutic efficacy, complications, and follow-up results were retrospectively evaluated among three groups: ileocecal region, colon, and rectum.
Results The mean size of all resected neoplasias was 35 ± 15 mm (range, 20–80 mm) and that of all resected specimens was 41 ± 15 mm (range, 23–82 mm). The mean procedural time was 121 ± 90 min (range, 22–420 min). The difference in mean values among the three groups was not significant. The overall rate of en bloc resection was 91% (30/33). Histopathologically, both the lateral and vertical margins in the specimens resected en bloc tested negative (30/30). The rate for en bloc resection in the ileocecal region did not differ significantly from that for the other two groups ($p = 0.20$ compared with the rate for the colon and $p = 0.12$ compared with the rate for the rectum). Complications such as perforation and postoperative bleeding did not occur in the ileocecal group. No recurrence was observed in any cases during the mean follow-up period of 20 ± 12 months (range, 4–44 months).
Conclusions The ESD approach is safe and effective for treating large superficial neoplasias of the ileocecal region such as other colorectal neoplasias.

Keywords Colorectal cancer · Colorectal neoplasia · EMR · Endoscopic mucosal resection · Endoscopic submucosal dissection · ESD · Ileocecal lesion · Ileocecal region

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Early-stage gastrointestinal neoplasias show a low frequency of the lymph node and distant metastasis, which allows for less invasive treatments. Recently, endoscopic submucosal dissection (ESD) has been applied to colorectal neoplasias because it provides a higher en bloc resection rate and is less invasive than surgical resection, although this technique has disadvantages such as a longer operative time and a higher complication rate [1–4]. When an ileocecal segment is removed, alterations in the absorption processes sometimes impair vitamin B12 metabolism as well as fat and bile salt absorption, which can cause chronic diarrhea [5–8].

It is recognized that large superficial neoplasias of the ileocecal transition pose an increased degree of complexity for endoscopic resection, and surgical treatment is sometimes required in the case of incomplete resection. The safety and efficacy of this new technique for neoplasias located in the ileocecal region that enables preservation of

the ileocecal segment have not been investigated adequately. This study aimed to evaluate the safety and efficacy of ESD for large superficial neoplasias in the ileocecal region.

Patients and methods

A total of 33 superficial colorectal neoplasias including eight neoplasias in the ileocecal region of 33 patients were treated with ESD at St. Luke's International Hospital in Tokyo from December 2005 to April 2009. All these lesions were preoperatively evaluated with high-magnifying colonoscopes (CF-H260ZI or PCF-Q240ZI; Olympus, Optical Co, Ltd., Tokyo, Japan) after 0.4% indigo carmine dye or 0.05% crystal violet had been sprayed over the neoplasias to enhance their surface details.

The indications for ESD were a superficial large lesion (diameter, >20 mm); lesions with a IIIs, IIIL, IV, or VI pit pattern and no VN pit pattern seen via a high-magnifying colonoscope in the deep submucosal invasion cases according to Kudo's classification [9–11]; no lymph node involvement or distant metastasis observed on computed tomography; and no deep submucosal invasion observed by endosonography with a 20-MHz through-the-scope endoscopic ultrasound catheter probe (UM3R; Olympus Optical Co. Ltd.).

The locations of the neoplasias were divided into three groups: the ileocecal region (cecum and ileocecal junction), the colon (ascending colon, transverse colon, descending colon, and sigmoid colon), and the rectum. Based on preoperative endoscopic findings, all colorectal neoplasias treated with ESD were classified into the following types: pedunculated type (0-Ip), sessile type (0-Is), slightly elevated type (0-IIa), completely flat type (0-IIb), slightly depressed type without ulcer (0-IIc), and combined type according to the Paris endoscopic classification [12]. The semipedunculated type (0-Isp) lesions were managed as sessile type (0-Is) lesions. Use of this treatment was approved by the ethics committee of our hospital, and written informed consent was obtained from all patients.

ESD methods

First, 50 mg of pethidine hydrochloride was administered in all cases. Second, 1 mg of midazolam was given additionally based on the endoscopist's judgment. During ESD treatment, blood pressure, oxygen saturation (SpO_2), and electrocardiogram (ECG) were monitored, and 1–3 l/min of oxygen was given using a nasal cannula.

