

ORIGINAL ARTICLE

## AN INITIAL INSTITUTIONAL APPRAISAL OF LAPAROSCOPE-ASSISTED COLECTOMY FOR EARLY COLORECTAL CANCER

Hajime Morohashi, Akihiko Murata, Motoi Koyama, Yoshiyuki Sakamoto,  
Shinji Tsutsumi, Shinnosuke Yonaiyama, Hiroshi Ogasawara, Toru Yoshikawa,  
Takahiro Muroya, Makoto Nakai, Keinosuke Ishido,  
Naoki Wajima and Kenichi Hakamada

**Abstract Introduction:** The employment of laparoscopic resection for the treatment of colorectal cancer has been expanding rapidly. However, its indication is still on debate. We have been actively employing laparoscope-assisted colectomy (LAC) for patients with early colorectal cancer. Here we retrospectively review the 71 cases of early colorectal cancer treated with LAC and analyzed the initial institutional surgical outcome.

**Results:** LAC was indicated as an additional surgical resection after endoscopic treatment in 27 cases, while it was employed as a definitive non-endoscopic treatment in 44 cases. Mean operative time was 163 min, and mean blood loss was 57 ml. Complications were encountered in 8 cases (11.3%). Advanced lesions invading to the muscularis propria or the serosa were more included in the group initially treated with LAC alone ( $p=0.04$ ). The reasons for additional LAC were the depth of submucosal invasion  $>1000\ \mu\text{m}$  in 15 cases and lymphatic or microvascular invasion in 5 cases. Lymph node metastases were detected pathologically in 9 patients, in which one suffered relapse after surgery.

**Conclusion:** Implementation of LAC for early colorectal cancer seems an acceptable strategy in terms of both radicality and less invasiveness. Cooperation between endoscopists and laparoscopic surgeons is important to apply LAC appropriately for colorectal cancer.

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**Key words:** laparoscope-assisted colectomy; early colorectal cancer.

原 著

### 当科における早期大腸癌に対する腹腔鏡下大腸切除症例の検討

諸 橋 一 村 田 暁 彦 小 山 基 坂 本 義 之  
堤 伸 二 米 内 山 真 之 介 小 笠 原 紘 吉 川 徹  
室 谷 隆 裕 中 井 款 石 戸 圭 之 輔 和 嶋 直 紀  
袴 田 健 一

**抄録** 【目的】大腸癌に対する腹腔鏡手術は急速に拡大しているが、その適応については議論が多い。当科では早期大腸癌症例に対して積極的に腹腔鏡下大腸切除術を導入している。そこで、術前早期大腸癌と診断され腹腔鏡補助下大腸切除術を施行した71症例を対象として当施設の初期治療成績を後方視的に検討した。【結果】内視鏡的切除後腹腔鏡下大腸追加切除施行群は27例、内視鏡切除非施行腹腔鏡下大腸切除群は44例であった。平均手術時間は163分、平均出血量は57 ml、合併症は8例(11.3%)であった。深達度は内視鏡切除非施行群で術後筋層以深と判明した浸潤癌が多く認められた( $p=0.04$ )。内視鏡切除後腹腔鏡下大腸追加切除理由は、 $1000\ \mu\text{m}$ 以上のsm浸潤癌が14例、脈管浸襲陽性が5例であった。術後のリンパ節転移陽性例は全体で9例あり1例に再発が認められた。【結語】早期大腸癌に対する腹腔鏡下大腸切除は、根治性と低侵襲性の両面から妥当と考えられた。この場合、特に内視鏡医と腹腔鏡手術医との連携が重要である。

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**キーワード:** 腹腔鏡補助下大腸切除; 早期大腸癌.

