Surg Endosc
DOI 10.1007/s00464-012-2403-4

Endoscopic submucosal dissection for colorectal tumors—1,000 colorectal ESD cases: one specialized institute's experiences

Eun-Jung Lee · Jae Bum Lee · Suk Hee Lee · Do Sun Kim · Doo Han Lee · Doo Seok Lee · Eui Gon Youk

Received: 13 March 2012 / Accepted: 17 May 2012

Abstract
Purpose Endoscopic submucosal dissection (ESD) is a very useful endoscopic technique, making it possible to perform en bloc resection regardless of lesion size. Since the introduction of ESD at our hospital, we have performed 1,000 colorectal ESDs during 56 months. The purpose of this study was to evaluate the clinical outcomes of our colorectal ESD experience and to access the efficacy and safety of colorectal ESD.
Methods Between October 2006 and August 2011, we performed ESD on 1,000 consecutive colorectal tumors in 966 patients. We evaluated the clinical outcomes of all said cases.
Results The mean resected tumor size was 24.1 ± 13.3 (3–145) mm. Our overall endoscopic en bloc resection rate was 97.5 % (975/1,000), and our R0 resection rate was 91.2 % (912/1,000) respectively. Our perforation rate was 5.3 % (53/1,000). Of these 53 perforations, 50 cases were treated through conservative management with/without endoscopic clipping, whereas the remaining 3 patients received laparoscopic operation. Pathological examination showed adenocarcinoma in 37.2 % of cases (372/1,000) and neuroendocrine tumors in 11.2 % (112/1,000). We recommended additional radical surgery to 82 patients who had a risk of lymph node metastasis. Follow-up colonoscopies were performed on 722 patients. During the median follow-up period of 13 (1–62) months, there were three recurrences (0.4 %).
Conclusions ESD is technically difficult, with a substantial risk of perforation. However, ESD enabled en bloc resection and pathologically complete resection of large colorectal epithelial tumors and submucosal tumors. As experience with the technique increases, ESD may gradually replace piecemeal endoscopic mucosal resection and radical colon resection in the treatment of colorectal tumors.

Keywords Colorectal · Cancer · Polyps · G-I · Endoscopy

Endoscopic mucosal resection (EMR) is a useful therapeutic technique for colorectal tumors. However, for large tumors, the chance of piecemeal resection is high. If the tumor is resected using piecemeal methods, precise pathological evaluation is difficult. In this case, the risk of residual tumor requires additional operations. In addition, local recurrence rates are very high (5–45 %) [1, 2].

Endoscopic submucosal dissection (ESD) was originally developed for the resection of early gastric cancer [3], yet more recently has been used to perform resection of colorectal tumors [4]. This enables en bloc resection regardless of the size of the tumor. However, the technique is very difficult, and the risk of perforation is high (5–14 %), making ESD less popular than EMR for the treatment of colorectal tumors [4, 5].

We adopted electrosurgical knives in October 2006 and performed EMR-P (EMR-precutting) as a step toward familiarity with the ESD procedure [6]. After some improvement in the skills needed to use the electrosurgical

Presented at the SAGES 2012 Annual Meeting, March 7–March 10, 2012, San Diego, CA.

E.-J. Lee · J. B. Lee · D. S. Kim · D. H. Lee · D. S. Lee · E. G. Youk (✉)
Department of Surgery, Daehang Hospital, 481-10 Bangbae Seocho, Seoul 137-820, Korea
e-mail: ejlee@daehang.com

S. H. Lee
Department of Pathology, Daehang Hospital, Seoul, Korea

Published online: 23 June 2012

knives, we began performing the ESD procedure for colorectal tumors in May 2007 more consistently. Since October 2006, we have performed more than 1,000 colorectal ESD cases. This study was designed to analyze the outcome of our colorectal ESD cases and to assess the efficacy and safety of colorectal ESD.

Patients and methods

Inclusion and exclusion criteria for ESD

Between October 2006 and August 2011, 966 consecutive patients with a total of 1,000 colorectal tumors were enrolled. We included all colorectal tumors without stalk that were endoscopically estimated to be 20 mm or larger. We also included colorectal tumors that were smaller than 20 mm and expected to be impossible to resect by using the en bloc method due to fibrosis and difficulty involved with the location of the tumor. Giant or oversized, pedunculated colorectal polyps with large stalks and submucosal tumors also were included. We also performed ESD for recurrent or residual tumors after endoscopic treatment.

We excluded strongly suspected "massive" submucosal invasive cancers after chromoendoscopy and submucosal injection. The endoscopic characteristics of massive submucosal invasion were reported to be consistency, an expansive appearance, fold convergency, ulceration, surface irregularity, spontaneous bleeding, type V_N (nonstructural) pit pattern, etc. [7–10]. Another indication for not performing ESD is the presence of a nonlifting sign. A positive nonlifting sign suggests massive submucosal or proper muscle invasion and makes resection technically difficult or impossible [11, 12]. We excluded strongly suspected massive submucosal invasive cases that had the presence of either previously mentioned endoscopic characteristics or a positive nonlifting sign for ESD.

ESD procedures

Adequate cleansing of the whole colorectum was conducted before performing endoscopic treatment, and the patients were restricted to a low-fiber diet the day before the procedure (Fig. 1). The patients ingested 4 liters of polyethylene glycol solution (Colyte Powder, Taejoon Pharm, Seoul, Korea) or 90 ml of oral sodium phosphate solution (Fleet Phospho-soda, C.B. Fleet Company, Lynchburg, USA) before each procedure to achieve good bowel preparation. We chose each solution according to the patient's age and their hepatic and renal functions.