The ESD technique, a novel procedure for dissecting the submucosal layer directly using specialized devices, allows en bloc resection [1–4, 13–16]. After routine bowel preparation with a polyethylene-glycol solution, ESD was performed with a single-accessory-channel endoscope (GIF-Q260J or PCF-240I; Olympus Optical Co, Ltd.) by one endoscopist who had treated more than 100 gastric neoplasias using the ESD technique. An electrosurgical current generator (ICC200, used from December 2005 to March 2006, or VIO300D, used from April 2006 to April 2009; ERBE, Tubimugen, Germany) was used for ESD treatment.

Because the margin of the lesions could be identified clearly with 0.4% indigo carmine dye spraying, marking dots for mucosal incision were not needed in all cases (Fig. 1). A small-caliber-tip transparent hood (DH-15GR, DH-15CR; Fujinon-Toshiba, Saitama, Japan) was fitted onto the tip of the endoscope to control the depth of the mucosal incision and to maintain a satisfactory view during the submucosal dissection [1]. From December 2005 to September 2007, 0.5% sodium hyaluronate solution comprising a mixture of 1.0% sodium hyaluronate (Artz 1%, average molecular weight 800,000 daltons; derivative type, rooster comb; Kaken Pharmaceutical Co., Tokyo, Japan) and the same amount of normal saline with 0.00005% epinephrine and 0.004% indigo carmine dye was used as an injection solution. From October 2007 to April 2008, 0.4% sodium hyaluronate solution (MucoUp; Johnson and Johnson Medical Co., Tokyo, Japan) was used for the injection [17].

After 0.4% indigo carmine dye spraying, sodium hyaluronate solution was injected into the submucosal layer around the lesion, and a circumferential incision was made with a flex knife (Flex Knife; KD-630L, Olympus, Optical Co, Ltd.) set to about 2 mm in length (Fig. 2) [2]. For this

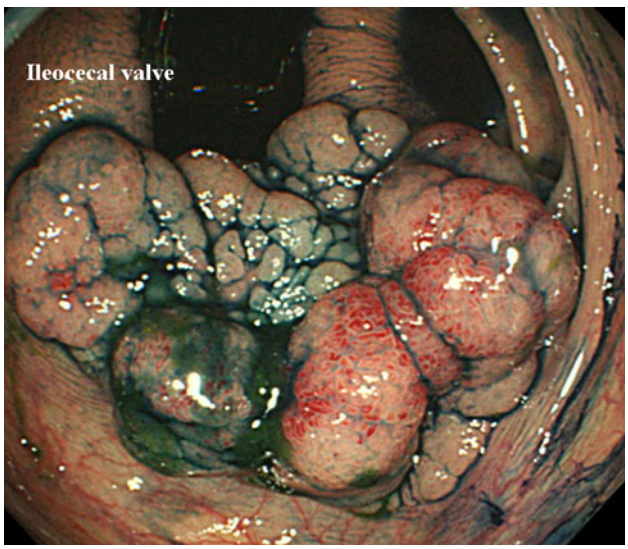

Fig. 1 Chromoendoscopy with 0.4% indigo carmine dye spraying showing a slightly elevated and sessile type (IIa + Is) neoplasia in the ileocecal region

Fig. 2 Flex knife

procedure, the electrosurgical generator output was set at 60 W of endocut mode, effect 2 in ICC200 or at duration 2 and interval 3 of endocut I, effect 1 in VIO300D. After an additional injection beneath the lesion to lift it apart from the muscularis propria sufficiently, the submucosal layer was dissected directly using the flex knife set to about 1 mm in length, with the electrosurgical generator output set at 20 W of forced coagulation mode in ICC200 or at 20 W of swift coagulation mode, effect 3 in VIO300D (Figs. 3, 4).

The hemostatic forceps (SDB2422; Pentax Co, Tokyo, Japan) was used to control bleeding during ESD treatment. The output of the electrosurgical generator was set at 60 W of soft coagulation mode in ICC200 or at 60 W of soft coagulation mode, effect 5 in VIO300D.

