



# The short-term outcomes of laparoscopic–endoscopic cooperative surgery for colorectal tumors (LECS-CR) in cases involving endoscopically unresectable colorectal tumors

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## Abstract

**Purpose** Laparoscopic and endoscopic cooperative colorectal surgery (LECS) is widely used for the removal of endoscopically unresectable colonic polyps. We evaluated the invasiveness of LECS in comparison to conventional laparoscopic surgery (CLS) for endoscopically unresectable colorectal tumors.

**Method** We retrospectively analyzed the data of patients with colorectal adenoma or mucosal cancer and submucosal tumors who underwent either LECS or CLS at a single, high-volume center in Japan between 2004 and 2017. The short-term and oncological outcomes were compared between groups.

**Results** Of the 83 eligible patients, 15 underwent LECS and 68 underwent CLS. There was no conversion to open surgery in either group. En bloc resection was achieved in all cases in both groups. The median time to solid diet intake was the same in both groups (2 days,  $p=0.39$ ). The median duration of hospital stay after surgery was 6 days (range 4–12 days) in the LECS group and 10 days (range 5–68 days) in the CLS group ( $p=0.01$ ). Clavien–Dindo grade  $\geq 3$  postoperative complications only occurred in the CLS group (two cases,  $p=0.37$ ).

**Conclusion** Our results indicated that LECS is a safe and feasible technique that results in high-quality colorectal polyp resection with quicker recovery and favorable 30-days postoperative outcomes.

**Keywords** Colonic polyps · Colorectal neoplasms · Colorectal surgery · Endoscopic surgical procedure · Laparoscopic surgery

## Introduction

Colorectal cancer (CRC) is a leading cause of cancer-related death in the developed world [1]. Colonic polyps are a precursor for colorectal cancer; thus, the removal of colonic adenomas is associated with a reduction in the incidence of CRC. The National Polyp Study in 1993 demonstrated that the consistent removal of polyps was associated with a clear reduction in the risk of colorectal carcinoma development [2].

Recently, a study by Winawer et al. [3] showed that the endoscopic removal of colorectal adenomas can reduce the incidence of colorectal cancer by 76–90%. Endoscopic removal was generally considered to include polypectomy, endoscopic mucosal resection (EMR), and endoscopic submucosal dissection (ESD). While up to 15% of colonic polyps require advanced polypectomy techniques because of their size, location, or appearance [4], another 10–15%

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are considered very difficult to remove by conventional flexible endoscopy [5]. These require surgical resection. The difficulty in the endoscopic removal of certain colonic polyps is attributable to their location, such as the diverticulum or appendiceal orifice; their size; or the presence of fibrosis.

Laparoscopic and endoscopic cooperative surgery for colorectal tumors (LECS-CR) was, therefore, proposed by our institution to overcome the burden associated with endoscopically unresectable polyps [6]. This operation was developed based on a novel procedure for gastric submucosal tumors called laparoscopic and endoscopic cooperative surgery (LECS), which was reported in 2008 by Hiki et al. [7]. LECS-CR has an advantage over conventional laparoscopic blind wedge resection in its capability of determining and achieving an appropriate and safe margin from the tumor via direct endoscopic intraluminal visualization. In addition, LECS-CR may be less invasive in comparison to conventional laparoscopic colorectal resection, which is commonly used to treat tumors that are difficult to resect endoscopically. Thus, in the present study, we retrospectively investigated the short-term outcomes of LECS-CR in comparison to conventional laparoscopic surgery (CLS).

## Methods

This was an observational study of consecutive patients undergoing LECS-CR or CLS for mucosal colorectal cancer or adenoma and submucosal tumors. A retrospective analysis of prospectively collected data was performed. Data were collected on specific data sheets and stored in a prospectively maintained database using the Microsoft Excel software program. The study was approved by our local institutional review board and all of the patients gave their written consent for the use of data from their medical records in the present study (UMIN000017503).

## Patients

Six thousand one hundred forty-six colorectal tumor patients underwent radical surgery at the Department of Gastroenterological Surgery of Cancer Institute Hospital (CIH) between January 2004 and December 2017. Among these, 83 patients were diagnosed with mucosal cancer or adenoma and submucosal tumor (SMT). LECS-CR was indicated and performed in 15 of the 83 cases between 2011 and 2017. The reasons for choosing surgical resection included a tumor surrounded by multiple diverticula, a tumor located in the appendiceal orifice, the presence of scar tissue caused by previous endoscopic mucosal resection, or SMT (Table 2).