ESD procedures were performed by one of four endoscopists (EJL, JBL, DSL, EGY) who are highly experienced in diagnostic and therapeutic colonoscopy. Individually, they have each performed at least 7,000 diagnostic colonoscopies and are highly experienced in therapeutic procedures, such as EMR.

ESD was performed by using a single-channel HD colonoscope (Olympus CF-H260AI, Olympus Optical Co., Tokyo, Japan) and a high-frequency generator with an automatically controlled system, VIO300. A transparent attachment (D-201-13404 or D-201-14304; Olympus Optical Co, Ltd.) was used to apply tension to the connective tissue for submucosal dissection. We used a CO_2 insufflation system to reduce any discomfort the patient may have experienced during ESD and to promote the absorption of leaked air from perforation.

We used a mixed solution of hyaluronic acid [13] (sodium hyaluronate injection, Huons, Seoul, Korea), glycerol (Cerol injection, Choongwae Pharma Co., Seoul, Korea), epinephrine, and indigo carmine for submucosal injection. After the tumor was lifted, a mucosal incision was made with the tip of a flex knife (from October 2006) or dual knife (from July 2011). We adjusted the tip of the flex knife or dual knife to a length of only 1–2 mm and gently pressed onto the mucosa to produce a cutting effect using Endocut I or dry cut mode. The distal one-third of the mucosa was incised first, and submucosal trimming was performed for the introduction of the attachment between the tumor and the muscle layer. After trimming, we dissected the submucosal layer with a flex or dual knife using forced or swift coagulation mode. In situations in which dissection was difficult and the risk of muscular injury was high, we used a hook knife (Olympus KD-620LR). To control bleeding, hemostatic forceps, such as a Coagrasper (Olympus FD-410LR), were used in soft coagulation mode (output 80 W). Then, an additional mucosal incision to the proximal part was performed, and an additional submucosal dissection was done. To prevent leakage of submucosal solution, circumferential mucosal incisions were staggered with submucosal dissection until the tumor was completely resected. After resection of the tumor, visible vessels in the exposed layer were treated with a Coagrasper in soft coagulation mode [14, 15].

All procedures were performed in the inpatient setting, and unless complications occurred, the length of stay was 2 or 3 days.

Informed, written consent from all patients for each specific colonoscopic treatment and all scheduled follow-up examinations were received by clinicians.

Complications

Perforation was diagnosed endoscopically or by the presence of free air on an abdominal plain radiograph or by