Histopathologic evaluation

The resectability of ESD specimens was carefully evaluated histopathologically by one pathologist in slices at

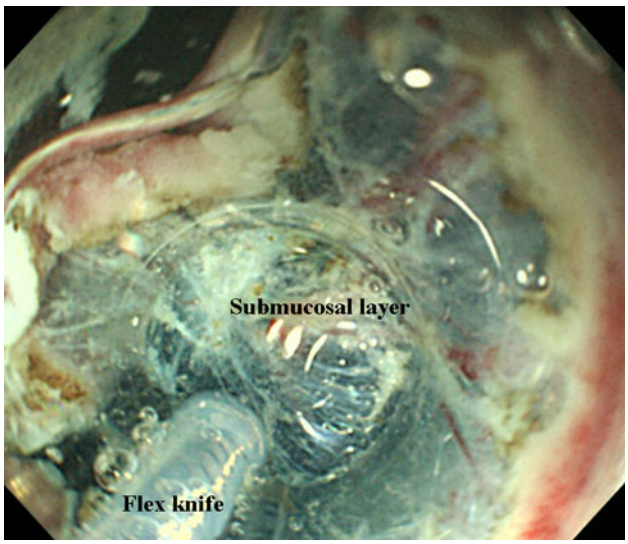

Fig. 3 Submucosal layer directly visualized endoscopically and dissected using the flex knife

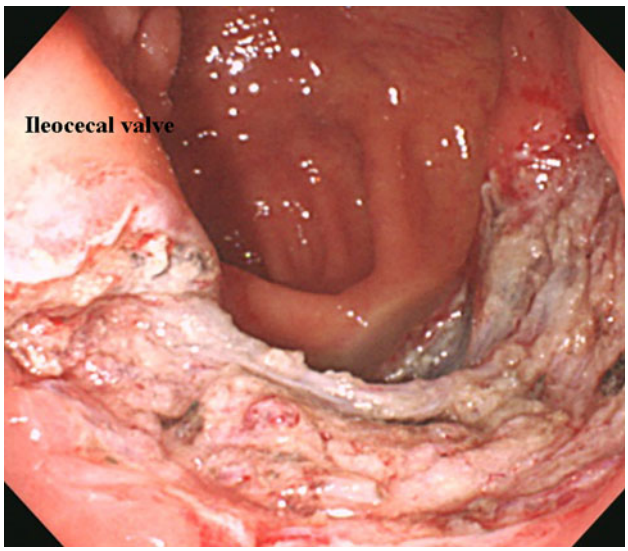

Fig. 4 Region after endoscopic submucosal dissection (ESD)

2-mm intervals according to the Vienna classification of epithelia neoplasia of the gastrointestinal tract [18]. They were examined microscopically for histopathologic type, depth of invasion, lateral and vertical resection margins, and lymph vascular involvement. En bloc resection was defined as resection of the entire lesion in a single piece and not piecemeal.

Curative resection (minimum probability of nodal and distant metastasis or local recurrence) was defined by four findings: (1) the lesion was resected in a single piece; (2) the histopathologic type was low- to high-grade dysplasia or well to moderately differentiated adenocarcinoma; (3) the neoplasia invasion was limited to that up to sm1 (a submucosal invasion of less than 1,000 μm below the muscularis mucosae) [19]; and (4) there was no lymph vascular or lateral or vertical margin involvement in the resected specimens.

The size of the neoplasias was determined histopathologically for the en bloc resected specimens and endoscopically for the piecemeal resected specimens. Patients with submucosal carcinoma that did not meet the curative criteria were recommended for additional surgery with lymph node dissection.

Follow-up evaluation

Colonoscopic examinations were performed 2, 6, and 12 months after ESD and every year thereafter to check for local recurrence and metachronous lesions. After the previously resected sites had been sprayed with 0.4% indigo carmine dye, they were evaluated by high-magnifying views. Computed tomography was performed for intramucosal carcinomas and submucosal carcinomas 6 and

12 months after ESD and every year thereafter to check for lymph node and distant metastasis.

Statistical analysis

All results are expressed as means ± standard deviation and range. To compare the size of the neoplasias, that of the resected specimens, and the procedural time, the mean value was statistically evaluated by a nonparametric Mann–Whitney *U* test. Statistical significance was defined as a p value less than 0.05.

Results

Patient characteristics

The clinicopathologic characteristics of the patients are presented in Table 1. Type 2a colorectal neoplasia was the most prevalent.

