**Table 4.** Colorectal carcinoma: multivariate analysis of factors predictive of cancer-specific survival

| Variable | Relative risk | 95% CI | *P* value |
|---|---|---|---|
| Peritoneal cytology | | | |
| Negative | 1 | | |
| Positive | 2.733 | 1.130–6.608 | 0.0256 |
| pN classification | | | |
| pN0 | 1 | | |
| pN1 | 1.341 | 0.616–2.919 | 0.4599 |
| pN2 | 4.252 | 1.923–9.404 | 0.0004 |

CI = confidence interval.

### Independent Prognostic Factors for Survival

Univariate analysis demonstrated that the cancer-specific and disease-free survivals of the patients investigated were significantly related to microscopic peritoneal dissemination and lymph node metastasis (Table 3). Multivariate analysis revealed that lymph node metastasis (pN2: $P = 0.0004$) followed by peritoneal cytology (positive: $P = 0.0256$) were independent predictors of cancer-specific survival (Table 4).

## DISCUSSION

Recently, several studies have demonstrated, in patients with colorectal carcinoma, the incidence of free malignant cells in the peritoneal cavity at the time of surgery and its prognostic significance by means of conventional cytology and immunocytology (7–12). On the other hand, Wind et al. (13) reported that conventional cytology provides no prognostic information in Dukes B and C patients and Vogel et al. (14) showed that there was no significant influence of microscopic peritoneal tumor cell dissemination on survival using conventional cytology and immunocytology in patients with colorectal carcinoma who underwent curative resection. However, the numbers of patients registered in these studies (66 and 64, respectively) are clearly limited and the follow-up period of the latter (median follow-up: 44.7 months) was not long enough to draw a definite conclusion. The results of the current study clearly demonstrated that conventional peritoneal cytology influences disease-free and cancer-specific survival after curative resection in patients with pT3/T4 colorectal carcinoma at the median follow-up of 103 months and it appears to be a useful diagnostic procedure to predict recurrence, especially peritoneal recurrence.

In the present study, only conventional peritoneal cytology was chosen as a means to detect cancer cells, because it is a universal and inexpensive method that can be easily performed at any institution worldwide (10). Moreover, the quality of the immunocytological methods on colorectal carcinoma was not fully established during the study period. However, one of the pitfalls of conventional cytology is that peritoneal inflammation can hinder the distinction between malignant cells and atypical or reactive mesothelial cells in body fluids (15,16). In the present study, patients with suspicious morphological evidence of malignancy by microscopy were included in the positive cytology group and it may account for the 45.5% (5/11) 'false-positive' rate on recurrence in the positive cytology group. Recently, several studies have demonstrated that immunocytology was more sensitive than conventional cytology for the detection of malignant cells and that it has greater specificity concerning prognosis (7,10,12). Technical advances now permit molecular detection of micrometastasis in lymph nodes and bone marrow in patients with colorectal carcinoma (17–20). Clearly, utilization of these newly developed technologies is indispensable for further investigation.

In summary, this study demonstrated that conventional peritoneal cytology serves as a new prognostic marker after curative resection in patients with pT3/T4 colorectal carcinoma. It appears to be a universal and inexpensive diagnostic procedure to predict recurrence, especially peritoneal recurrence, and would be useful for deciding adjuvant intraperitoneal and/or systemic chemotherapy. However, the utilization of newly developed methods, immunocytology and molecular technology, is necessary in further investigations.

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# Weekly Hepatic Arterial Infusion of 5-Fluorouracil and Subsequent Systemic Chemotherapy for Liver Metastases from Colorectal Cancer

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**Objective:** To determine the antitumor activity and toxicity of weekly hepatic arterial infusion (HAI) of 5-fluorouracil (5-FU) for liver metastases from colorectal cancer. In addition, the present study also evaluated the efficacy of second-line chemotherapy after termination of HAI.
**Methods:** A retrospective study was designed to evaluate the clinical outcome in patients treated with HAI. Twenty-six patients with liver metastases from colorectal cancer were treated with 5-FU 1000 mg/m$^2$ over 5 h once per week on an outpatient basis. The treatment was continued until disease progression, unacceptable toxicity or the patient's refusal to continue treatment occurred. One of three kinds of second-line systemic chemotherapy, irinotecan alone, protracted venous infusion of 5-FU or methotrexate (MTX) and 5-FU, was chosen after termination of HAI.
**Results:** An objective tumor response to HAI was observed in 46% (95% confidence interval, 26.9–65.2%) of 26 patients. The most common adverse events were mild nausea and vomiting (35%) and occurrence of gastroduodenal ulcers (15%). Hematological toxicity was minimal. No responder was observed to improve following second-line chemotherapy after termination of HAI.
**Conclusion:** Weekly HAI of 5-FU is both active and well tolerated. However, extrahepatic progression was observed in one-third of patients with termination of HAI and the efficacy of second-line chemotherapy was not demonstrated. Regional treatment with systemic chemotherapy should be conducted to achieve good results in terms of survival.