## Operative techniques

CLS was performed by experienced surgeons certified by the Japan Society for Endoscopic Surgery. LECS-CR was performed by one experienced surgeon and some experienced endoscopists. We previously reported the procedure for LECS-CR [6].

## LECS-CR

After confirming the tumor's location by endoscopy and laparoscopy, a hook knife with water-jet system (Olympus, Tokyo, Japan) was used for ESD. A full-thickness incision of the colon wall was created cooperatively using both endoscopic and laparoscopic approaches. The resected specimen was retrieved intraluminally using an endoscopic forceps. The colon wall defect was then closed in an axial direction using multiple linear staplers.

## Outcome measurements

The primary outcome of interest was intraoperative adverse events. This was scored according to the National Cancer Institute Common Terminology Criteria for Adverse Events, version 5.0 [8]. Postoperative complications within 30 days were stratified according to the Clavien–Dindo classification system. Operative time, blood loss, and length of hospital stay were also compared between the two groups [9].

Anastomotic leakage was diagnosed by computed tomography (CT) and enema as well as associated clinical signs. Surgical site infection was defined as wound pain associated with fever ( $> 38.5$  °C), leukocytosis ( $> 11 \times 10^9$  white blood cells/L), or imaging findings of local inflammation or pus collection within the wound associated with the need for treatment.

## Statistical analysis

Data extraction and statistical analyses were performed using JMP® 14 (SAS Institute Inc., Cary, NC, USA). Continuous variables are described as the median (range) and were compared using Student's *t* test or the Mann–Whitney *U* test, depending on their distribution. Categorical variables are described as percentages and were compared using the  $\chi^2$  test.

Univariate analyses were used to determine differences in preoperative variables based on whether patients underwent LECS-CR or CLS. A multivariate logistic regression model was used to compare the outcomes of LECS-CR versus conventional laparoscopic surgery. Preoperative factors for which a significant difference between the cohorts

was identified by a univariate analysis were included in the multivariate logistic regression model. *P* values of <0.05 were considered to indicate statistical significance, and 95% confidence intervals (CIs) were described for all odds ratios (ORs).

## Results

### Patient characteristics

The demographic characteristics of the patients in this series are summarized in Table 1. The median age, gender, body mass index, tumor location, history of abdominal surgery, and preoperative carcinoembryonic antigen level did not differ between the two groups. The median tumor size was smaller in the LECS group ( $p = 0.005$ ). The LECS group included two submucosal tumors. The median follow-up period was 12 months (95% CI 0.6–41.8 months) in the

LECS group and 52.5 months (95% CI 13–89.5 months) in the CLS group.

The indications for LECS are presented in Table 2. The most frequent reason for performing LECS was the tumor location. The tumor was located on the appendiceal orifice in six cases and in the diverticulum in three cases. Four cases had severe fibrosis after previous endoscopic resection. These cases were diagnosed as having adenoma or cancer

**Table 2** Indications for LECS

Cause	<i>N</i>
Location	9
Appendiceal orifice	6
Diverticulum	3
Fibrosis	2
Scar	2
SMT	2

SMT submucosal tumor

**Table 1** The clinicopathological characteristics of the patients

	LECS <i>N</i> = 15	Conventional laparoscopic surgery <i>N</i> = 68	<i>P</i> value
Age (years)	64 (50–77)	68 (21–86)	0.96
Gender			0.51
Male	10	39	
Female	5	29	
BMI (kg/m <sup>2</sup> )	22.9 (18.4–30.3)	22.5 (14.9–30.5)	0.22
Location			0.53
Cecum	6	28	
Ascending colon	4	15	
Transverse colon	3	10	
Descending colon	1	1	
Sigmoid colon	0	7	
Upper rectum	1	5	
Lower rectum	0	2	
Tumor size (mm)	20 (5–33)	34 (6–90)	0.005**
Final pathology			0.0004**
Adenoma	3	9	
Sessile serrated adenoma	1	0	
Mucosal cancer	5	57	
Cartinoid	1	0	
Schwannoma	1	0	
Prior abdominal surgery			0.62
Yes	7	27	
No	8	41	
CEA (ng/mL)	2.1 (1.3–3.9)	2.2 (0.5–7.1)	0.75

BMI body mass index, CEA carcinoembryonic antigen, LECS laparoscopic endoscopic cooperative surgery

\* $P < 0.05$

\*\* $P < 0.01$

on the fibrosis or scar. Two SMT cases met the criteria for LECS-CR.