Department of Gastrointestinal Surgery, Hirosaki  
University Graduate School of Medicine  
Correspondence: K. Hakamada  
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## Introduction

Along with advancement of endoscopic diagnostics for colorectal cancer and its wider use in both medical check-ups and clinical settings, the incidence of colorectal cancer found in earlier stage has been increasing in both Japan and USA<sup>1)</sup>. The latest 2010 version of the Guidelines for the Treatment of Colorectal Cancer by the Japanese Society for Cancer of the Colon and Rectum<sup>2)</sup> now recommends that endoscopic excisional biopsy, either endoscopic mucosal resection (EMR) or endoscopic submucosal dissection (ESD), should be done as a first-step treatment modality if the lesions are estimated to be limited to mucosa or within submucosa to some extent<sup>3)</sup>. However, in cases that endoscopic treatment seems technically difficult from anatomical reasons or in cases that endoscopic excision seems not feasible because pretreatment endoscopy demonstrates the sign of massive invasion to the submucosa or deeper layer<sup>4)</sup>, surgery still has its role as the definitive treatment modality. Moreover, in cases that the depth of lesion is underestimated by the initial endoscopic evaluation and later found to exceed the submucosa pathologically, additional surgical resection is adopted as a rescue therapy because lymph node metastasis occurs in as high as 10% if the lesions invades to the deeper submucosal layer<sup>5)</sup>.

As for surgical procedure, laparotomy is still the standard approach of radical resection for colorectal cancer. Recently, various kinds of minimally invasive surgeries like laparoscope-assisted colectomy<sup>6, 7)</sup> and hand-assisted laparoscopic colectomy<sup>8)</sup> have been developed to reduce patients' burden associated with damage to the abdominal wall<sup>8)</sup>. These procedures are preferred especially in cases with earlier stage in which cancer is not exposed to the serosal surface and complete lymph node clearance can be achievable. However, the

efficacy of laparoscopic approach in comparison to open surgery is still on debate. We have been actively employing laparoscope-assisted colectomy (LAC) for early colorectal cancer together with open colectomy. We herein review the medical records of patients undergoing LAC for early colorectal cancer retrospectively and analyzed the initial institutional surgical outcome during the learning curve.

## Patients and Methods

Between October 2001 and November 2010, 71 patients diagnosed as having early colorectal cancer preoperatively underwent LAC at Hirosaki University Hospital. Early colorectal cancer was defined as the lesion limited to the mucosa or within the submucosa and that without any distant metastasis. The preoperative diagnostic methods included colorectal endoscopy and multi-detector row computed tomography in all cases. Other image studies like PET-scan or MRI were adopted in some patients when indicated. The clinical and pathological records of all 71 patients were reviewed in terms of gender, age, tumor location, tumor size, implementation of preoperative endoscopic treatment (EMR or ESD), operative time, blood loss, degree of lymph node clearance, histological differentiation, depth of invasion, presence of vascular invasion, presence of lymph node metastasis, operative morbidity and mortality, and length of hospital stay. Late recurrence was also evaluated.

Principally, the lesions were evaluated by the endoscopists first. They allocated each case to either endoscopic treatment or surgical resection as an initial intervention according to the technical feasibility and the tumor extension. Additional surgical resection after endoscopic treatment was indicated for cases with positive specimen margin, presence of microscopic vascular or lymphatic invasion, or

**Table 1** Patient Data (N = 71)

Gender	Male 34 (47.9%), Female 37 (52.1 %)
Age	63.6 (39-85)
Tumor location	
Cecum	6(8.5%)
Ascending colon	15(21.1%)
Transverse colon	8(11.3%)
Descending colon	2(2.8%)
Sigmoid colon	20(28.2%)
Rectosigmoid colon	14(19.7%)
Rectum above the peritoneal reflection	3(4.2%)
Rectum below the peritoneal reflection	3(4.2%)
Preoperative EMR or ESD	(+) 27 (38.0%), (-) 44 (62.0%)
Operation	
Degree of lymph node dissection*	D1 15, D2 54, D3 1
Operative time	163 min (53-455min)
Blood loss	57 ml (0 - 514ml)
Outcome	
Morbidity	(+) 8 (11.3%), (-) 63 (88.7%)
Mortality	0
Length of hospital stay	10.0 days (3-21 days)

\*According to the Japanese Classification of Colorectal Carcinoma

EMR : endoscopic mucosal resection ESD : endoscopic submucosal dissection

depth of submucosal invasion more than >1000  $\mu\text{m}$  according the Guideline<sup>2)</sup>. In all cases, the detailed reasons why LAC was performed as an initial step without endoscopic intervention or as additional surgical resection were analyzed.

