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ORIGINAL RESEARCH ARTICLE

Short-term outcomes of endoscopic submucosal dissection versus laparoscopic surgery for colorectal neoplasms: An observational study

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Abstract:

Objectives: With endoscopic submucosal dissection and laparoscopic surgery, treatment for colorectal neoplasms has become minimally invasive. However, few studies have compared endoscopic submucosal dissection with laparoscopic surgery for colorectal neoplasms, excluding deeply invasive cancer on preoperative diagnosis. Methods: We retrospectively reviewed the files of patients who had undergone endoscopic submucosal dissection or laparoscopic surgery for colorectal neoplasms between November 2005 and December 2015. We limited patients who were not suspected preoperatively to have aggressive submucosal invasion >1,000 μm. Results: Ninety-five patients underwent endoscopic submucosal dissection and 37 underwent laparoscopic surgery. Cases of endoscopic submucosal dissection tended to involve rectal neoplasms more often than colonic neoplasms, shorter operative times, and shorter lengths of hospital stay compared with laparoscopic surgery. The perforation rate during colonic endoscopic submucosal dissection in the early period (November 2005 to December 2010) and late period (January 2011 to December 2015) was 14.8% and 2.9%, respectively. In all cases of perforation during colonic endoscopic submucosal dissection, the ability to maneuver the endoscope was compromised. Though tumors were larger in patients who underwent rectal endoscopic submucosal dissection compared with colonic endoscopic submucosal dissection, the perforation and postoperative bleeding rates with rectal endoscopic submucosal dissection were both 3.2%. The most common indication for laparoscopic surgery was difficulty performing endoscopic submucosal dissection. Serious complications were rare. Conclusions: For colonic neoplasms, laparoscopic surgery should be considered when endoscopic submucosal dissection is technically difficult in the early period. For rectal neoplasms, endoscopic submucosal dissection is desirable even for those of large size.

Keywords:

endoscopic submucosal dissection, laparoscopic surgery, colorectal neoplasm

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Introduction

With endoscopic submucosal dissection (ESD) and laparoscopic surgery (LS), treatment for colorectal neoplasms has become minimally invasive. In many institutions, gastrointestinal physicians have performed endoscopic resection, and gastrointestinal surgeons have performed surgical resection. In our institution, gastrointestinal surgeons perform both ESD and LS for colorectal neoplasms. Consequently, we can offer optimal, personalized treatment to individual patients with a full understanding of the advantages and disadvantages of each method.

In April 2012, colorectal ESD was introduced in Japan. ESD enables endoscopic resection of tumors measuring >2

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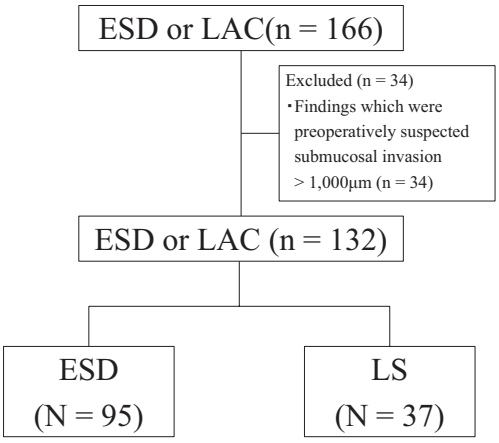

Figure 1. Selection for ESD and LS. (ESD: endoscopic submucosal dissection, LS: laparoscopic surgery)

cm, an upper limit that is easily resectable en bloc by endoscopic mucosal resection. Furthermore, ESD allows for detailed pathological examination and functional preservation of organs if curative resection is feasible[1].

In colon cancer, several randomized trials have revealed the benefits of LS compared to open surgery in terms of short-term outcomes. These advantages include improved pain management, faster recovery of bowel function, reduced wound-related complications, shorter hospital stays and improved cosmetic results[2-8]. Furthermore, long-term outcomes of LS have been proven to be equal to those of open surgery[3,4,8].