### Surgical outcomes

The surgical outcomes are shown in Table 3. The median operating time was 182 min (range 127–255 min) in the LECS group and 174.5 min (range 52–410 min) in the CLS group ( $p=0.96$ ). The median estimated blood loss was 5 mL (range 3–40 mL) in the LECS group and 10 mL (range 3–555 mL) in the CLS group ( $p=0.20$ ). En bloc resection was achieved for all cases in both groups without conversion to open surgery. The median time to solid diet intake was the same in both groups (2 days,  $p=0.39$ ). Conversely, the median duration of hospital stay after surgery in the LECS group (6 days; range 4–12 days) was significantly shorter than that in the CLS group (10 days; range 5–68 days) ( $p=0.01$ ). Clavien–Dindo grade  $\geq 3$  postoperative complications only occurred in the CLS group (2 cases,  $p=0.37$ ). When all grades of complication were included, postoperative complications still only occurred in the CLS group (6 cases,  $p=0.11$ ).

The median maximum C-reactive protein (CRP) level after surgery tended to be lower in the LECS group ( $p=0.07$ ); however, the difference was not statistically significant. Similarly, the median maximum white blood cell (WBC) count after surgery did not differ between the groups to a statistically significant extent ( $p=0.53$ ). Recurrence was only noted in the CLS group (1 case,  $p=0.53$ ). The inflammatory biomarker levels of the two groups, which were

measured for several days after surgery, did not differ to a statistically significant extent (Fig. 1).

### Discussion

To the best of our knowledge, this is the first study evaluating the short-term outcomes of LECS-CR and CLS. After analyzing the data for the enrolled patients, the median duration of hospital stay after surgery was found to be shorter in the LECS group, whereas Clavien–Dindo grade  $\geq 3$  postoperative complications were only observed in the CLS group.

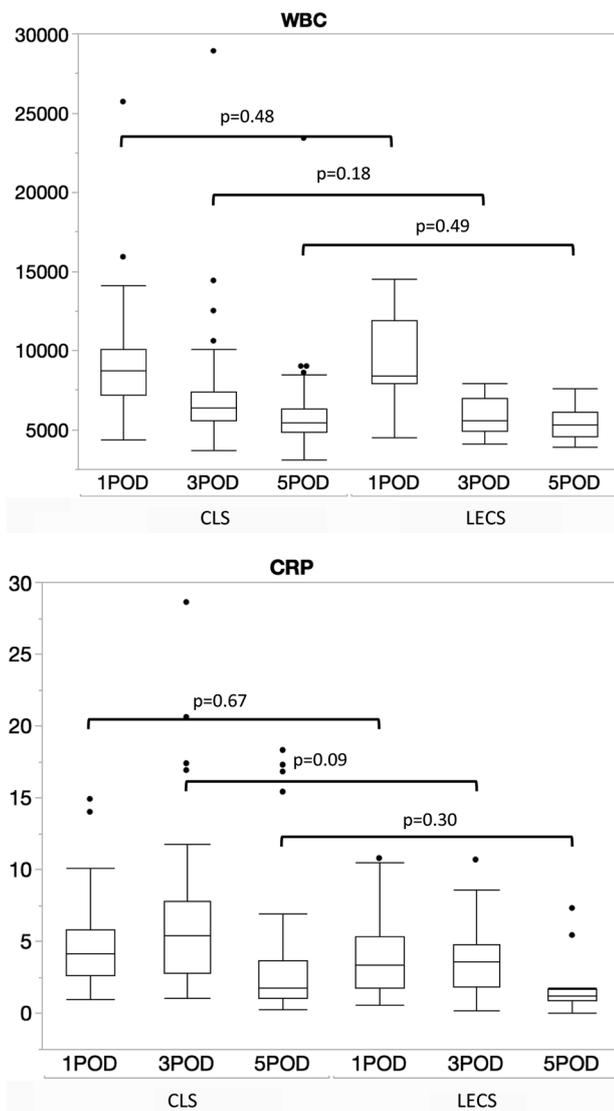
Polyps are regarded as endoscopically unresectable mostly based on their location and size. To overcome these issues, a novel laparoscopic-assisted polypectomy technique called combined endoscopic and laparoscopic surgery (CELS) was first described in 1993 [10]. The largest study of this technique to date, which was performed by Franklin and Portillo, included the long-term follow-up of 160 patients with 209 polyps. After a median follow-up period of 65 months (range, 6–196 months), no completely resected polyps showed signs of recurrence [11]. Endoscopic full-thickness resection (EFTR) is another procedure using an over-the-scope technique for polyps that are judged to be slightly difficult to resect by endoscopy alone. Schmidt et al. [12] conducted a prospective multicenter study of EFTR and concluded that EFTR has reasonable technical efficacy with acceptable complication rates. However, they reported that the curative resection rate for early cancers was too low to recommend its primary use. Thus, there is a need to develop