## Results

Of the 71 patients who underwent LAC, 34 were male and 37 were female. The mean patient age was 63.6 years. Fifty-one patients (71.8%) had colon cancer and 20 (28.2%) had rectal cancer. Sigmoid colon was the most prevalent site (28.2%). Forty-four (62.0%) patients underwent LAC as an initial treatment, while 27 (38%) were converted to LAC according the results from EMR or ESD. Degree of lymph node clearance was D1 in 15 cases (21.1%) and D2 in 54 cases (76.1%). Mean operative time was 163 (53-455) min, with a mean blood loss of 57 (0-514) ml. Postoperative complications were encountered in 8 cases (11.3%); wound infection in 4, intestinal obstruction in 2, intra-pelvic abscess in 1, and

anastomotic failure in 1 case (Table 1).

The depth of invasion in patients diagnosed as having early cancer preoperatively and undergoing LAC as a first step treatment was underestimated in 13 (29.5%), in which the lesions invaded to muscularis propria in 9 and to subserosa in 4 cases. Consequently, stages of the two groups were different according to the implementation of preoperative endoscopic treatment or not. However, histological features including cancer differentiation, presence of vascular or lymphatic invasion, and presence of lymph node metastasis were not different between the two groups (Table 2). The reasons why endoscopic treatments were skipped before LAC were signs of massive submucosal invasion in 27 patients (61.4%), a tumor size of >20 mm in 13 (29.5%), technical difficulty in 2 (4.5%), and unfavorable histology of undifferentiated adenocarcinoma in 1 (2.3%) (Table 3). The reasons for surgical resection after endoscopic treatment included submucosal invasion exceeding 1000  $\mu\text{m}$  in 14 cases (51.9%), and microvascular and/or lymphatic invasion

**Table 2** Tumor profile in patients undergoing LAC with or without preoperative endoscopic treatment.

	LAC after endoscopic treatment N=27 (Colon : 16 Rectum : 11)				LAC alone N=44 (Colon : 20 Rectum : 24)				P value
Macroscopic type*	Ip : 4	Is :5	Isp :10	IIa :4	Is : 9	Isp:9	IIa : 3	IIa+IIc:5	0.48
Maximum size	13.6 (4-28) mm				22.1 (7-58) mm				0.09
Cancer differentiation	tub1: 16		tub2: 10		tub1: 13		tub2: 10		0.36
Depth of invasion	sm:27 <1000 $\mu$ m: 4 (14.8%) >1000 $\mu$ m:23 (85.2%)				m : 8    sm:23    mp : 9    ss : 4				0.04
Positive margin with endoscopic treatment	(+) : 4 (14.8%)		(-) : 23 (85.2%)						
Lymphatic invasion*	ly0: 18	ly1 : 3	ly2 : 1		ly0 : 27	ly1 :10	ly2 : 4	ly3 :3	0.17
Vascular invasion*	v0: 16	v1 : 5	v2 : 2		v0: 30	v1: 9	v2: 3	v3: 2	0.45
Lymph node involvement	(+) : 2 (7.4%)		(-) : 25 (92.6%)		(+) : 7 (15.9%)		(-) : 37 (84.1%)		0.21

\*According to the Japanese Classification of Colorectal Carcinoma

tub1: well-differentiate tubular adenocarcinoma, tub2: moderately differentiated tubular adenocarcinoma

sm: submucosa, m: mucosa, mp: muscularis propria, ss: subserosa

**Table 3** The reason for LAC without preoperative endoscopic treatment (N=44)

	Number
Sign suggestive of deep submucosal invasion	27 (61.4%)
Larger size (>20mm)	13 (29.5%)
Undifferentiated carcinoma	1 (2.3%)
Technical difficulty	2 (4.5%)
Others	1 (2.3%)

**Table 4** The reasons for LAC after endoscopic treatment (N=27)

	Number
sm invasion >1000 $\mu$ m	14 (51.9%)
Microvascular and/or lymphatic invasion	5 (18.5%)
Positive specimen margin	4 (14.8%)
Undifferentiated carcinoma	1 (3.7%)
Local recurrence after EMR	3 (11.1%)

in 5 cases (18.5%). Four patients (14.8%) were specimen margin-positive, 3 patients (11.1%) suffered from local recurrence after EMR, and 1 patient (3.7%) had undifferentiated adenocarcinoma (Table 4).