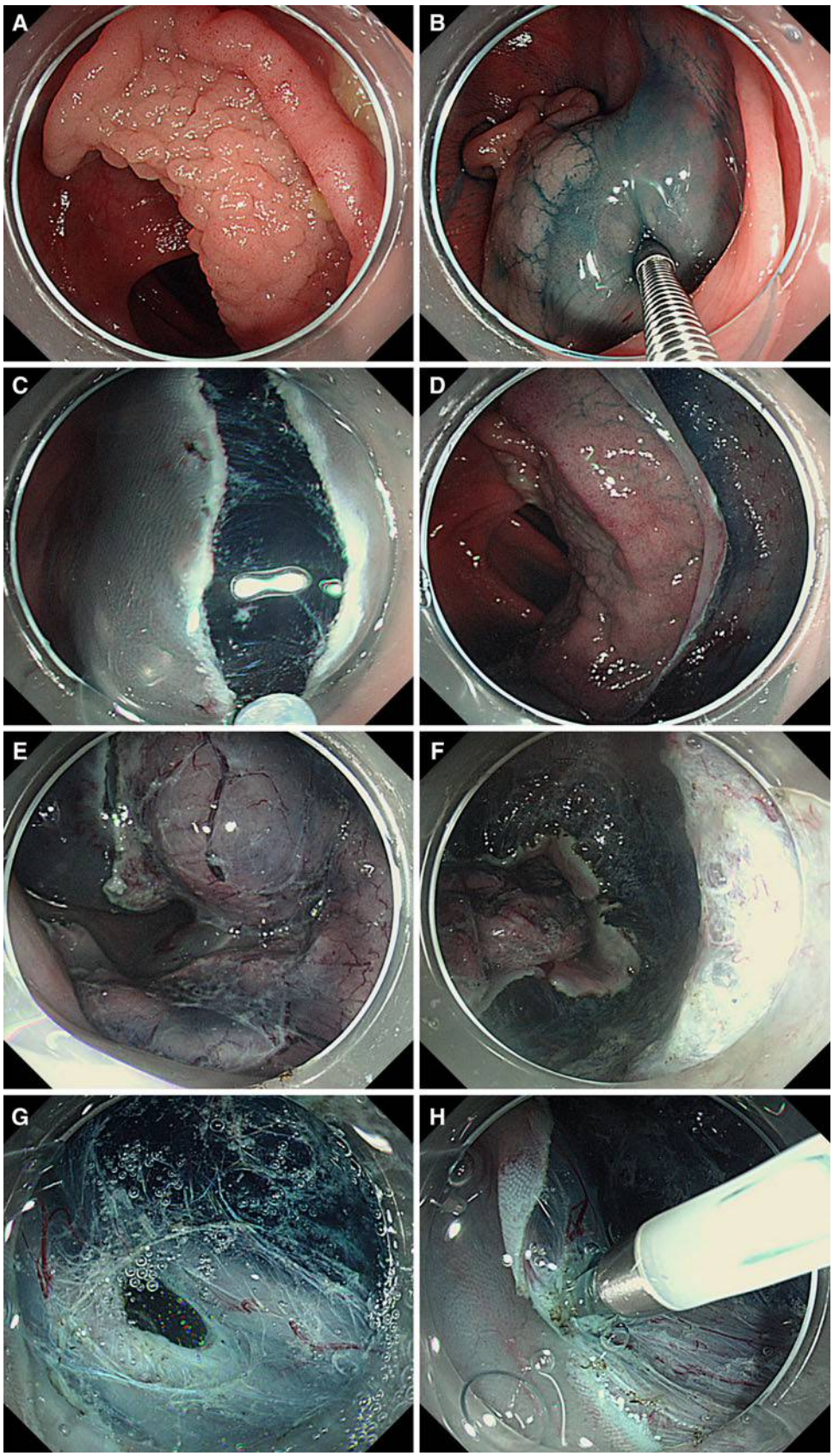

Fig. 1 ESD procedure for a 95-mm LST on the ascending colon of a 55-year-old woman. **a** 95-mm–sized laterally spreading tumor in the ascending colon. The tumor is encircling 60 % of the lumen. **b** Submucosal injection with hyaluronic acid. **c** Mucosal incision with a Flex knife. **d** Submucosal dissection. **e** The end point of submucosal dissection. **f** Approximately 70 % of the whole circumference was resected. **g** Minor bowel injury. **h** The injured bowel was repaired by endoscopic clipping

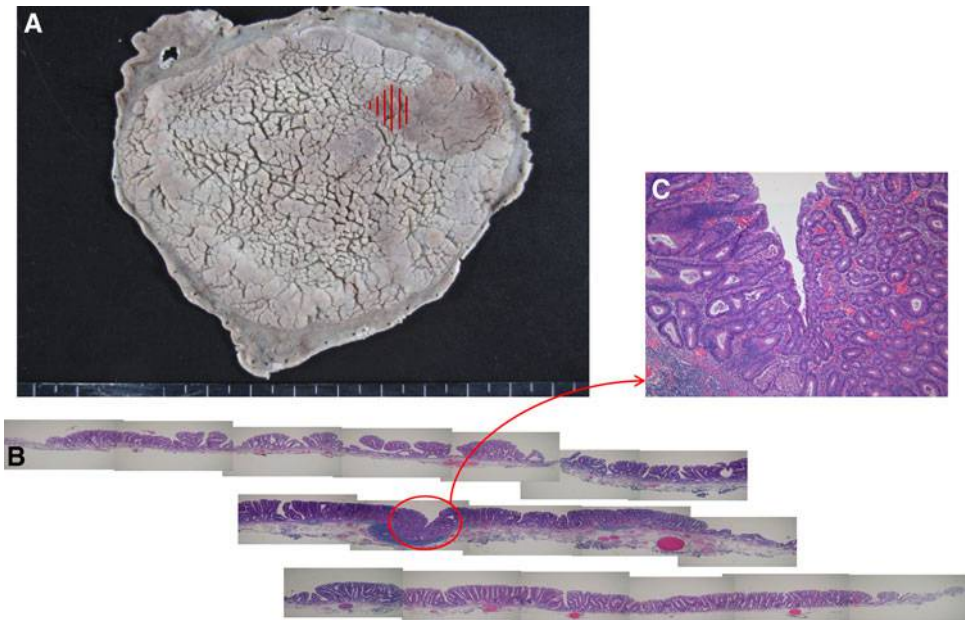

Fig. 2 Pathological examination of the Fig. 1 case. **a** The specimen was fixed with formalin and sliced in 2–2.5 mm intervals. Red lines indicate the adenocarcinoma after mapping. **b** Images arranged in line (hematoxylin and eosin [H&E] stain). **c** Adenocarcinoma was confined in the mucosal layer (H&E stain, x200)

computed tomography. Delayed perforation was defined as occurring after completion of the ESD procedure [16]. Delayed bleeding was defined as hematochezia or melena in the patient after completion of ESD that required endoscopic hemostasis or transfusions.

Pathological evaluation

We defined "en bloc resection" as the one-piece resection of an entire lesion as observed endoscopically (Fig. 2) [16]. All specimens were evaluated after being cut into 2- to 2.5-mm slices and examined microscopically for histological type, depth of invasion, lateral (mucosal) resection margin, and basal (submucosal) resection margin. Extension of tumor cells to the resected margin was evaluated as complete (R0) resection with the lateral and basal resection margins free of tumor (en bloc resection is essential), incomplete (R1) resection when the tumor extended into the lateral or basal margins, or not evaluable (Rx) when the margins were not evaluable as a result of the artificial effects of coagulation necrosis or multipiece resection [17]. We also evaluated differentiation, lymphatic invasion, vascular involvement, and tumor budding. We measured the submucosal invasion depth according to the previous report [18]. When the submucosal invasion depth is less than 1,000 μm from muscularis mucosae for nonpedunculated tumors and 3,000 μm for pedunculated tumors, we use the definition "minimal submucosal invasion." When submucosal invasion depth is 1,000 μm or deeper than 1,000 μm for nonpedunculated tumors and 3,000 μm for pedunculated tumors, we use the definition "massive submucosal invasion" [18]. When the tumor showed massive submucosal invasion or had unfavorable pathological risk factors related to lymph node metastasis (i.e., lymphovascular invasion, poor differentiation, or tumor budding), we recommended surgical resection accompanied with lymph node dissection. Pathological diagnoses were based on the Vienna classification.