Some studies have compared the clinical outcomes of ESD and LS[9-11]. In those studies, tumor depths on preoperative diagnosis differed between patients who underwent ESD and LS. Few studies have compared ESD with LS for colorectal neoplasms, excluding deeply invasive cancer on preoperative diagnosis. Therefore, we limited our analysis to patients, who were not suspected preoperatively to have aggressive submucosal invasion > 1,000 μm. Furthermore, we limited our analysis to patients, whose tumor size was more than 20 mm, because the insurance provided by the Japanese government covers ESD for colorectal cancer measuring >20 mm. In this retrospective study, we sought to examine the short-term outcomes of ESD and LS for colorectal neoplasms, excluding deeply invasive cancer on preoperative diagnosis, and to provide guidance for when to select one over the other.

Methods

Patients and lesions

One hundred thirty-two patients underwent ESD or LS for colorectal tumors at our institution between November 2005, when we first introduced colorectal ESD, and December 2015. None of the patients were suspected preoperatively to have aggressive submucosal invasion >1,000 μm, and all had a tumor size >20 mm. Retrospective examination was performed by extracting the following information from medical records: preoperative diagnosis, reason for selection of modality, age, gender, location of tumor, rate of complete en bloc resection after ESD, operative procedure of LS, operation time, intraoperative blood loss of LS, largest tumor diameter, histological diagnosis, postoperative complications, and postoperative hospital stay. This retrospective study was approved by the ethics committee of our hospital. We re-evaluated the data following the Japanese Society for Cancer of the Colon and Rectum 2014 Guidelines for the Treatment of Colorectal Cancer[12].

Indications for endoscopic resection and surgical resection

We perform endoscopic diagnosis by white light with indigo-carmine dye, magnifying endoscopy with Crystal violet staining, narrow-band imaging or flexible spectral imaging color enhancement, and endoscopic ultrasonography. According to the Japanese Society for Cancer of the Colon and Rectum 2014 Guidelines for the Treatment of Colorectal Cancer[12], we selected endoscopic resection if we did not suspect aggressive submucosal invasion >1,000 μm, and surgical resection if we suspected aggressive submucosal invasion >1,000 μm. However, when we did not suspect aggressive submucosal invasion >1,000 μm, we sometimes selected surgical resection with consideration of the advantages and disadvantages of each treatment method (Figure 1). We applied the older version of the Japanese Society for Cancer of the Colon and Rectum Guidelines for the Treatment of Colorectal Cancer before the new version was published.

Indications for ESD

The first indication was a laterally spreading tumor-nongranular type >20 mm. The second indication was a local recurrence after endoscopic resection without submucosal invasion. The third indication was a laterally spreading tumor-granular type >20 mm, for which preoperative diagnosis was malignant, and for which endoscopic mucosal resection was likely to result in a piecemeal resection.

Rating method for endoscope maneuverability

We performed a precheck colonoscopy before ESD or LS for colorectal neoplasms, excluding deeply invasive cancer in preoperative diagnosis. We selected ESD, if the ESD operator decided that the maneuverability of the endoscope for the ESD procedure was not poor. We selected LS, if the ESD operator decided that the maneuverability of the endoscope for the ESD procedure was poor.

Table 1. Clinical Outcomes of the Patients That Underwent ESD.

	N=95
Operative time (min)	116 (20-431)
En bloc resection	90 (93.7%)
Largest tumor diameter (mm)	38 (20-123)
Histological diagnosis	
Adenoma	41
Tis	37
T1 (≤1000μm)	10
T1 (>1000μm)	7
Complications	
Perforation	6 (6.3%)
Postoperative bleeding	2 (2.1%)
Postoperative hospital stay (days)	5 (3-13)
Curative resection	83 (87.4%)

ESD: endoscopic submucosal dissection
Tis: intramucosal carcinoma
T1: carcinoma with submucosal invasion

ESD techniques

The ESD technique was previously described[13]. We used an endoscope (CF-Q260AI, or CF-H260AZI; Olympus, Tokyo, Japan) with a hood, a flush knife (Flush Knife; FujiFilm, Tokyo, Japan) and an electrosurgical unit (VIO200D; Erbe Elektromedizin, Tübingen, Germany). We injected 0.1% adrenaline and indigo-carmine locally in small doses, and 1% hyaluronic acid solution (MucoUp; Johnson & Johnson, Tokyo, Japan) was diluted 1.5 times with saline solution. The basic procedure for ESD was as follows. The diluted hyaluronic acid solution was injected into the submucosa distal to the tumor. Subsequently, an incision was made into the mucosa distal to the tumor. The submucosa was dissected just above the muscle layer toward the proximal side of the tumor. When an adequate amount of submucosal dissection was completed, the mucosal incision was extended proximally to make a circumferential mucosal incision. Finally, the remaining submucosal layer was dissected and the tumor was resected en bloc.