Lymph node metastases were detected pathologically in 9 patients with their extent being N1 in 7 and N2 in 2. Histological features of their primary tumors were moderately differentiated adenocarcinomas (tub2) in 7 (77.8%), presence of lymphatic invasion in

6 (66.7%) and microvascular invasion in 5 (55.6%). During the observation period, about 10 months after surgery, recurrence occurred in one patient whose cancer had invaded to the subserosal layer of the rectosigmoid colon and metastasized to N2 lymph node (Table 5).

## Discussion

Laparoscopic surgery has been applied to the treatment of almost all colorectal diseases,

**Table 5** Nine cases with positive lymph node metastasis

No	Age	Sex	Site*	Morphological type*	Size (mm)	Histology*	Depth*	ly*	v*	Number of positive lymph node	N*	Preoperative EMR/ESD	D*	Recurrence
1	59	F	S	Is	8	tub1	sm	ly0	V1	3	N1	EMR	D2	(-)
2	56	F	S	Is	5	tub2	sm	ly0	V0	1	N1	EMR	D2	(-)
3	72	M	RS	2	30	tub2	mp	ly3	V1	4	N2	(-)	D2	(-)
4	63	F	A	Isp	30	tub1	sm	ly0	V0	1	N1	(-)	D1	(-)
5	55	F	RS	Is	14	tub2	mp	ly1	V3	1	N1	(-)	D2	(-)
6	50	F	RS	2	30	tub2	ss	ly1	V0	4	N2	(-)	D2	(+)
7	64	F	D	Ila	16	tub2	mp	ly1	V0	1	N1	(-)	D2	(-)
8	73	M	S	2	21	tub2	mp	ly1	V1	1	N1	(-)	D2	(-)
9	82	F	A	1	13	tub2	mp	ly2	V1	1	N1	(-)	D2	(-)

\*According to the Japanese Classification of Colorectal Carcinoma

S: sigmoid colon, RS: rectosigmoid, A: ascending colon, D: descending colon, ly: lymphatic invasion, v: vascular invasion, N: degree of lymph node metastasis, D: degree of lymph node dissection

either benign or malignant, since Jacobs et al.<sup>9)</sup> first introduced it as an alternative procedure to the conventional open surgery in 1991. Indeed, minimum invasiveness to the abdominal wall has an absolute cosmetic benefit and probably shows accelerated postoperative recovery due to less pain<sup>6, 7)</sup>. However, this approach has also been criticized for technical difficulties which require much more operative time and may predispose an increased risk of procedure-specific complications.

In our institutional learning curve, operative time elongated to a mean of 163 min, while blood loss was as minimum as 57 ml. Operative morbidity of 11% with zero mortality and a mean hospital stay of 10 days were comparable to those of open surgery at the same period (data not shown). Lourenco et al.<sup>10)</sup> also reported shorter length of hospital stay and earlier recovery associated with less blood loss, although the operative time became longer than that of open surgery. They described no significant difference in the incidence of anastomotic failure and wound infection between the two arms. Hasegawa et al.<sup>11)</sup> reported the operative morbidity of 14.3%, with the incidences of wound infection, intestinal obstruction, intraabdominal abscess and anastomotic failure being 8.2%, 2.2%, 1.1%,

and 2.9%, respectively, which were very similar to those in our hospital. So far, we have not experienced late occurrence of incisional hernia at the port sites, which are unique to the laparoscopic approach<sup>12)</sup>.