Clinical outcomes and clinical courses

The clinical outcomes of this study are presented in Table 2, and the study's clinical courses are summarized in Fig. 5. The mean size of the resected neoplasias and that of the resected specimens in ileocecal region did not differ significantly from those in the other two groups (colon and rectum neoplasias). The mean procedural time in the ileocecal region was longer than in the other two groups, although the difference was not significant.

The overall rate of en bloc resection was 91% (30/33). Histopathologic evaluation confirmed that both the lateral and vertical margins in the specimens resected en bloc were considered negative (30/30). The rate of en bloc resection in ileocecal region did not significantly differ from the rates in the other two groups ($p = 0.20$ compared with the values for the colon and $p = 0.12$ compared with values the values for the rectum). Histopathologic evaluation confirmed that these colorectal neoplasias consisted of four low-grade intraepithelial neoplasias, eight high-grade intraepithelial neoplasias, 18 intramucosal carcinomas (lamina propria invasion), and three submucosal carcinomas. Three intramucosal carcinomas were locally recurrent lesions treated with endoscopic mucosal resection (EMR) in prior hospitals. However, all three cases could be resected en bloc without any complications such as postoperative bleeding or perforation.

The overall rate of curative resection was 82% (28/33). The rate of curative resection for the ileocecal region was significantly lower than for the rectum ($p < 0.05$), but the difference was not significant compared with that for colon ($p = 0.33$).

Three submucosal carcinomas were resected en bloc, and histopathologic evaluation demonstrated that both the vertical and lateral margins were negative in the resected specimens. Although they were diagnosed as intramucosal carcinomas preoperatively, deep submucosal invasion was demonstrated in all three cases histopathologically (1,500, 1,700, and 2,000 μm below the muscularis mucosae, respectively), and lymph vascular involvement was demonstrated in the latter two cases. Because the three patients in these cases were elderly and had comorbid pulmonary disease, they did not receive additional surgery with lymph

Table 1 Clinicopathologic characteristics of 33 colorectal neoplasias

Sex (M/F)	20/13
Mean age: years (range)	66 ± 12 (42–89)
Mean follow-up period: months (range)	20 ± 12 (4–44)
Location: ileocecal region/colon/rectum	8/16/9
Macroscopic type: Is/IIa/IIa + Is/IIa + IIc	3/25/4/1

Is, sessile type; IIa, slightly elevated type; IIa + Is, slightly elevated and sessile type; IIa + IIc, slightly elevated and depressed type

Table 2 Results of endoscopic submucosal dissection (ESD)

	Overall ($n = 33$)	Ileocecal region ($n = 8$)	Colon ($n = 16$)	Rectum ($n = 9$)
Mean neoplasis size: mm (range)	35 ± 15 (20–80)	41 ± 13 (26–60)	33 ± 16 (20–80)	34 ± 16 (20–58)
Mean resected specimen size: mm (range)	41 ± 15 (23–82)	45 ± 11 (31–61)	38 ± 17 (23–82)	40 ± 14 (25–65)
Mean procedural time: min (range)	121 ± 90 (22–420)	142 ± 81 (45–270)	110 ± 73 (32–305)	122 ± 126 (22–420)
En bloc resection rate: % (n)	91 (30/33)	75 (6/8)	94 (15/16)	100 (9/9)
Histpathologic type (LGIEN/HGIEN/IMC/SMC)	4/8/18/3	1/2/4/1	3/4/7/2	0/2/7/0
Lymph vascular involvement (negative/positive)	31/2	7/1	15/1	9/0
Curative resection rate: % (n)	82 (27/33)	63 (5/8)	81 (13/16)	100 (9/9)[a]
Perforation (penetration): % (n)	3 (1/33)	0 (0/8)	6 (1/16)	0 (0/9)
Postoperative bleeding: % (n)	3 (1/33)	0 (0/8)	6 (1/16)	0 (0/9)

LGIEN, low-grade intraepithelial neoplasia; HGIEN, high-grade intraepithelial neoplasia; IMC, intramucosal carcinoma (lamina propria invasion); SMC, submucosal carcinoma

