Laparoscopic and endoscopic cooperative surgery (LECS) to overcome the limitations of endoscopic resection for colorectal tumors





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ABSTRACT

Background and study aims We developed a laparoscopy endoscopy cooperative surgery (LECS) to overcome the limitations of endoscopic resection for colorectal tumors. The aim of this study was to evaluate the feasibility of LECS,

which combines endoscopic submucosal dissection (ESD) and laparoscopic partial colectomy.

Patients and methods We performed LECS for 17 colorectal tumors in 17 patients (male:female 10:7; mean age, 66.5 years). The clinicopathological outcomes of these 17 cases and the feasibility of LECS were evaluated retrospectively. Indications for LECS were as follows: 1) intramucosal cancer and adenoma accompanied by wide and severe fibrosis; 2) intramucosal cancer and adenoma involving the diverticulum or appendix; and 3) submucosal tumors.

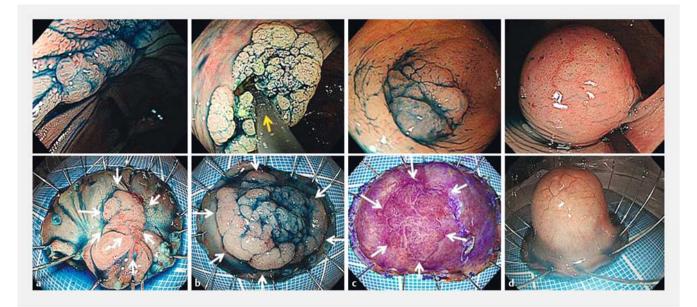
Results We successfully performed LECS procedures in 17 cases (intramucosal cancer [n=6], adenoma [n=9], schwannoma [n=1], and gastro-intestinal stromal tumour [GIST] [n=1]. Mean tumor diameter was 22.4mm (range, 8–41 mm). LECS was successfully performed in all 17 cases without conversion to open surgery; the R0 rate was 100%. LECS was applied to the following situations: involving the appendix (n=6), tumor accompanied by severe fibrosis (n=5), involving the diverticulum (n=3), submucosal tumor (n=2), and poor endoscopic operability (n=1). We experienced no adverse events (e.g., leakage or anastomotic stricture) and the median hospital stay was 6.4 dayus (range, 4 to 12). All 17 patients who were followed for ≥ 3 months (median, 30.8 months; range, 3–72 months) showed no residual/local recurrence.

Conclusion LECS was a safe, feasible, minimally invasive procedure that achieved full-thickness resection of colorectal tumors and showed excellent clinical outcomes.

Introduction

While endoscopic resection (ER) such as endoscopic mucosal resection (EMR) and endoscopic submucosal dissection (ESD) has progressed and spread globally, we have experienced several cases in which ESD was difficult to perform for various reasons (e.g., involvement of a diverticulum or the appendix, firm submucosal fibrous change due to previous conventional endoscopic treatment). We identified the limitations and factors affecting the safety of ESD procedure in these cases.

To overcome the limitations of ER, we established a laparoscopic and endoscopic cooperative surgery (LECS) procedure [1–2] that combines ESD and laparoscopic partial colectomy. In this procedure, local full-thickness resection is performed using a combination of laparoscopic-assisted colectomy (LAC) and ESD. This combined procedure is considered to be an epoch-making minimally invasive treatment that preserves colorectal function. The aim of this study was to establish the feasibility of LECS applied with an ESD technique to achieve safe local full-thickness resection with adequate surgical margin.



▶ Fig. 1 Indications for the LECS procedure for colorectal tumors. Pictures show an endoscopic image and a resected specimen. a Case with severe degree fibrosis. b Case with the diverticulum. c Case that progressed to appendix. d Case of submucosal tumor.

Patients and methods

LECS was performed to treat colorectal tumors in 17 patients (male:female, 10:7; mean age, 66.5 years) from July 2012 to January 2018 and clinicopathological outcomes of full-thickness resection were analyzed for a retrospective study. We examined the following points: 1) clinical outcomes (macroscopic configuration, tumour size, localization of the tumor in the colorectal wall, operating time, intraoperative bleeding volume, postoperative hospital stay, adverse events (AEs); 2) postoperative peripheral blood and chemistry findings, body temperature and bowel movement; 3) histology of the resected specimen, en bloc resection rate and R0 resection rate; and 4) the postoperative follow-up period and the incidence of residual/local recurrence.