Rating method for submucosal fibrosis

The degree of submucosal fibrosis was classified into three categories (F0-2)[14]. F0 indicated no fibrosis; F1 indicated mild fibrosis; F2 indicated severe fibrosis.

Endoscopic curative resection and indication for additional surgery

Endoscopic curative resection of colorectal cancer is defined as that satisfying the following criteria based on the Japanese Society for Cancer of the Colon and Rectum 2014 Guidelines for the Treatment of Colorectal Cancer[12]: negative vertical margin, papillary or tubular adenocarcinoma, depth of submucosal invasion <1,000 μm, no vascular invasion, and no budding. We always perform additional surgery, if the vertical margin is positive, and consider it if one of the other above factors is present without a positive vertical margin.

Indications for LS

We do not select LS for patients with swelling of multiple lymph nodes.

LS technique

The LS technique was previously described[15]. An incision is made longitudinally on the umbilicus, and the first trocar for the camera is introduced. The second and third trocars are introduced in the right side of the abdomen, and the fourth and fifth trocars are introduced in the left side of the abdomen. The mesocolon is lifted, and the dissection of the mesocolon from the retroperitoneum occurs in a medial to lateral approach. The extent of lymph node dissection is based on the Japanese Society for Cancer of the Colon and Rectum 2014 Guidelines for the Treatment of Colorectal Cancer[12], namely, D1 or D2. In the case of the right colon, after the umbilical incision is enlarged for externalization of the colon, the resection and anastomosis are done outside of the abdomen. In the case of the left colon, the anal side of the tumor is divided using an endostapler (Tri-Staple Technology, Covidien, Mansfield, MA, USA, or Eshelon, Ethicon, Cincinnati, OH, USA) laparoscopically. After the umbilical incision is enlarged for the externalization of the colon, the oral side of the tumor is divided. The end-to-end anastomosis is created by a double stapling technique using circular staplers (EEA28 mm, Covidien, Mansfield, MA, USA, or CDH29 mm, Ethicon, Cincinnati, OH, USA) laparoscopically. A drain is placed near the anastomosis via the trocar. Finally, the wound is closed.

Statistical analysis

Statistical calculations were made with SPSS vl9.0 (SPSS Inc., Chicago, IL, USA). Data are presented as medians with ranges. Statistical analyses were performed with the Mann-Whitney U test or the x^2 test with Fisher's exact test. Statistical significance was defined as p values of <0.05.

Results

There were 132 patients for whom we did not suspect aggressive submucosal invasion >1,000 μm preoperatively. Conversely, there were 34 patients that we suspected of having aggressive submucosal invasion >1,000 μm preoperatively (Figure 1), and they were excluded.

Ninety-five of 132 patients analyzed underwent ESD, and 37 underwent LS.

Clinical outcomes of the patients that underwent ESD are

Table 2. Perforation Rate of ESD.

	Colon	Rectun	P value
All period (%)	4/32 (12.5%)	2/63 (3.2%)	0.09
Early period (2005.11-2010.12) (%)	2/5 (40.0%)	2/22 (9.1%)	<0.01
Late period (2011.1-2015.12) (%)	2/27 (7.4%)	0/41 (0%)	<0.01

ESD: endoscopic submucosal dissection

Table 3. Perforation Cases of Colonic ESD.