[a] $p < 0.05$ compared with values of the ileocecal region

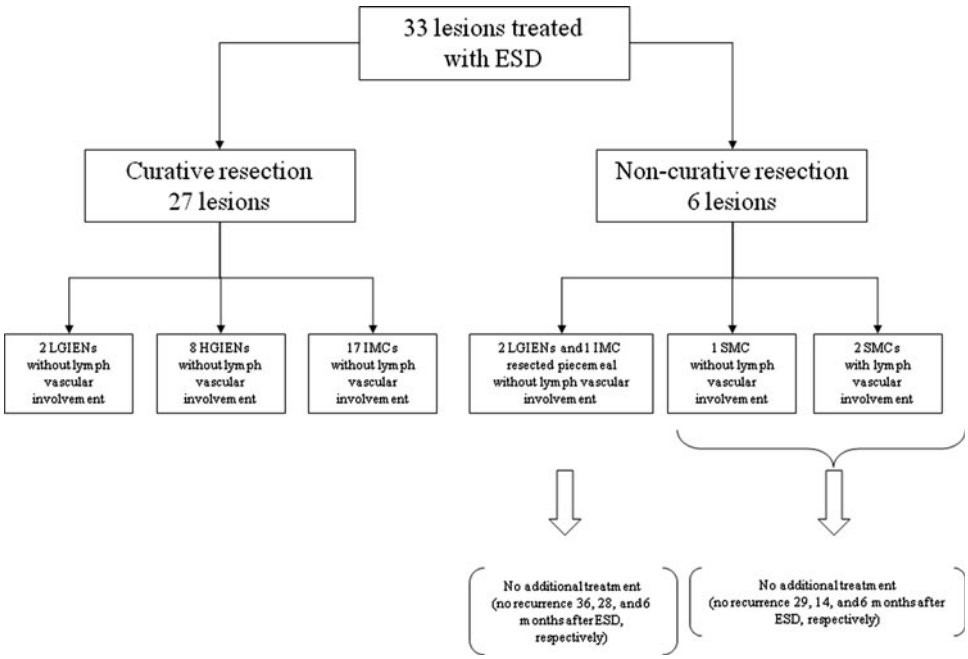

Fig. 5 Clinical courses of superficial colorectal neoplasias after endoscopic submucosal dissection (ESD)

node dissection because of their decisions. No recurrence was observed during 29, 14, and 6 months of follow-up evaluation after ESD treatment, respectively.

Penetration toward the mesenterium occurred in one sigmoid colon case (3%). Because endoscopic closure with endoclips was performed, the amount of intraperitoneal air was small, as shown on computed tomography, and abdominal pain hardly occurred after ESD. This case could be conservatively managed by medical treatment, and neither laparoscopy nor emergent surgery was needed.

Postoperative bleeding occurred in one ascending colon case (3%) 6 h after ESD. This complication was successfully managed by endoscopic hemostasis with endoclips. No recurrence was observed in any of the cases during the mean follow-up period of 20 ± 12 months (range, 4–44 months).

Discussion

Endoscopic mucosal resection is indicated for the treatment of early-stage gastrointestinal neoplasias, which show a low frequency of lymph node and distant metastasis [20–25]. Since EMR is inadequate for en bloc resection of large superficial colorectal neoplasias (diameter, >20 mm) and neoplasias with submucosal infiltration or fibrosis caused by prior EMR, local recurrence is frequently observed [25, 26]. Some authors have suggested that incomplete EMR for colorectal carcinomas may accelerate growth of the remaining carcinoma and promote metastasis [27, 28]. Therefore, en bloc resection is desirable.

Recently, ESD has been applied to colorectal neoplasias because it provides a higher en bloc resection rate and is less invasive than surgical resection [1–4]. In our study, the overall rate of en bloc resection was 91% (30/33), which was as high as the rates in recent two reports (84% and 91.5%, respectively) [3, 4]. Because the horizontal margin of neoplasias and the submucosal layer beneath the neoplasia could be directly visualized during the procedures and ESD could provide adequate thickness of mucosa and submucosa, both the lateral and vertical margins in the specimens resected en bloc all were negative histopathologically (30/30). With the ESD technique, the neoplasias extending beyond sm1 (1,000 μm below the muscularis mucosae) could be resected en bloc with pathologically free margins, although the number of these neoplasias was small in our study. The rate of en bloc resection for the ileocecal region did not significantly differ from that for the other two groups (colon and rectum neoplasias), although it is possible that if more cases had been included, the en bloc resection rate would have proved to be significantly lower for the neoplasias located in the ileocecal region. In our study, the rate of curative resection for ileocecal region was significantly lower than for the rectum. In the ileocecal region group, one submucosal carcinoma that extended beyond sm1 was included, but not in rectal group. That could have had an impact on this result.