This study was performed in accordance with the Declaration of Helsinki and the abovementioned protocol was approved by the Institutional Review Board of the Cancer Institute Hospital. All patients received detailed information about the significance of the procedure and potential complications before surgery and gave their informed consent. All patients were informed that if a histological analysis revealed risk factors for lymph node metastasis, such as deep submucosal cancer invasion, lympho-vascular involvement, or tumor budding in a resected specimen, then a subsequent radical operation might be necessary.

En bloc full-thickness resection was defined by lateral and vertical margins that were both negative and resected on a macroscopic examination. Similarly, R0 resection was defined as histologically complete en bloc resection with a negative lateral margin. In addition, we evaluated adverse events according to Clavien-Dindo classifications [3]. Macroscopic-type colorec-

tal tumors were classified according to the Paris Classification [4] as follows; 0-ls, 0-ls + lla, 0-lla, 0-lla + llc and 0-llc.

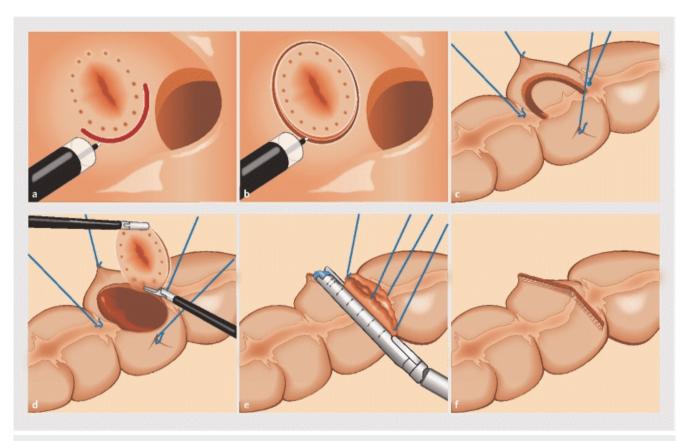
Indications for LECS in patients with colorectal tumors

LECS is indicated in cases in which ER is associated with a high risk of perforation, or safety cannot be secured. LECS is also indicated for lesions that are considered to be curable by local resection without lymph node dissection.

Indications for LECS were considered to be as follows: 1) intramucosal cancer and adenoma with high-grade atypia (Vienna Classification, Category 3, 4) [5] accompanied by widespread and severe fibrosis in the submucosal layer (tumor recurrence after endoscopic or surgical resection); 2) intramucosal cancer and adenoma with high-grade atypia involving the appendix or diverticulum; and 3) intraluminal or intramural growth-type submucosal tumors (**> Fig. 1**).

Indications for LECS were determined by magnifying endoscopy and image-enhanced endoscopy (IEE) (i.e., narrow-band imaging [NBI)]), for the purpose of diagnosis by exclusion of submucosal invasive cancer requiring lymph node dissection.

Similarly, lesions with multiple firm scars in regions 1 cm or more in size were judged against an ESD limit lesion, in particular, recurrent lesions after piecemeal EMR. These lesions were regarded as good indicators for LECS in terms of safety and curability. Furthermore, we performed preoperative biopsy to confirm that a lesion was indicative of LECS by virtue of adenoma and an intramucosal carcinoma. In addition, we evaluated the growth pattern of the submucosal tumor (SMT) using endoscopic ultrasonography (EUS). Moreover, lesions were excluded if they were larger than one-third of the colorectal wall, submucosal invasive cancer or lower rectal lesions.



▶ Fig. 2 Basic technique of LECS procedure for the colorectal tumor -the lesion involving the diverticulum for a case. a Mucosal incision along the marking around the lesion b Cutting of seromuscular layer by using Hook knife. c Laparoscopic view of seromuscular incision, and the lesion lifting by using "Crown method." d Cutting of the last part by using laparoscopic device. e Closure by using Endo-GIA. f Picture of completion.

Basic technique of LECS

The basic technique for full-thickness resection by LECS is shown in ▶ Fig. 2 and in ▶ Video 1. Prior to surgery, we performed bowel preparation using polyethylene glycol (PEG), similarly to a colonoscopy.