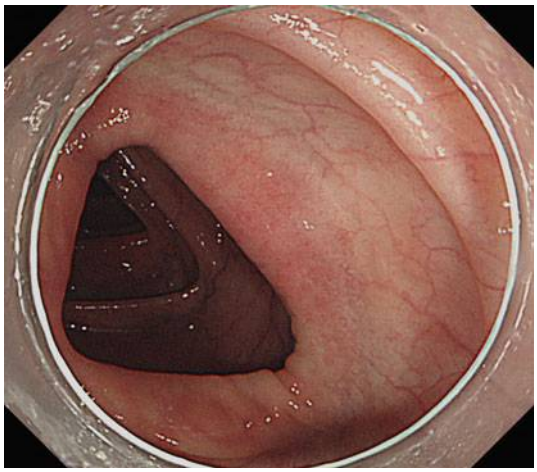

Fig. 3 Follow-up colonoscopy after 6 months. The case in Fig. 2 shows complete healing and no stricture. There was no evidence of recurrence

Follow-up

Follow-up colonoscopies were performed once every 6–12 months during the first year after the procedure and once every year thereafter to assess local recurrence (Fig. 3). We sprayed indigo carmine dye on ESD scars and evaluated them for any recurrence. If a recurrence was

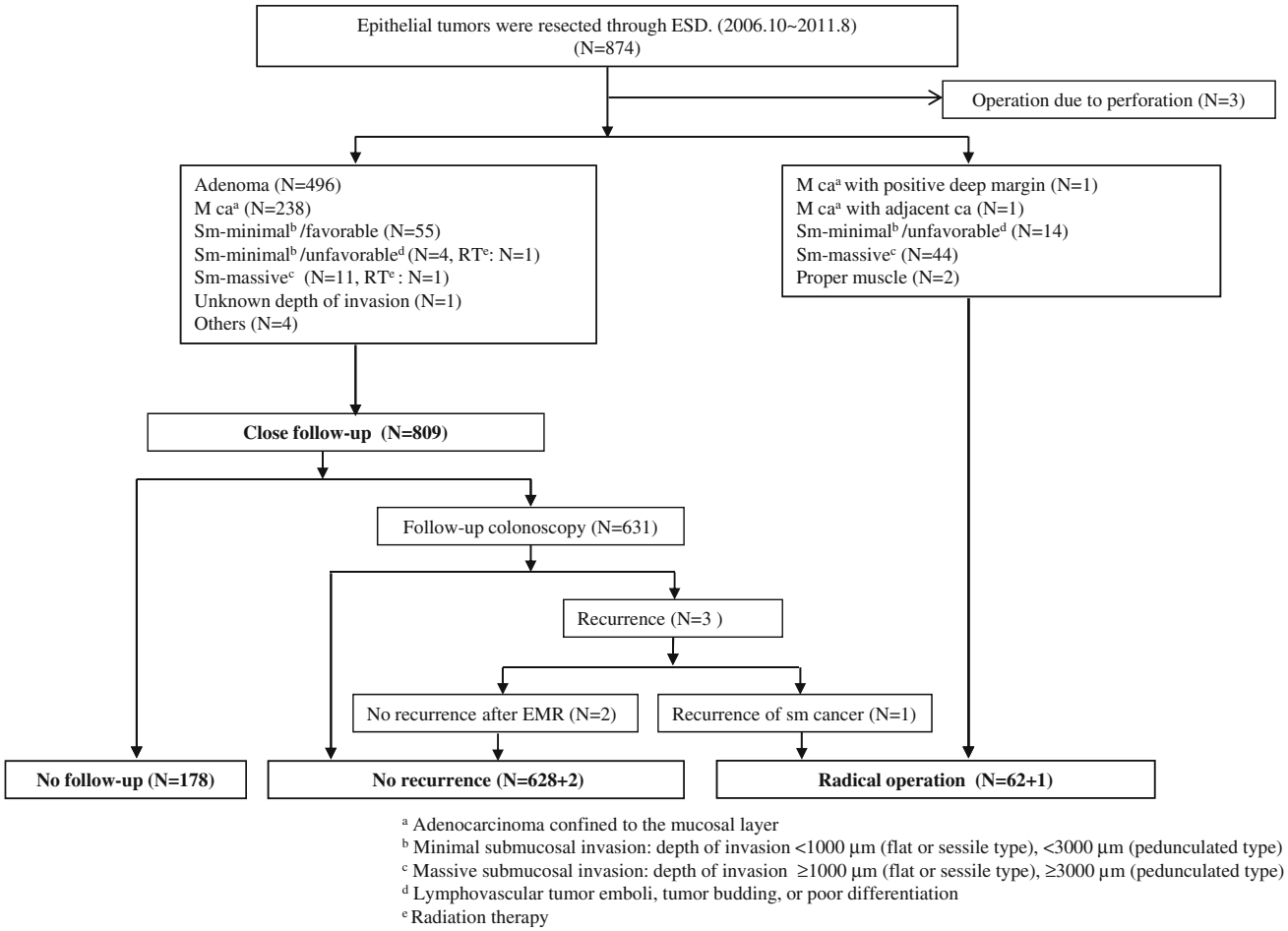

Fig. 4 Flow chart shows patient's clinical course after endoscopic submucosal dissection for colorectal epithelial tumors

suspected, we confirmed our findings through biopsy. The flowcharts of Figs. 4 and 5 show a patient's clinical course after ESD.

Results

We divided all patients into two groups: epithelial tumors and submucosal tumors. Tables 1 and 2 show patient demographics and clinicopathological outcomes of colorectal ESD according to the two respective groups. In epithelial tumors, 437 cases (50 %) were located in the right colon and 181 cases (20.7 %) in the rectum. According to the gross morphology, 617 cases (70.6 %) were laterally spreading tumors (LST). Among LSTs, 278 cases were nongranular types and 339 cases were granular types. Of submucosal tumors, 90.5 % were located in the rectum. Among 1,000 cases, 20 residual tumors and 4 recurrent tumors were included.

The mean resected tumor size was 24.1 ± 13.3 (range, 3–145) mm. The mean size of the epithelial tumors was 26.5 ± 12.3 (range, 5–145) mm, whereas the mean size of the submucosal tumors was 7.1 ± 4.7 (range, 3–50) mm. Our overall endoscopic en bloc resection rate was 97.5 % (975/1,000) and R0 resection rate was 91.2 % (912/1,000), respectively.