	Year	Age	Sex	Location	Magnification	Time (min)	Tumor size (mm)	Fibrosis of submucosa	Histological diagnosis	maneuverability of endoscope
①	2007	67	Female	Transverse colon	LST-NG	140	40	F2	Adenoma	poor
②	2007	65	Male	Descending colon	LST-NG	20	20	F1	Adenoma	poor
③	2015	82	Female	Ascending colon	LST-G	283	35	F2	Adenoma	poor
④	2015	51	Male	Transverse colon	LST-NG	59	29	F1	Adenoma	poor

ESD: endoscopic submucosal dissection
LST-NG: laterally spreading tumor-non granular type
LST-G: laterally spreading tumor-granular type

Table 4. Indications of Laparoscopic Surgery.

	N=37
Endoscopic resection is difficult	29
Maneuverability of the endoscope	12
Location	9
Degree of circumference	4
On the scar	2
Secure the field of view	1
Unable to be resected by ESD	1
Multiple lesions	3
Patient desired the surgery	3
Perforation during EMR	1
Other	1

ESD: endoscopic submucosal dissection
EMR: endoscopic mucosal resection

summarized in Table 1. The en bloc resection rate was 93.7%, median cutting time was 116 min, and median tumor diameter was 38 mm. The rates of perforation and postoperative bleeding were 6.3% and 2.1%, respectively. In all postoperative bleeding cases, hemostasis was achieved endoscopically. The median postoperative hospital stay was 5 days. Histological diagnosis included adenoma in 41 patients, intramucosal carcinoma (Tis) in 37 patients, and carcinoma with submucosal invasion (T1) in 17 patients. Curative resection was achieved in 87.4% of patients and the recurrence rate was 3.2%. Curative resection was achieved in all patients in the adenoma and Tis groups and in 5 patients in the T1 group. Twelve patients with T1 were not cured by ESD, and additional surgery was indicated. Seven of the 12 patients underwent additional surgery, and five of the 12 patients did not.

Perforation rates of ESD are shown in Table 2. Compared with the perforation rate of colonic and rectal ESD in the early period (November 2005 to December 2010), the rate in the late period (January 2011 to December 2015) was lower. However, the perforation rate during colonic ESD was higher than that during rectal ESD. Cases of perforation during colonic ESD are described in Table 3. All four cases were accompanied by at least F1 fibrosis of the submucosa. In all four cases, maneuverability of the endoscope was poor. All perforation cases were treated successfully by endoscopic clip application and antibiotics.

There were three cases with incomplete ESD. Though no case was incomplete because of scope operability, two cases were incomplete because of fibrosis of the submucosa, and one case was incomplete because of disturbance. Two cases whose ESD was incomplete because of fibrosis of the submucosa underwent additional surgery with lymph node dissection.

Indications for LS are described in Table 4. In 29 of 37 cases (78%), the indication for LS was difficulty with endoscopic resection. In 12 of the 29 cases, the difficulty with endoscopic resection was poor maneuverability of the endoscope. Clinical outcomes of the patients that underwent LS are described in Table 5. LS for rectal tumors was performed in only three of 37 cases. The median operative time was 228 min, intraoperative blood loss was negligible, and the median tumor diameter was 37.5 mm. Though there was only one anastomotic leak, this case did require reoperation. The median postoperative hospital stay was 9 days. Histological diagnosis was adenoma in 9 patients, Tis in 26 patients, and T1 in 2 patients. Curative resection was

achieved in all cases.

We compared short-term outcomes between ESD and LS. We excluded the initial term of introducing ESD, from 2005 to 2009. The patient group that underwent ESD had significantly more rectal lesions ($P < 0.01$), shorter operative times ($P < 0.01$), and shorter postoperative hospital stay ($P < 0.01$) compared to the LS cohort (Table 6). With regard to tumor size, although there was no significant difference between the colonic ESD group and the colonic LS group ($P = 0.71$), there was a significant difference between the colonic ESD group and the rectal ESD group ($P < 0.01$).

Table 5. Clinical Outcomes of the Patients That Underwent LS.