**Table 3** Perioperative findings

	LECS <i>N</i> = 15	Conventional laparoscopic surgery <i>N</i> = 68	<i>P</i> value
Operation time (min)	182 (127–255)	174.5 (52–410)	0.96
Blood loss (mL)	5 (3–40)	10 (3–555)	0.20
Conversion, <i>n</i> (%)	0 (0)	1 (1.5)	0.53
En bloc resection, <i>n</i> (%)	15 (100)	68 (100)	–
Time to solid diet administration (days)	2 (2–6)	2 (2–41)	0.39
Hospital stay after surgery (days)	6 (4–12)	10 (5–68)	0.01*
Complications			
(Clavien–Dindo Grade $\geq 3$ ), <i>n</i> (%)	0 (0)	2 (2.9)	0.37
(Clavien–Dindo Grade $\geq 1$ ), <i>n</i> (%)	0 (0)	6 (8.8)	0.11
Anastomotic leakage	0 (0)	2 (2.9)	
Surgical site infection	0 (0)	3 (4.4)	
Chylous ascites	0 (0)	1 (1.5)	
Maximum CRP after surgery (mg/dL)	3.6 (0.58–11)	5.7 (1.4–28.6)	0.07
Maximum WBC after surgery ( $\mu$ L)	8400 (4500–13,660)	8850 (4400–28,900)	0.65
Recurrence, <i>n</i> (%)	0 (0)	1 (1.5)	0.53

LECS laparoscopic–endoscopic cooperative surgery, CRP C-reactive protein, WBC white blood cells

\* $P < 0.05$



**Fig. 1** Inflammatory biomarkers in the postoperative course

and assess better resection techniques for such cases. Overall, LECS-CR was found to be an effective surgical approach for endoscopically unresectable polyps in the present study.

Although laparoscopic colectomy is associated with less invasiveness, less pain, quicker recovery of the bowel function, and a faster return to daily life in comparison to open colectomy [13], laparoscopic segmental colectomy still associated with considerable morbidities, including anastomotic leakage, bleeding, and small bowel obstruction. It is, therefore, important to avoid unnecessary bowel resection when a tumor is benign or in a very early cancer stage and is expected to be curable by endoscopic resection.

CELS is reported to be associated with a success rate of 80.9% [7]; in contrast, the success rate of LECS-CR in our study was 100%. This difference could be attributable to

the different technical concepts in use: CELS is based on polypectomy, whereas LECS-CR is based on ESD, which is a far superior to polypectomy in terms of its ability to obtain a sufficient margin.

In one paper, EFTR was reported to have a technical success rate of 89.5% and an R0 resection rate of 76.9% [12]; these rates are far lower in comparison to those of LECS-CR in the present study such as 100%. In addition, the same paper demonstrated that the adverse event rate after EFTR was very high (9.9%); 2.2% of the cases required emergency surgery, and a recurrent/residual tumor was evident in 15.3% of cases. Thus, they concluded that the curative resection rate for early cancers was too low to recommend its primary use [12]. Additionally, EFTR for polyps on the appendiceal orifice has the potential to cause acute appendicitis [12].