*Key words: hepatic arterial infusion – 5-fluorouracil – liver metastasis – colorectal cancer – second-line treatment*

## INTRODUCTION

Hepatic metastases are the most common visceral metastases from colorectal carcinoma and are observed in 18% of patients on initial diagnosis of their primary tumor and will occur in 60% of patients who subsequently develop advanced disease (1). Although hepatic resection is the only potentially curative treatment, the value of which has been proven with a 5-year survival rate of 25–35% (2), curative resection of liver metastases is possible in less than 25% (3).

For unresectable lesions, systemic 5-fluorouracil (5-FU) therapy is marginally active in prolongation of survival. The rationale for hepatic arterial infusion (HAI) is as follows. The normal liver has a dual blood supply. Liver metastases obtain most of their blood supply from the hepatic artery, whereas normal liver cells derive most of their blood supply from the portal vein (4). Hence direct hepatic arterial infusion increases drug concentrations at the tumor site, and at the same time decreases systemic drug exposure (5).

Prospective, randomized studies of patients with unresectable liver disease have reported response rates from 42 to 62% in the group given HAI, compared with rates of 10–21% in the groups treated with systemic chemotherapy (6–11). It is therefore common practice in Japan to perform continuous arterial infusion of 5-FU, because the response rate of HAI is significantly higher than that of systemic chemotherapy. An encouraging result was obtained from a phase II clinical trial of intermittent HAI with high-dose 5-FU (12), which demonstrated a response rate of 78% and a survival time of 25.8 months without any serious toxicities.

There have been few reports about the impact of second-line systemic chemotherapy in patients refractory to HAI. Hence the role of second-line chemotherapy is still unclear.

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The objectives of this study were to evaluate the antitumor activity and toxicity of weekly HAI of 5-FU for liver metastases from colorectal cancer and the efficacy of second-line chemotherapy after HAI.

## PATIENTS AND METHODS

### PATIENT ELIGIBILITY

Patients with liver metastases from colorectal carcinomas were eligible for this retrospective study if they had histologically confirmed and resected primary colorectal carcinoma, had at least one measurable lesion, had not had prior chemotherapy and had an Eastern Cooperative Oncology Group performance status of 0–2. Further entry criteria were adequate hepatic function (serum total bilirubin ≤2 mg/dl), adequate hematological function (white blood cells ≥4000/mm$^3$, platelets ≥100 000/mm$^3$) and adequate renal function (serum creatinine ≤1.5 mg/dl). Written informed consent was obtained from all patients.

### TREATMENT

A catheter was inserted into the hepatic artery via the subclavian artery for patients with metachronous metastases and into the gastroduodenal artery at the time of resection of the primary site for patients with synchronous metastases. The proximal end of the catheter was connected to an implanted port system. 5-FU was administered at a dose of 1000 mg/m$^2$ over 5 h once per week on an outpatient basis and this treatment was continued until the occurrence of disease progression, unacceptable toxicity or the patient's refusal to continue treatment. In all patients, gastrointestinal vessels were occluded with steel coils or ligated to preclude gastrointestinal tract perfusion. In addition, we confirmed the hepatic distribution of the drug and checked for the absence of extrahepatic perfusion using angiography by the port before HAI.

### SECOND-LINE SYSTEMIC CHEMOTHERAPY

In 17 (74%) patients who terminated HAI, systemic chemotherapy was performed. For patients refractory to HAI, we mainly administered irinotecan, and for patients who terminated HAI due to complications of the catheter system and gastroduodenal ulcer formation probably related to misdistribution of 5-FU, we administered either protracted venous infusion of 5-FU or MTX and 5-FU. Eleven patients were treated with irinotecan, three patients received protracted venous infusion of 5-FU and three patients MTX and 5-FU. The three treatment schedules were as follows:

(1) irinotecan 100 mg/m$^2$ given as a 90 min intravenous infusion weekly or irinotecan 150 mg/m$^2$ given as a 90 min intravenous infusion once every 2 weeks;
(2) 5-FU given as a protracted venous 24 h infusion at 250 mg/m$^2$ per day;
(3) MTX 100 mg/m$^2$ followed by 5-FU 600 mg/m$^2$ 3 h after MTX, each given every 2 weeks; all patients received leucovorin rescue, 10 mg/m$^2$ orally every 6 h for six doses, 24 h after MTX injection.