	N=37
Operation procedure	
Ileocecal resection	17
Sigmoidectomy	9
Partial resection	5
Right hemicolectomy	2
Low anterior resection	2
Anterior resection	1
LECS	1
Operative time (min)	228 (83-595)
Intraoperative blood loss (ml)	10 (10-740)
Largest tumor diameter (mm)	32 (20-85)
Histological diagnosis	
Adenoma	9
Tis	26
T1 (≤1000μm)	1
T1 (>1000μm)	1
Postoperative complications	
Leakage	1 (2.7%)
SSI	1 (2.7%)
Ileus	0 (0%)
Postoperative hospital stay (days)	9 (5-29)
Curative resection	37 (100%)

LS: laparoscopic surgery
LECS: laparoscopy and endoscopy cooperative surgery
Tis: intramucosal carcinoma
T1: carcinoma with submucosal invasion
SSI: surgical site infection

Discussion

In this study, the perforation rate during ESD was higher than the rate of anastomotic leakage after LS. The perforation rate during ESD in the early period was higher than, that in the late period. There seems to be two reasons for this, namely, the infrequency of cases and immaturity of the technique, especially in the early period. In the early period, despite there being only five colonic ESD cases, there were two perforations. In the late period, the perforation rate for all ESD cases was 2.9%, which is consistent with another report[16]. However, the perforation rate during colonic ESD was higher than that during rectal ESD, and in all four cases of perforation during colonic ESD, the maneuverability of the endoscope was poor. Some studies have reported that poor maneuverability of the endoscope and submucosal severe fibrosis affect the technical difficulty of ESD for colorectal tumors[16-18]. Though fibrosis of the submucosa is not able to be determined preoperatively, the maneuverability of the endoscope can be predicted. In colonic cases wherein postoperative incontinence and anastomotic leakage are not common[2], poor maneuverability of the endoscope may be considered to be an indication for LS in the early period. Balloon-assisted ESD should be considered to be an other option, because balloon-assisted ESD may enhance the maneuverability of the endoscope[19,20]. On the other hand, these data may indicate that colonic tumor size is not necessarily an absolute indication for LS, because there was no significant difference between the colonic ESD group and the colonic LS group with regard to tumor size. Furthermore, tumor sizes in the perforation cases were all less than 50 mm.

Among 63 rectal cases, 60 cases underwent ESD, and

Table 6. Clinicopathological Characteristics between Patients That Underwent ESD or LS.

	ESD (n=71)	LS (n=37)	P value
Age	66 (40-85)	70 (40-84)	0.29
Gender (Male:Female)	50:21	15:22	<0.01
Tumor location (Colon:Rectum)	27:44	34:3	<0.01
Operative time (min)	126 (54-431)	228 (83-595)	<0.01
Largest Tumor diameter (mm)	38 (20-123)	32 (20-85)	0.10
Histological diagnosis (Adenoma:Tis:T1)	34:25:12	9:26:2	<0.01
Postoperative hospital stay (days)	5 (3-11)	9 (5-29)	<0.01

ESD: endoscopic submucosal dissection
LS: laparoscopic surgery
Tis: intramucosal carcinoma
T1: carcinoma with submucosal invasion

only 3 cases underwent LS. The reason for this is that, LS for rectal tumors can be difficult because of the limited space in the pelvis[21], and post-proctectomy incontinence and anastomotic leakage are significant complications when they occur[22]. Furthermore, the maneuverability of the endoscope for rectal tumors is often relatively good. Though the tumor size in the rectal ESD group was larger than that in the colonic ESD group in this study, the perforation rate during rectal ESD was lower than that during colonic ESD. These data indicate that ESD may be preferable even for large rectal neoplasms.

This study has some limitations, including retrospective analyses with limited cases in a single institution, study group bias, and inconsistency of both resection techniques through the study period. In the future, a multicenter study with many cases is needed to evaluate not only outcome but also quality of life with ESD and LS.

In counseling patients regarding ESD or LS for colorectal neoplasms, the endoscopist and the surgeon must have a full understanding of the advantages and disadvantages of each method. Furthermore, it is necessary to select the safest treatment method according to the resources available within each facility. We have suggested that LS should be considered when ESD for colonic neoplasms is technically difficult in the early period and ESD for rectal neoplasms is desirable even for those of large size.

Conflicts of Interest

There are no conflicts of interest.

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