During the procedure, the patient was placed under general anesthesia in the lithotomy position. Five ports were used for laparoscopy under carbon dioxide pneumoperitoneum (8 mmHg). The laparoscope was inserted using a 12-mm trocar placed in the periumbilical area. For a right-sided colon tumor, the operator stood on the left side with a laparoscopist on the left side. For rectal tumors or in cases involving tumors located on the left side, the operator stood on the right side of the patients, while the endoscopist stood between the patient's legs.

Before endoscopic mucosal incision, we perform a detailed observation of the lesion using an indigo-carmine dye spraying method and NBI, to precisely diagnose the lateral extension of the tumor. After the abovementioned endoscopic examination, we made several marker dots around the lesion using a Hook knife in coagulation mode.

Next, the endoscopist punctured the area around the lesion using a 23G endoscopic fine needle (NM-400U-0623, Olympus, Tokyo, Japan) and showed the lesion site to the laparoscopic surgeon. The laparoscopic surgeon marked the site of puncture

around the lesion using a laparoscopic device in coagulation mode.

The mesentery of the colon was incised in cases in which the tumor was located on the mesentery side. In cases located in the rectum, we dissected the peritoneal reflection and exposed the rectal wall under a laparoscopic approach.

For the ESD procedure, a Hook knife (KD-6200QR, Olympus, Tokyo, Japan) was used for submucosal dissection, a Coagrasper (FD-411QR, Olympus) endoscopic device was used for hemostasis, and a high-frequency surgical unit (ERBOTOM ICC 300/350 and VIO 300 D, ERBE, Tübingen, Germany) with an automatically controlled cutting mode was used for cutting (effect 3, duration 2, interval 2) and coagulation (effect 3, 30–40 W).

After elevating the tumor with submucosal injection of saline and glycerol solution, the circumference of the mucosa was carefully cut outside the marks made with the Hook knife. After the circumference had been cut, we trimmed the incised part and made a rail.

During the next laparoscopic procedure, several anchoring sutures were placed around the lesion to allow the surrounding wall to be lifted using a "Crown method" to prevent the tumor from coming into contact with the visceral tissue and spilling intestinal contents [1].



▶ Video 1 We present the LECS procedure for submucosal tumor located at the upper rectum of a 74-year-old man. First, we exfoliate the retroperitoneum and expose the rectal wall. Next, we make several markings around the tumor and make a circumference cutting after having performed local injection of saline solution. Next, we trim the incised part and make a rail with the ESD technique. Subsequently, we puncture the outside of the incision line using an endoscopic fine needle, which reveals the fullthickness resection line to the surgeon. Next, several anchoring sutures are placed around the lesion. Subsequently, the seromuscular layer is cut along the rail of the mucosal incision using a Hook knife. During the above-mentioned procedure, the lesion is lifted using several anchoring sutures, in a "Crown method," to prevent pollution by intestinal juice. The last part is the cut using a laparoscopic device. The specimen is retrieved transanally by an endoscopic procedure using grasping forceps. The open part of the wall is closed by multiple linear staplers in the axial direction. Histology of the specimen revealed gastrointestinal stromal tumor and negative lateral margin.

Subsequently, the seromuscular layer was endoscopically cut along the rail of the mucosal incision using a Hook knife. Approximately three-fourths of the rail around the circumference can be cut endoscopically using the ESD technique.

To prevent the tumor from coming into contact with the visceral tissue, the tumour was turned towards the intra-colonic cavity by traction on the stitches. Finally, dissection of the full-thickness of the wall (approximately a quarter of the circumference) was performed laparoscopically and the specimen was retrieved transanally by an endoscopic procedure. The specimen was then fixed in formalin for a histological analysis.

The open part of the colon wall was closed with multiple linear staples in the axial direction. Finally, after absence of stenosis was confirmed endoscopically, all ports were removed and the skin closed after achieving hemostasis.