In addition to procedure-related outcomes, oncological aspects of LAC are another major concern. In our initial experience, recurrence was observed in one case, the tentative recurrence rate being 1.4%. This case was underestimated as early cancer first. However, it was later found that tumor cells invaded to the serosal layer and metastasized to the N2 lymph node. So it remains unclear whether the recurrence occurred due to oncological features of more advanced stage or due to procedure-related problems. There are some reports that both recurrence and survival rates after LAC are the same as those of conventional laparotomy<sup>13-15)</sup>. Indeed the long-term outcome should be discussed according to randomized control trials (RCTs) between LAC and open surgery. According to the meta-analysis of 3346 patients from 23 RCTs<sup>16)</sup>, rates of recurrence at the site of the primary tumor were similar (colon cancer: 4 RCT, 938 pts, 5.2% vs 5.6%,  $p=0.57$ ; rectal cancer: 4 RCT, 714 pts, 7.2% vs 7.7%,  $p=0.46$ ). No differences were observed in the occurrence of port-site/wound recurrences

( $p=0.16$ ), and similar cancer-related mortality was found after laparoscopic surgery compared to open surgery (colon cancer: 5 RCT, 1575 pts, 14.6% vs 16.4%,  $p=0.15$ ; rectal cancer: 3 RCT, 578 pts, 9.2% vs 10.0%,  $p=0.16$ ).

However, these analyses included different stages of tumors in different series of learning curves. Five-year survival of 50% in Stage III of these analyses seems lower when compared to the historical data from Japan<sup>2</sup>). Theoretically, LAC is more technically feasible in early cancer, because of less possibility of procedure-related tumor dissemination and less incidences of distant lymph node metastases. The Japanese Guideline 2010 now recommends that LAC should be carefully applied according to the institutional availability of skilled surgeons, the precise preoperative staging (invading depth is mucosa or submucosa and lymph node metastasis is not pointed out) and the appropriate tumor location technically feasible to the laparoscopic approach. Taking these issues into account, we decided to implement LAC for early stage colorectal cancer first. In a learning curve, Left sided colectomy was performed in more than 50% cases because of its technical easiness.

Another reason why we indicated LAC for early cancer is increased numbers of colorectal cancer diagnosed in earlier stage. This may be due to a rapid expansion of the use of endoscopy as a routine diagnostic tool after positive occult blood at the medical check-up in Japan<sup>1</sup>). Endoscopic approach, either EMR or ESD, is used for both diagnostic and treatment purposes. Favorable outcome by the endoscopic intervention would be expected if the tumor is in a controllable size and shows the features indicating less possibility of lymph node metastasis. Japanese Guideline 2010 advocates that invasion to the deeper submucosal tumor more than 1000  $\mu\text{m}$ , presence of microvascular and lymphatic invasion, unfavorable histology

with poorly differentiation and presence of budding<sup>17</sup>) at the invasive front increase the risk for regional lymph node involvement as high as 10%, and thus recommends that additional surgical resection should be performed to eradicate enough lymph nodes<sup>2, 5</sup>). Indeed, 7.4% (2/27) of cases treated additional LAC according to this criteria showed lymph node metastases in our series. In turn, the majority of the patients with early colorectal cancer have tended to undergo unnecessarily invasive surgery for lymph node clearance. Therefore, we have to reduce excess patients' burden by balancing radicality and invasiveness of each surgical procedure. LAC is an ideal treatment in this respect.

Another role of LAC is a definitive treatment for the cases that endoscopic intervention is not feasible. In high risk cases with lymph node metastasis as indicated above criteria, LAC must be a better approach because EMR and ESD cannot control the lesion outside the intestinal wall absolutely. Moreover, because of limitation in diagnostic power of endoscopy, these cases suggestive of deeper submucosal invasion are potentially advanced, in which the role of lymph node dissection becomes more important. In our series, endoscopy underestimated in 30% (13/44) of cases, in which preoperative diagnoses of submucosal lesions were later found to be invaded to the muscularis propria or the subserosal layer. We should not hesitate to adopt LAC if such ominous signs indicating lymph node metastasis or deeper invasion are demonstrated by endoscopy.

In summary, our initial experience has shown that LAC is an acceptable and perhaps preferable alternative to conventional open surgery for early colon cancer, with both comparable procedure-related short-term results and oncological outcomes. Implementing LAC for early cancer first seems to be an acceptable strategy to develop a new institutional

program of laparoscopic colorectal surgery. Anyway, cooperation between endoscopists and laparoscopists is very important for expanding the indications of LAC appropriately.

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