On the other hand, the ESD technique has disadvantages such as a longer procedural time and a higher complication rate. Although it is true that the procedural time was long in our study (the mean operative time was 121 ± 90 min), the rate of en bloc resection was high for large superficial

colorectal neoplasias including neoplasias of the ileocecal region (91%), and no recurrence was observed in any of the cases. Moreover, the mean procedural time for the ileocecal region was not significantly different from that for other two groups.

During colorectal ESD, perforation can easily occur if the tip of the knife comes into contact with the floor of the ulcer because the wall of the colon is thinner than that of stomach, and its muscular layers are sparse. Therefore, safer procedures are required for colorectal ESD. Saito et al. [3] and Fujishiro et al. [4] reported that almost all perforations were diagnosed during ESD procedures and could be managed by endoscopic closure with endosclips, although the incidence of perforation associated with ESD (4–5%) was higher than for conventional EMR.

In our study, penetration toward the mesenterium occurred during dissection of the submucosal layer in one sigmoid colon case (3%). However, it could be conservatively managed by medical treatment after endoscopic closure with endoclips, as described in previous reports, and emergent surgery was not needed.

In this study, we applied a combination of flex knife and small-caliber-tip transparent hood to colorectal ESD such as esophageal ESD [29]. The flex knife has special features [2]. It is easy to handle in any direction—vertically, horizontally, or diagonally. It is soft and has a unique looped shape to minimize the possibility of tissue perforation. The length of the knife tip is adjustable so that the distance and depth of mucosal incision and submucosal dissection can be controlled precisely.

By using a small-caliber-tip transparent hood in our study, the knife was set in the center of the lumen so that it was easier to handle in any direction during both mucosal incision and submucosal dissection without rotating the endoscope. While performing submucosal dissection, we could obtain a clear field of the submucosal tissue and control bleeding easily by using a small-caliber-tip transparent hood. Thus, severe complications such as perforation and intolerable bleeding during ESD treatment could be minimized even in the ileocecal region.

The ileocecal valve has two functions: to prevent regurgitation of material from the cecum into the ileum and to delay passage of ileal contents into the cecum, allowing more time for digestion and absorption of foodstuffs to occur in the ileum [5–8]. Bile acids absorbed in the terminal ileum are essential to an intact enterohepatic cycle and lipid digestion. Therefore, malabsorption and diarrhea sometimes occur, causing the quality of life for the patients to decrease after ileocecal resection.

Complete resection using standard EMR technique in the ileocecal area is much more difficult, especially for larger lesions, and surgical treatment is sometimes required in the case of incomplete resection. By applying ESD for the treatment of large superficial neoplasias in our study, the ileocecal valve could be preserved in all cases involving the ileocecal region without any complications.

Several studies have demonstrated that lymph node metastasis in cases of submucosal carcinomas is closely associated with the depth of submucosal invasion, the poor differentiation, lymph vascular invasion, and tumor budding [19, 30–32]. Ueno et al. [32] reported that the nodal involvement was extremely low (0.7%) in cases of submucosal carcinomas without an unfavorable tumor grade, vascular invasion, tumor budding, or extensive submucosal invasion (width exceeding 4,000 μm or depth exceeding 2,000 μm), and proposed a wait-and-see policy after sufficient resection of these carcinomas. Hence, an expanded indication of endoscopic treatment for these submucosal carcinomas can be considered. To that end, en bloc resection is needed to evaluate tumor grade, the extent of submucosal invasion, lymph vascular involvement, and tumor budding in the resected specimens. Because ESD improves the completeness of en bloc resection of large colorectal neoplasias including the neoplasias of the ileocecal region, provides adequate thickness of the mucosa and the submucosa, and is less invasive than surgical resection, it may be considered the treatment of choice for these submucosal carcimonas, especially for patients with comorbid diseases.

Although the number of patients who underwent ESD and the follow-up periods was limited in the current study, ESD with a combination of small-caliber-tip transparent hood and flex knife is safe and effective for the treatment of large superficial neoplasias in the ileocecal region such as other colorectal neoplasias.