Follow-up evaluation

All patients underwent intensive follow-up at our institution. During the first postoperative follow-up examination, at 3 to 6 months, serology (including measurement of serum CEA level) and colonoscopy were performed. Colonoscopy was performed to check for anastomotic stricture and residual/local recur-

Patients	Male 10 cases Female 7 cases
Age (mean)	66.5 yr (50 – 81 yr)
Location	
Cecum	7 cases
Ascending colon	4 cases
Transverse colon	4 cases
Descending colon	1 case
Sigmoid colon	None
Rectum	1 case
Side of the colorectal wall	
Mesentery side	6 cases
Anterior side	3 cases
Posterior side	1 case
Orifice of the appendix to cecum	7 cases
Macroscopic classification (Paris classific	ation)
0-IIa	9 cases
0-Is	4 cases
0-Is+lia	4 cases
Tumor size (mean)	22.4 mm (8 – 41 mm)
Indications for LECS	
Involving the appendix	6 cases
Severe degree of fibrosis	5 cases
Involving the diverticulum	3 cases
Submucosal tumor (SMT)	2 cases
Technical difficulty of ESD	1 case
Histology	
Adenoma (including SSA/P)	9 cases
Intramucosal cancer	6 cases
Gastrointestinal stromal tumor (GIST)	1 case
Schwannoma	1 case

LECS, laparoscopic and endoscopic cooperative surgery; ESD, endoscopi submucosal dissection; SSA/P, sessile serrated adenoma/polyp

rence. Thereafter, all patients had a follow-up colonoscopy at 3 to 6 months and 1, 3, and 5 years after the LECS procedure and abdominal ultrasonography or computed tomography (CT) scans as required.

► Table 2 Clinical outcomes.	
Conversion to open surgery	none
En bloc resection rate (%)	17/17 cases (100%)
R0 resection rate (%)	17/17 cases (100%)
Operating time (median)	183.3 min (68 – 332 min)
Estimated blood loss (mean)	7.8 g (2 – 20 g)
Intraoperative adverse events	none
Postoperative course	
CRP (mean)	4.07 mg/dL (0.58 – 10.76 mg/dL)
WBC (mean)	9,111 (4,500 – 13,100)
Body temperature (mean)	37.2°C (36.7 – 37.6°C)
Initial flatus (mean)	1.5 POD (1 – 2 POD)
Postoperative hospital stay (mean)	6.4 days (4 – 12 days)
Follow-up periods (mean)	30.8 months (3 – 72 months)
Postoperative adverse events	none
Residual/local recurrence	none
Long-term adverse events	none
Adverse event: Grade 3 or more of Clavien-Dindo classification	
Intraoperative adverse events: technical failure of LECS procedure, injury	of other organs, massive bleeding, etc.
Postoperative adverse events: anastomotic leakage, abscess, infection, e	etc.
Long-term adverse events: anastomotic stricture, intestinal obstruction,	etc.
CRP, C-reactive protein; WBC, white blood cell; POD, postoperative day	

Results

We successfully performed full-thickness resection in 17 cases (100%) using LECS (► Table 1, ► Table 2). The one-piece resection rate and the R0 rate were both 100%. Median operation time was 183.3 minutes (range, 68 – 332), and mean estimated blood loss was 7.8 g (range 2 – 20 g). Postoperative inflammatory reactions were minimal, as shown in ► Table 2.

The LECS procedures were accomplished safely without conversion to open surgery. Furthermore, there were no post-operative AEs, and postoperative movement of the intestine was restored at an early stage. Mean hospital stay was 6.4 days (range 4–12). In one patient who simultaneously underwent a radical operation due to other advanced tumors, the surgery took 332 minutes for surgery and the patient was hospitalized for 12 days.

Pathological results of the 17 cases as follows: intramucosal cancer (n=6), adenoma (n=9), schwannoma (n=1), and gastrointestinal stromal tumor (GIST) (n=1). Locations included the cecum (n=7), ascending colon (n=4), transverse colon (n=4), descending colon (n=1), and upper rectum (n=1). Macroscopic configurations of the 15 cases (with the exception of the SMT) were type 0-lIa (n=9), type 0-ls+IIa (n=4), and type 0-Is (n=2). Median tumor diameter was 22.4 mm (range, 8-41).