Our perforation rate was 5.3 % (53/1,000). For 50 patients, perforation was treated by conservative management with or without endoscopic clipping; the other three patients received laparoscopic surgery. There was no delayed perforation. There were four cases of delayed bleeding, and all cases were managed with conservative treatment, such as endoscopic clipping or soft coagulation with a Coagrasper. No case required transfusion or surgical intervention. The complications of each group are presented in Table 3 separately. There was no complication in the submucosal tumor group.

Pathological examination showed adenocarcinoma in 37.2 % of cases (372/1,000). There were 112 neuroendocrine tumors (NET; i.e., carcinoid tumors) among 126 submucosal tumors. The mean size of NETs was 6.4 ± 2.0 (range, 3–13) mm. We immediately recommended radical operation for the NET cases whose size was 10 mm or larger. Our data included seven NET cases of which the

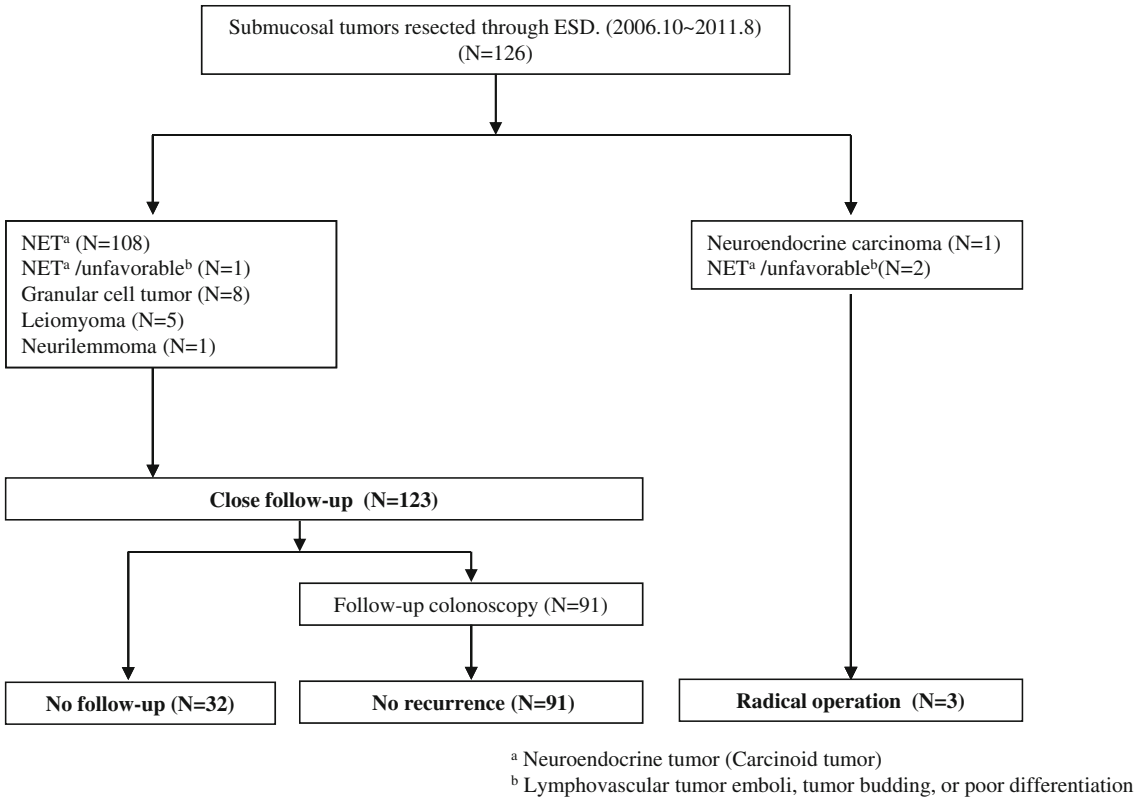

Fig. 5 Flow chart shows patient's clinical course after endoscopic submucosal dissection for colorectal submucosal tumors

sizes were between 10 mm and 13 mm. These patients refused radical operation in place of ESD procedure.

We recommended additional surgical resection accompanied with lymph node dissection to 82 patients who had risk of lymph node metastasis. These included mucosal cancer with uncertain margin (1 case), mucosal cancer with adjacent submucosal cancer (1 case), minimal submucosal invasion with unfavorable pathology (18 cases), unknown depth of submucosal invasion (1 case), massive submucosal invasion (55 cases), invasion to proper muscle (2 cases), neuroendocrine carcinoma (1 case), and NET with unfavorable pathology (3 cases). Among those 82 cases, 65 received radical operations. Two patients received radiation therapy. The other patients chose close follow-up. Among the 65 cases who received radical operations, lymph node metastasis was found in 7 cases.

Follow-up colonoscopies were performed on 722 patients. During the median follow-up period of 13 (range, 1–62) months, there were three recurrences (0.4 %). The first case was a 25-mm-sized nongranular type LST (sessile serrated adenoma) and was resected on a piecemeal basis because of perforation. At the follow-up colonoscopy 6 months after ESD, the tumor recurred as a small sessile serrated adenoma on the ESD scar. The second case was a 3-cm–sized sessile polyp (noninvasive carcinoma in high-grade adenoma) located in the ascending colon. The pathological mucosal resection margin was clear. At the follow-up colonoscopy 6 months after ESD, the tumor recurred as a small tubular adenoma on the ESD scar. This recurrent tumor was resected through EMR. Each recurrent tumor required one additional EMR. Curative resections were achieved in these two recurrent cases.