General complications associated with ESD are bleeding and perforation. Bleeding, with an incidence of up to 7% [14], is the most common complication, but it is rarely serious. However, this issue can be overcome by laparoscopic confirmation and by arresting the bleed using an energy device or stapler during LECS-CR. The incidence of colonic perforation after ESD is reported to be 5–10% [15]. In the LECS-CR procedure, a full-thickness incision is intentionally performed, and the colonic defect is securely closed by staplers. Because of the cooperatively endoscopic procedure in LECS-CR, an air leak test is simultaneously carried out. When leakage is detected, it can be closed laparoscopically by suturing or additional stapling. We also consider a hand-sewn approach for the closure of colonic defects. However, this approach takes longer than closure by staplers and is consequently associated with a higher risk of intra-abdominal contamination. Because we took care to avoid intra-abdominal contamination, the inflammatory biomarker levels did not show a considerable increase in the LECS-CR group.

While performing LECS-CR, three other points need to be considered. Firstly, there is a risk of stenosis after closing the colonic defect using staplers. It is generally important to ensure that the staple line for closure runs axially to the colon. Thus, the two edges of the staple line should be carefully determined to ascertain the axial direction before stapling and should be subsequently stitched to ensure that the sutures remain in place. No stenosis was found on follow-up colonoscopy in the present study. Second, care should be taken to avoid colonic ischemia. In particular, for lesions located on the mesenteric aspect, several blood vessels to the related part of the colon should be divided. When portions of the lesion are not similar internally and externally, the arteries supplying different parts of the lesion are divided to cause partial colonic ischemia. It is important to align the site of the lesion internally and externally. In our series, there were no cases of ischemia that resulted in leakage or stenosis. Third, issues may occur related to the intentional

perforation in this procedure. Oncologically, peritoneal seeding is a concern if the lesion is a mucosal cancer. Lifting up the surrounding wall before opening the wall is important to avoid spilling the contents of the large bowel into the abdominal cavity. Another measure for the prevention of seeding is washing out the lumen with adequate amounts of saline solution before opening the wall. There was no recurrence due to peritoneal seeding in our case series. In addition, no abdominal abscesses due to bacterial exposure were observed after this procedure in our study, which may also be a result of the abovementioned measures. In two cases, excessive spillage of lavage fluid from the colon resulted in an increased CRP level ( $> 10$  mg/L). Thus, the prevention of intra-abdominal contamination is very important.

In the current study, we investigated and compared some factors representing the invasiveness of the surgery between LECS-CR and CLS. The avoidance of segmental bowel resection contributes to a significantly shorter hospital stay and reduces the incidence of postoperative complications. Postoperative ileus, including bowel paralysis, is likely to occur in conventional procedures. However, it is not encountered in LECS-CR cases. Unfortunately, the inflammatory changes after LECS-CR were not reduced in comparison to those after CLS in this study; however, favorable trends may have existed and are expected in the future.

The most common reason for LECS-CR was the tumor location, which was the appendiceal orifice in six of nine cases. In these circumstances, CLS (e.g., laparoscopic cecectomy) is generally considered. However, it is difficult to achieve a safe margin with CLS because of the lack of intraluminal visualization. In fact, negative margins were only achieved in two cases in the CLS group.

There was a significant difference in the tumor diameter between the two groups. Although the size of the tumor is not a contraindication for surgery, the diagnosis of the depth becomes more difficult when the tumor is larger. These factors should be considered before performing this procedure. However, the short-term results of this procedure may be purely due to technical differences rather than the size of the tumor.

This study was associated with several limitations. First, it was a single-center retrospective study, and a randomized controlled trial was not conducted. Second, the sample size was small. Third, the median follow-up period of the LECS-CR group was shorter than that of the CLS group and could have been inadequate for the assessment of the long-term oncological effectiveness of the procedure, in terms of recurrence. Thus, the study cannot be termed a comparative study. Fourth, five cases in the LECS-CR group were diagnosed with cancer through the final pathological examination. These patients need to be assessed by cytoscreening of intra-abdominal fluid after LECS-CR. Finally, the difference in demographic characteristics between the two groups, in

particular the higher prevalence of malignancy in the CLS group, could have influenced the results.

In conclusion, LECS-CR was performed safely and with reasonable operation times, less bleeding, and an acceptable and favorable complication rate in comparison to conventional segmental colonic resection. No patients experienced recurrence after LECS-CR. To the best of our knowledge, this is the first report to demonstrate the feasibility and safety of LECS-CR for the resection of endoscopically unresectable laterally spreading colorectal tumors and submucosal tumors. Larger randomized case–control comparative studies should be designed to validate the benefits of this procedure.

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### Compliance with ethical standards

**Conflict of interest** The authors declare no conflict of interest in association with the present study.

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