Disclosures Drs. Naoki Ishii, Toshiyuki Itoh, Noriyuki Horiki, Michitaka Matsuda, Takeshi Setoyama, Shoko Suzuki, Masayo Uemura, Yusuke Iizuka, Katsuyuki Fukuda, Koyu Suzuki, and Yoshiyuki Fujita have no conflicts of interest or financial ties to disclose.

References

1. Yamamoto H, Kawata H, Sunada K, Sasaki A, Nakazawa K, Miyata T, Sekine Y, Yano T, Satoh K, Ido K, Sugano K (2003) Successful en bloc resection of large superficial tumors in the stomach and colon using sodium hyaluronate and small-caliber-tip transparent hood. Endoscopy 35:690–694
2. Yahagi N, Fujishiro M, Imagawa A, Kakushima N, Iguchi M, Omata M (2004) Endoscopic submucosal dissection for the reliable en bloc resection of colorectal mucosal tumors. Dig Endosc 16:89–92
3. Saito Y, Uraoka T, Matsuda T, Emura F, Ikehara H, Mashimo Y, Kikuchi T, Fu KI, Sano Y, Saito D (2007) Endoscopic treatment of large superficial colorectal tumors: a case series of 200 endoscopic submucosal dissections (with video). Gastrointest Endosc 66:966–973