The third recurrent case was a 16-mm–sized submucosal invasive carcinoma in the sigmoid colon. The submucosal invasion depth was 800 μm coupled with tumor budding. We recommended radical operation to the patient due to the risk of lymph node metastasis but he refused, choosing to monitor the tumor through close follow-ups. The recurrent tumor was detected in a follow-up colonoscopy 13 months later, confirmed as adenocarcinoma through biopsy. He received a radical operation, and the pathological result revealed the adenocarcinoma extending to the pericolic fat tissue with lymph node metastasis.

Discussion

The ESD procedure that was initially developed for early gastric cancer facilitates en bloc and complete resection of large colorectal tumors. Through high R0 resection, ESD shows a lower recurrence rate than EMR [19, 20]. However, ESD has not been widely accepted for colorectal

Table 1 Patient demographics and clinicopathological outcomes of epithelial tumors

	Epithelial tumors (n = 874)
Median age, yr (range)	62 (25–86)
Gender (M:F ratio)	517:357
Location of tumor, n (%)	
Right colon	437 (50)
Left colon	256 (29.3)
Rectum	181 (20.7)
Gross finding, n (%)	
LST	617 (70.6)
Granular type	339
Non-granular type	278
Sessile	205 (23.5)
Pedunculated	52 (5.9)
Tumor size (range), mm	26.5 ± 12.3 (5–145)
Pathology, n (%)	
Adenoma	186
Adenoma with high grade dysplasia	312
Adenocarcinoma	372 (42.6)
Intramucosal cancer	241
Submucosal invasive cancer	129
Minimal invasion[a]	73
Massive invasion[b]	55
Unknown depth of invasion	1
Proper muscle invasion	2
Procedure time (range), min	53.8 ± 38.9 (6–321)
Hospital stay (range), days	3.47 ± 1.3 (2–17)
En bloc resection, n (%)	847 (97.1)
R0 resection[c], n (%)	791 (90.5)

[a] Minimal submucosal invasion: depth of invasion <1,000 μm (flat or sessile type), <3,000 μm (pedunculated type)

[b] Massive submucosal invasion: depth of invasion ≥ 1,000 μm (flat or sessile type), ≥ 3,000 μm (pedunculated type)

[c] R0 resection (1) En bloc resection, and (2) Pathologically margin negative (mucosal and submucosal resection margin)

Table 2 Patient demographics and clinicopathological outcomes of submucosal tumors

	Submucosal tumors (n = 126)
Median age, yr (range)	51 (27–79)
Gender (M:F ratio)	73:53
Location of tumors, n (%)	
Right colon	8 (6.3)
Left colon	4 (3.2)
Rectum	114 (90.5)
Tumor size (range), mm	7.1 ± 4.7 (3–50)
Pathology	
Neuroendocrine tumor	112
Granular cell tumor	8
Leiomyoma	5
Neurilemmoma	1
Procedure time (range), min	12.5 ± 13.8 (3–89)
Hospital stay (range), days	2.5 ± 0.7 (1–5)
En bloc resection, n (%)	126 (100 %)
R0 resection, n (%)	120 (95.2 %)

Table 3 Complications of colorectal ESD

Complications, n (%)	Epithelial tumors 874 cases	Submucosal tumors 126 cases
Perforation	53 (6.1)	0 (0)
Delayed perforation	0 (0)	0 (0)
Bleeding	4 (0.5)	0 (0)

tumors because of the greater technical difficulty involved and the risk of perforation and resultant peritonitis [5]. Nowadays, through technical refinement and the development of new devices and equipment, many centers have started trying to perform colorectal ESDs. As a result, reports of colorectal ESD are increasing. There have been many reports in Japan, several reports in Korea, and a few in Europe [4]. However, in Korea all reports were done on a small scale. This report is the first large study of colorectal ESD performed at a specialized center in Korea.

Our perforation rate was relatively low and most perforation was managed without surgical treatment. There was no case of delayed perforation in contrast to Japanese data (0.3–0.7 %) [5, 16, 21–23]. Although conservative treatment might be possible, most delayed perforations are typically large in size and require surgical intervention [5]. Excessive thermal injury during ESD might be the cause of delayed perforation. Fortunately, we have not experienced this complication because of sharp dissection and low coagulation power during ESD. However, we have to keep in mind that delayed perforation might occur after ESD, especially in patients who have several concurrent diseases [21].

Procedure time was 53.8 ± 38.9 (range, 6–321) minutes for epithelial tumors and 12.5 ± 13.8 (range, 3–89) minutes for submucosal tumors. ESD required relatively long procedure times. However, if a CO_2 insufflation system is used, patients feel less discomfort and sometimes none at all during long procedures. These factors make the long procedure time for ESD less significant.

Piecemeal resection of submucosal cancer lesions prevents the pathologist from reliably determining the status of the resection margins. Kobayashi et al. [20] showed a change of treatment strategy for laterally spreading tumors, improving the en bloc resection rate and reducing the surgical resection rate through the introduction of colonic ESD. They recommended ESD both for treatment and to

obtain an adequate specimen for histopathological diagnosis. This study stated that a more accurate histopathological evaluation using en bloc specimens revealed the "true" invasion depth of the lesions. Histopathological diagnosis using a multi-fragmented specimen may result in underestimation of the invasion depth. At times, we are concerned about this underestimation and recommend radical operation to patients who have suspicious massive submucosal invasion in the resected fragment. In our previous study [6], three patients received operations after EMR due to suspicion of massive submucosal invasion. If we could have performed exact pathological examinations, it is possible that some of these patients could have avoided unnecessary surgery.