Indications for LECS included involvement of the mucosa of the appendix (n=6), severe fibrosis (n=5), involvement of a diverticulum (n=3), submucosal tumor (n=2), and poor endoscopic operability (n=1). No grade 3 or higher AEs, using the Clavien-Dindo classification, were seen in any of the 17 cases

Follow-up outcomes

All 17 patients were followed up for 3 months or more according to the follow-up schedule. No cases of residual/local recurrence were detected with a median follow-up period of 30.8 months (range, 3–72). Furthermore, the patients followed a favorable course, without complications such as postoperative anastomotic stricture or small bowel obstruction due to adhesion.

Discussion

When ESD is performed to treat lesions with a severe degree of fibrosis in the submucosal layer, the perforation rate reportedly ranges from 5.6% to 11.0% [6-9]. Similarly, lesions involving a diverticulum or the appendix are associated with a high risk of perforation during ESD.

Although the abovementioned lesions are curable by local excision without lymph node dissection, the procedures are difficult to perform. For these reasons, we devised the LECS proce-

► Table 3 Literature on full-thickness wedge resection of the colon wall in combination with endoscopy and laparoscopy.

LAER, laparoscopy-assisted endoscopic resection; EAWR, endoscopy-assisted laparoscopic vedge resection; EATR, endoscopy-assisted laparoscopic segment resection; LACP, laparoscopic polypectomy; CLER, combined laparoscopic surgery; LER, laparoscopic polypectomy; CLER, combined laparoscopic surgery; LER, laparoscopic resection; LAEP, laparoscopic polypectomy; LECS, laparoscopy endoscopy cooperative surgery; EFTR, endoscopic resection laparoscopic polypectomy; LECS, laparoscopy endoscopy cooperative surgery; EFTR, endoscopic full-thickness resection latest

► Table 3	(Continuation)	ition)											
Author	Year	Literature	Method	Case	Completion	R0	Conversion to LAC or open sur- gery	Adverse	Leak- age	Subsequent operation due to SM invasion, recurrence, or other	Postoperative hospital stay	Residual/ local recurence	Mortality
Lee SW [21]	2013	Dis Colon Rectum	CELS: 65	65 cases 65 lesions	48/65 (73.8%)	I	17/65 (26.2%)	2/48 (4.4%)	I	1/48 (2.1%)	1 (0-6)	5/48 (10.4%)	none
Goh C [22]	2014	Colorectal Dis	ELP: 65	30 cases 30 lesions	22/30 (73%)	I	8/30 (26.7%)	4/30 (13.3%)	I	2/30 (6.7%)	2 (1.0–3.0)	none	none
Fukunaga Y [2]	2014	Dis Colon Rectum	LECS: 3	3 cases 3 lesions	3/3 (100%)	3/3 (100%)	none	none	none	none	7	none	none
Schmidt A [25]	2015	Endoscopy	EFTR: 25	25 cases 25 lesions	24/25 (96.0%)	18/24 (75%)	I	none	I	2/24 (8.3%)	4 (1–12)	5/24 (20.8%)	none
Richter- Schrag HJ [26]	2016	Chirurg	EFTR: 20	20 cases 20 lesions	15/20 (75.0%)	16/20 (80.0)%	3/20 (15.0%)	1/20 (5.0%)	none	2/20 (10%)	I	1/20 (5.0%)	none
Andrisani G [27]	2017	Digestive and liver dis- ease	EFTR: 20	20 cases 20 lesions	20/20 (100%)	20/20 (100%)	none	1/20 (5.0%)	none	1/20 (5.0%)	I	none	none
Schmidt A [28]	2017	Gut	EFTR:181	181 lesions	162/181 (89.5%)	139/ 181 (76.9%)	I	18/181 (9.9%)	per- fora- tion: 6/181 (3.3%)	14/154 (9.1%)	1	18/154 (15.3%)	none
Valli PV [29]	2018	Surg Endosc	FTR¹: 60 (colorectal: 55)	60 cases 60 lesions	51/58 (87.9%)	46/58 (79.3%)	I	4/60 (6.7%)	Ī	2/60 (3.3%)	I	none	none
Our case			LECS: 17	17 cases 17 lesions	17/17 (100%)	17/17 (100%)	none	none	none	none	7.4 (4-12)	none	none

dure to facilitate safe and radical local resection of colorectal tumors.