4. Fujishiro M, Yahagi N, Kakushima N, Kodashima S, Muraki Y, Ono S, Yamamichi N, Tateishi A, Oka M, Kawabe T, Ichinose M, Omata M (2007) Outcomes of endoscopic submucosal dissection for colorectal epithelial neoplasms in 200 consecutive cases. Clin Gastroenterol Hepatol 5:678–683
5. Sako K, Blackman GE (1962) The use of a reversed jejunal segment after massive resection of the small bowel: an experimental study. Am J Surg 103:202–205
6. Hofmann AF, Poley JR (1972) Role of bile acid malabsorption in pathogenesis of diarrhea and steatorrhea in patients with ileal resection: I. Response to cholestyramine or replacement of dietary long chain triglyceride by medium chain triglyceride. Gastroenterology 62:918–934
7. Cosnes J, Gendre JP, Le Quintrec Y (1978) Role of the ileocecal valve and site of intestinal resection in malabsorption after extensive small bowel resection. Digestion 18:329–336
8. Mitchell JE, Breuer RI, Zuckerman L, Berlin J, Schilli R, Dunn JK (1980) The colon influences ileal resection diarrhea. Dig Dis Sci 25:33–41
9. Kudo S, Tamura S, Nakajima T, Yamano H, Kusaka H, Watanabe H (1996) Diagnosis of colorectal timorous lesions by magnifying endoscopy. Gastrointest Endosc 44:8–14
10. Kudo S, Kashida H, Tamura T, Kogure E, Imai Y, Yamano H, Hart AR (2000) Colonoscopic diagnosis and management of nonpolypoid early colorectal cancer. World J Surg 24:1081–1090
11. Kudo S, Rubio CA, Teixeira CR, Kashida H, Kogure E (2001) Pit pattern in colorectal neoplasia: endoscopic magnifying view. Endoscopy 33:367–373
12. Group Endoscopic Classification Review (2005) Update on the Paris classification of superficial neoplastic lesions in the digestive tract. Endoscopy 37:570–578
13. Gotoda T, Yanagisawa A, Sasako M, Ono H, Nakanishi Y, Shimoda T, Kato Y (2000) Incidence of lymph node metastasis from early gastric cancer: estimation with a large number of cases at two large centers. Gastric Cancer 3:219–225
14. Yamamoto H, Yube T, Isoda N, Sato Y, Sekine Y, Higashizawa T, Ido K, Kimura K, Kanai N (1999) A novel method of endoscopic mucosal resection using sodium hyaluronate. Gastrointest Endosc 50:251–256
15. Ono H, Kondo H, Gotoda T, Shirao K, Yamaguchi H, Saito D, Hosokawa K, Shimada T, Yoshida S (2001) Endoscopic mucosal resection for treatment of early gastric cancer. Gut 48:225–229
16. Neuhaus H, Costamagna G, Deviere J, Fockens P, Ponchon T, Rosch T (2006) Endoscopic submucosal dissection (ESD) of early neoplastic gastric lesions using a new double-channel endoscope (the "R-scope"). Endoscopy 38:1016–1023
17. Yamamoto H, Yahagi N, Oyama T, Gotoda T, Doi T, Hirasaki S, Shimoda T, Sugano K, Tajiri H, Takakoshi T, Saito D (2008) Usefulness and safety of 0.4% sodium hyaluronate solution as a submucosal fluid "cushion" in endoscopic resection for gastric neoplasms: a prospective multicenter trial. Gasrtointest Endosc 67:830–839
18. Stolte M (2003) The new Vienna classification of epithelia neoplasia of gastrointestinal tract: advantages and disadvantages. Virchows Arch 442:99–106
19. Kitajima K, Fujimori T, Fujii S, Takeda J, Ohkura Y, Kawamata H, Kumamoto T, Ishiguro S, Kato Y, Shimoda T, Iwashita A, Ajioka Y, Watanabe H, Watanabe T, Muto T, Nagasako K (2004) Correlations between lymph node metastasis and depth of submucosal invasion in submucosal invasive colorectal carcinoma: a Japanese collaborative study. J Gastroenterol 39:534–543
20. Tada M, Murakami A, Karita M, Yanai H, Okita K (1993) Endoscopic resection of early gastric cancer. Endoscopy 25:445–450
21. Inoue H, Tani M, Nagai K, Kawano T, Takeshita K, Endo M, Iwai T (1999) Treatment of esophageal and gastric tumors. Endoscopy 31:47–55
22. Kudo S (1993) Endoscopic mucosal resection of flat and depressed types of early colorectal cancer. Endoscopy 25:455–461
23. Yokota T, Sugihara K, Yoshida S (1994) Endoscopic mucosal resection for colorectal neoplastic lesions. Dis Colon Rectum 37:1108–1111
24. Ahmad NA, Kochman ML, Long WB, Furth EE, Ginsberg GG (2002) Efficacy, safety, and clinical outcomes of endoscopic mucosal resection: a study of 101 cases. Gastrointest Endosc 55:390–396
25. Walsh RM, Ackroyd FW, Shellito PC (1992) Endoscopic resection of large sessile colorectal polyps. Gastrointest Endosc 38:303–309
26. Tanaka S, Oka S, Kaneko I, Hirata M, Mouri R, Kanao H, Yoshida S, Chayama K (2007) Endoscopic submucosal dissection for colorectal neoplasia: possibility of standardization. Gastrointest Endosc 66:100–107
27. Hackelsberger A, Fruhmorgen P, Weiler H, Heller T, Seeliger H, Junghanns K (1995) Endoscopic polypectomy and management of colorectal adenomas with invasive carcinoma. Endoscopy 27:153–158
28. Kawamura YJ, Sugamata Y, Yoshino K, Abo Y, Nara S, Sumita T, Setoyama R, Kiribuchi Y, Kawano N (1999) Endoscopic resection for submucosally invasive colorectal cancer: is it feasible? Surg Endosc 13:224–227
29. Ishii N, Horiki N, Itoh T, Uemura M, Maruyama M, Suzuki S, Uchida S, Izuka Y, Fukuda K, Fujita Y (2009) Endoscopic submucosal dissection with a combination of small-caliber-tip transparent hood and flex knife is a safe and effective treatment for superficial esophageal neoplasias. Surg Endosc. doi: 10.1007/s00464-009-0560-x
30. Nascimbeni R, Burgart LJ, Nivatvongs S, Larson DR (2002) Risk of lymph node metastasis in T1 carcinoma of the colon and rectum. Dis Colon Rectum 45:200–206
31. Sakuragi M, Togashi K, Konishi F, Koinuma K, Kawamura Y, Okada M, Nagai H (2003) Predictive factors for lymph node metastasis in T1 stage colorectal carcinomas. Dis Colon Rectum 46:1626–1632
32. Ueno H, Mochizuki H, Hashiguchi Y, Shimazaki H, Aida S, Hase K, Matsukuma S, Kanai T, Kurihara H, Ozawa K, Yoshimura K, Bekku S (2004) Risk factors for an adverse outcome in early invasive colorectal carcinoma. Gastroenterology 127:385–394