We also performed ESD for 52 giant pedunculated polyps. A pedunculated polyp is not indicated for ESD because of less frequent submucosal invasion, easier en bloc resection and a low incidence of lymph node invasion. Large, pedunculated colonic polyps have a greater risk of both early and late postpolypectomy bleeding because of the presence of large blood vessels within the stalk [24, 25]. There are occurrences when complete visualization or successful encirclement with the snare is impossible either due to larger tumor size or angulated and difficult location. However, if we adopt ESD for these giant pedunculated polyps, vessels in a stalk can be precisely detected as submucosal dissection is performed under direct visualization of the submucosal tissue, allowing precise hemostasis to be performed using hemostatic forceps. Therefore, we attempted to perform ESD for some cases of oversized pedunculated polyps with huge stalk and there were no post-ESD bleeding cases.

We also performed ESD for four locally recurrent cases and 20 residual tumors after EMR. Generally, these lesions show severe fibrosis and a nonlifting sign. Repeated EMR for these lesions (especially large lesions) is technically impossible or risky due to submucosal fibrosis [26]. Such lesions often need repeated therapy, and some cases might need surgical resection. ESD can be a good treatment option for recurrent/residual lesions [27].

ESD can be performed not only for colorectal epithelial tumors but also submucosal tumors. We performed ESD for 126 submucosal tumors, most consisting of NETs. In rectal NETs, the size of the tumor is directly related to the frequency of lymph node metastasis. In NETs with sizes larger than 10 mm, the risk of lymph node metastasis increased remarkably. According to Korean and Japanese multicenter study, rectal NETs with sizes between 10 mm and 20 mm showed a lymph node metastasis rate of 23.5 and 27.6 % [28, 29]. We usually recommend radical operation as first-line treatment to those cases. However, in NETs with sizes smaller than 10 mm, the risk of lymph node metastasis was low [28]. Thus, it could be treated by regional treatments, including colonoscopic resection.

Complete resection of rectal NETs is difficult with conventional endoscopic resection, because these tumors extend to the submucosa [30, 31]. ESD is effective treatment for submucosal tumors because through this method, we can dissect tumors directly along the submucosal layer and clearly delineate submucosal resection margins [21]. Recently, several studies reported the better results of ESD compared to EMR for the treatment of rectal NETs [31, 32].

Our study shows high en bloc and R0 resection rates, whereas complication rates are acceptable. Our data are comparable to most Japanese data. ESD seems to be an extremely effective technique to achieve R0 resection of large colorectal lesions. The very low rate of surgery for complications also shows the potential safety of this approach.

Conclusions

ESD is technically difficult, with a substantial risk of perforation. However, ESD enabled en bloc resection of large colorectal epithelial tumors and submucosal tumors. As experience with the technique increases, ESD may gradually replace piecemeal EMR and radical colon resection in the treatment of colorectal tumors.

Disclosures Eun-Jung Lee, Jae Bum Lee, Suk Hee Lee, Do Sun Kim, Doo Han Lee, Doo Seok Lee, and Eui Gon Youk have no conflicts of interest or financial ties to disclose.

References

1. Conio M, Repici A, Demarquay JF, Blanchi S, Dumas R, Filiberti R (2004) EMR of large sessile colorectal polyps. Gastrointest Endosc 60:234–241
2. Fukami N, Lee JH (2006) Endoscopic treatment of large sessile and flat colorectal lesions. Curr Opin Gastroenterol 22:54–59
3. Ohkuwa M, Hosokawa K, Boku N, Ohtu A, Tajiri H, Yoshida S (2001) New endoscopic treatment for intramucosal gastric tumors using an insulated-tip diathermic knife. Endoscopy 33(3):221–226
4. Repici A, Hassan C, De Paula Pessoa D, Pagano N, Arezzo A, Zullo A, Lorenzetti R, Marmo R (2012) Efficacy and safety of endoscopic submucosal dissection for colorectal neoplasia: a systematic review. Endoscopy 44(2):137–150 Epub 2012 Jan 23
5. Taku K, Sano Y, Fu KI, Saito Y, Matsuda T, Uraoka T, Yoshino T, Yamaguchi Y, Fujita M, Hattori S, Ishikawa T, Saito D, Fujii T, Kaneko E, Yoshida S (2007) Iatrogenic perforation associated with therapeutic colonoscopy: a multicenter study in Japan. J Gastroenterol Hepatol 22:1409–1414
6. Lee EJ, Lee JB, Lee SH, Youk EG (2012) Endoscopic treatment of large colorectal tumors: comparison of endoscopic mucosal resection, endoscopic mucosal resection-precutting, and