There have been reports of full-thickness wedge resection of the colon wall in combination with endoscopy and laparoscopy instead of laparoscopic colorectal resection in round slices [10–22] (> Table 3). These surgical procedures are referred to as "combined laparoscopic-endoscopic resection (CLER)," "combined endoscopic and laparoscopic surgery (CELS)," and "endo-laparoscopic polypectomy (ELP)," etc. In reports on CLER, CELS and other combined procedures, the complete resection rate was very low, while AE, conversion and subsequent operation rates were relatively high.

According to a multicenter questionnaire survey about endoscopic treatment with JSCCR, ESD achieved an en bloc resection rate of 94.5% in treatment of 816 lesions (size, ≥ 20 mm). This was significantly superior to the en bloc resection rate of 56.9% in the 1,019 cases treated by conventional polypectomy or EMR [23]. Local recurrence after en bloc resection revealed that the rate of recurrence after ESD was 1.4%, while that after conventional endoscopic resection, including polypectomy and EMR, was 6.8%, which was significantly higher [24].

Our LECS procedure was quite different from CLER or CELS using conventional endoscopic resection, because we secured the surgical margin using an ESD technique. The ESD technique can be used in LECS to achieve a safe oncological margin in cases involving colorectal tumors. Thus, a high complete resection rate, with an adequate surgical margin and a lower local recurrence rate, can be expected.

Endoscopic full-thickness resection (EFTR) using a full-thickness resection device (FTRD; Ovesco Endoscopy, Tübingen, Germany) has been reported [25–30]. In that report of 181 cases treated by EFTR, the en bloc resection rate was 89.5%, and the R0 rate was 76.9% [28]. Three-month follow-up was performed for 154 cases and residual/local recurrence was evident in 15.3%. Furthermore, the AE rate was 9.9% with a 2.2% rate of emergency surgery. Thus, the results, in terms of the complete resection rate, radical curability and safety, did not seem satisfactory.

When LECS was used to treat colorectal tumors in the current study, the en bloc resection rate was 100%. Similarly, the R0 resection rate was 100%, mainly due to securing of lateral margin by ESD. Furthermore, no cases of residual/local recurrence were detected in the follow-up cases.

Laparoscopic colectomy is widely used as a minimally invasive surgery for colorectal cancer. Some randomized clinical trials have shown that it is associated with long- and short-term outcomes superior to those of open colectomy. Laparoscopic colectomy has also been used to treat colorectal tumors such as adenoma, intramucosal cancer and SMT, which could not be treated by conventional endoscopic techniques.

However, some of these cases might be curable by local full-thickness resection without lymph node dissection, such as adenoma and intramucosal cancer, which are associated with a severe degree of fibrosis, extension to a diverticulum or the appendix, and SMT, as noted in the indications for LECS procedure.

There were few cases of functional impairment, even after colorectal surgery, especially in right-side colectomy and low-anterior resection. We were able to maintain intestinal continuity by local full-thickness resection using our LECS procedure. This enabled the continuity of the Auerbach nerve plexus to be secured and bowel movement to be preserved.

For cecal lesions involving the appendix in particular, we can treat the lesions with an appropriate surgical margin and avoid unnecessary colectomy using the LECS procedure. This is different from cecal resection by LAC, because we can maintain ileocecal valve function, and enterohepatic circulation of bile acid.

It is essential during LECS procedures for epithelial neoplasms that tumor cells are not seeded into the peritoneal cavity. To prevent the tumor from coming into contact with visceral tissue, the tumor was turned towards the intracolonic cavity by placing traction on the stitches, and the resection line was pulled up using a "Crown method." In addition, we were able to prevent spilling of the intestinal content.

Postoperative inflammatory reactions after LECS were minimal, as shown in the clinical results, and recovery of intestinal tract function was favorable. Thus, LECS was useful for treating cases in which the ability to perform endoscopic treatment was limited. This method, which has low invasiveness, can be used to supplement LAC and ESD.

Our study, however, has several limitations. This retrospective study was limited to a single center and a small number of patients. Moreover, progress of this procedure is required to overcome the problem of the peritoneal seeding of tumor cells and others. Thus, additional cases and further investigation are required to clarify the feasibility of the LECS procedure.

Conclusions

LECS may be a feasible procedure that achieves full-thickness resection while preserving of colorectal function in patients with colorectal tumors that are considered to have a high risk of perforation with endoscopic treatment.

Competing interests

None

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