endoscopic submucosal dissection. Surg Endosc Jan 26. [Epub ahead of print]
7. 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
8. Hackelsberger A, Frühmorgen P, Weiler H, Heller T, Seeliger H, Junghanns K (1995) Endoscopic polypectomy and management of colorectal adenomas with invasive carcinoma. Endoscopy 27:153–158
9. Volk EE, Goldblum JR, Petras RE, Carey WD, Fazio VW (1995) Management and outcome of patients with invasive carcinoma arising in colorectal polyps. Gastroenterology 109:1801–1807
10. Horie H, Togashi K, Kawamura YJ, Ohta M, Nakajima Y, Kihara M, Nagai H, Lefor AT, Konishi F (2008) Colonoscopic stigmata of 1 mm or deeper submucosal invasion in colorectal cancer. Dis Colon Rectum 51:1529–1534
11. Kobayashi N, Saito Y, Sano Y, Uragami N, Michita T, Nasu J, Matsuda T, Fu KI, Fujii T, Fujimori T, Ishikawa T, Saito D (2007) Determining the treatment strategy for colorectal neoplastic lesions: endoscopic assessment or the non-lifting sign for diagnosing invasion depth? Endoscopy 39:701–705
12. Ishiguro A, Uno Y, Ishiguro Y, Munakata A, Morita T (1999) Correlation of lifting versus non-lifting and microscopic depth of invasion in early colorectal cancer. Gastrointest Endosc 50:329–333
13. Fujishiro M, Yahagi N, Nakamura M, Kakushima N, Kodashima S, Ono S, Kobayashi K, Hashimoto T, Yamamichi N, Tateishi A, Shimizu Y, Oka M, Ogura K, Kawabe T, Ichinose M, Omata M (2006) Successful outcomes of a novel endoscopic treatment for GI tumors: endoscopic submucosal dissection with a mixture of high-molecular-weight hyaluronic acid, glycerin, and sugar. Gastrointest Endosc 63:243–249
14. Lee EJ, Lee JB, Choi YS, Lee SH, Lee DH, Kim DS, Youk EG (2011) Clinical risk factors for perforation during endoscopic submucosal dissection (ESD) for large-sized, nonpedunculated colorectal tumors. Surg Endosc Dec 17. [Epub ahead of print]
15. Toyonaga T (2006) ESD atlas. Kanehara & Co. Ltd., Bunkyo-Ku
16. Saito Y, Uraoka T, Yamaguchi Y, Hotta K, Sakamoto N, Ikematsu H, Fukuzawa M, Kobayashi N, Nasu J, Michida T, Yoshida S, Ikehara H, Otake Y, Nakajima T, Matsuda T, Saito D (2010) A prospective, multicenter study of 1111 colorectal endoscopic submucosal dissections (with video). Gastrointest Endosc 72(6):1217–1225
17. Fujishiro M, Yahagi N, Nakamura M, Kakushima N, Kodashima S, Ono S, Kobayashi K, Hashimoto T, Yamamichi N, Tateishi A, Shimizu Y, Oka M, Ogura K, Kawabe T, Ichinose M, Omata M (2006) Endoscopic submucosal dissection for rectal epithelial neoplasia. Endoscopy 38:493–497
18. 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
19. Saito Y, Fukuzawa M, Matsuda T, Fukunaga S, Sakamoto T, Uraoka T, Nakajima T, Ikehara H, Fu KI, Itoi T, Fujii T (2010) Clinical outcome of endoscopic submucosal dissection versus endoscopic mucosal resection of large colorectal tumors as determined by curative resection. Surg Endosc 24(2):343–352
20. Kobayashi N, Saito Y, Uraoka T, Matsuda T, Suzuki H, Fujii T (2009) Treatment strategy for laterally spreading tumors in Japan: before and after the introduction of endoscopic submucosal dissection. J Gastroenterol Hepatol 24:1387–1392
21. Fujishiro M, Yahagi N, Kakushima N, Kodashima S, Muraki Y, Ono S, Yamamichi N, Tateishi A, Oka M, Ogura K, Kawabe T, Ichinose M, Omata M (2007) Outcomes of endoscopic submucosal dissection for colorectal epithelial neoplasms in 200 consecutive cases. Clin Gastroenterol Hepatol 5(6):678–683 quiz 645
22. Toyanaga T, Man-I M, Ivanov D, Sanuki T, Morita Y, Kutsumi H, Inokuchi H, Azuma T (2008) The results and limitations of endoscopic submucosal dissection for colorectal tumors. Acta Chir Iugosl 55:17–23
23. Isomoto H, Nishiyama H, Yamaguchi N, Fukuda E, Ishii H, Ikeda K, Ohnita K, Nakao K, Kohno S, Shikuwa S (2009) Clinicopathological factors associated with clinical outcomes of endoscopic submucosal dissection for colorectal epithelial neoplasms. Endoscopy 41:679–683
24. Dobrowolski S, Dobosz M, Babicki A, Glowacki J, Nalecz A (2006) Blood supply of colorectal polyps correlates with risk of bleeding after colonoscopic polypectomy. Gastrointest Endosc 63:1004–1009
25. Van Gossum A, Cozzoli A, Adler M, Taton G, Cremer M (1992) Colonoscopic snare polypectomy: analysis of 1485 resections comparing two types of current. Gastrointest Endosc 38:472–475
26. Rembacken BJ, Gotoda T, Fujii T, Axon AT (2001) Endoscopic mucosal resection. Endoscopy 33(8):709–718
27. Kuroki Y, Hoteya S, Mitani T, Yamashita S, Kikuchi D, Fujimoto A, Matsui A, Nakamura M, Nishida N, Iizuka T, Yahagi N (2010) Endoscopic submucosal dissection for residual/locally recurrent lesions after endoscopic therapy for colorectal tumors. J Gastroenterol Hepatol 25(11):1747–1753
28. Colonoscopy Study Group of Korean Society of Coloproctology (2011) Clinical characteristics of colorectal carcinoid tumors. J Korean Soc Coloproctol 27(1):17–20
29. Soga J (2005) Early-stage carcinoids of the gastrointestinal tract: an analysis of 1914 reported cases. Cancer 103:1587–1595
30. Park HW, Byeon JS, Park YS, Yang DH, Yoon SM, Kim KJ, Ye BD, Myung SJ, Yang SK, Kim JH (2010) Endoscopic submucosal dissection for treatment of rectal carcinoid tumors. Gastrointest Endosc 72(1):143–149
31. Yamaguchi N, Isomoto H, Nishiyama H, Fukuda E, Ishii H, Nakamura T, Ohnita K, Hayashi T, Kohno S, Nakao K, Shikuwa S (2010) Endoscopic submucosal dissection for rectal carcinoid tumors. Surg Endosc 24(3):504–508
32. Lee DS, Jeon SW, Park SY, Jung MK, Cho CM, Tak WY, Kweon YO, Kim SK (2010) The feasibility of endoscopic submucosal dissection for rectal carcinoid tumors: comparison with endoscopic mucosal resection. Endoscopy 42(8):647–651