**Table 1.** Patients' characteristics ($n$ = 26)

| Characteristic | Patient data |
|---|---|
| Age (years) | |
| Median | 56 |
| Range | 32–80 |
| Gender | |
| Male | 16 |
| Female | 10 |
| Performance status | |
| 0 | 22 |
| 1 | 4 |
| Location of primary tumor | |
| Rectum | 9 |
| Colon | 17 |
| Metastases | |
| Synchronous | 15 |
| Metachronous | 11 |
| Tumor differentiation | |
| Well | 10 |
| Moderate | 16 |

### RESPONSE AND TOXICITY CRITERIA

Response to measurable and evaluable sites of disease was assessed by computed tomography (CT) before the beginning of HAI and every 4 weeks during treatment. Response and toxicity were evaluated according to the World Health Organization guidelines (13).

### STATISTICAL ANALYSIS

Overall survival was measured from the start of HAI to the date of death. The Kaplan–Meier method was used to estimate the overall survival curves (14). Survival time was censored at the close out date if the patients were alive.

## RESULTS

### PATIENTS' CHARACTERISTICS

Twenty-six patients with liver metastases from colorectal cancer were entered in this study between October 1995 and October 1999 at the National Cancer Center Hospital. All 26 patients had either unresectable liver metastases or recurrent liver metastases after surgery for primary tumor or liver metastases. Patients' characteristics before HAI are summarized in Table 1. Eleven patients had undergone previous surgery and 15 patients had unresectable liver metastases. They had no metastases other than liver metastases. None of them had received previous chemotherapy.

**Table 2.** Response to hepatic arterial infusion

| | No. of patients | % |
|---|---|---|
| Complete response | 2 | 8 |
| Partial response | 10 | 38 |
| Stable disease | 9 | 35 |
| Progressive disease | 5 | 19 |
| Total | 26 | 100 |

**Table 3.** Reasons for termination of hepatic arterial infusion

| | No. of patients (%) |
|---|---|
| Total No. of patients | 23 |
| Tumor progression | 14 (61%) |
| Hepatic | 7 |
| Extrahepatic | 4 |
| Hepatic and extrahepatic | 3 |
| Complications of catheter system | 4 (17%) |
| Gastrointestinal complication | 3 (13%) |
| Hepatectomy | 1 (4%) |
| Patient refusal | 1 (4%) |

### Response and Duration of HAI

A summary of tumor response is shown in Table 2. An objective response was seen in 12 of 26 (46%; 95% confidence interval, 26.9–65.2%) patients, including two (8%) complete responses.

The median number of treatment cycles given was 21 (range 7–75) and the median duration of treatment was 5.6 months. Discontinuation of the treatment was necessary in 23 patients. The reasons for termination are summarized in Table 3. Extrahepatic progression was observed in seven of 23 patients (30%). These included lung in four patients, lung and abdominal lymph node in one patient, abdominal lymph node in one patient and bone in one patient. Although 14 patients continued HAI until tumor progression occurred, other patients terminated HAI because of technical complications and clinical conditions. In four patients, the treatment was discontinued owing to complications related to the catheter system, hepatic artery thrombosis in three patients and arterial–portal shunt in one patient. Three patients stopped HAI because of gastroduodenal ulcer formation probably related to misdistribution of the drugs. In one patient who was a responder, hepatectomy was performed, and one patient refused to continue the treatment after 30 injections.

### Toxicity in HAI

The toxicity observed in this study is summarized in Table 4. No treatment-related death was observed. Hematological toxicity was minimal, with one patient developing grade 3 leukocytopenia and another patient grade 3 thrombocytopenia.

**Table 4.** Toxicity of hepatic arterial infusion ($n$ = 26)

| Toxicity | Grade | | | |
|---|---|---|---|---|
| | 1 | 2 | 3 | 4 |
| Leukocytopenia | | | 1 | |
| Thrombocytopenia | | 2 | 1 | |
| Nausea/vomiting | 4 | 5 | | |
| Gastroduodenal ulcer | | 3 | 1 | |
| Stomatitis | 2 | 1 | | |
| Diarrhea | 2 | | 1 | |
| Hand–foot syndrome | 2 | 1 | | |
| Gastritis/duodenitis | 2 | | | |
| Esophagitis | 1 | | | |

**Table 5.** Response to second-line systemic chemotherapy

| | CR | PR | SD | PD |
|---|---|---|---|---|
| Irinotecan ($n$ = 11) | 0 | 0 | 5 | 6 |
| PVI 5-FU* ($n$ = 3) | 0 | 0 | 0 | 3 |
| MTX + 5-FU ($n$ = 3) | 0 | 0 | 1 | 2 |
| Total | 0 | 0 | 6 | 11 |

*Protracted venous infusion of 5-FU.

Nausea and vomiting were the most common adverse reactions in nine of 26 patients (35%), followed by gastroduodenal ulcers in four patients (15%). Stomatitis, diarrhea and hand–foot syndrome were minor problems. No chemical hepatitis or sclerosing cholangitis were observed.

Among four patients with gastroduodenal ulcers, one patient developed a severe complication, perforation of the duodenum and he was operated on. The other three patients recovered with only medical treatment.

### Results of Second-line Systemic Chemotherapy

Results of the second-line systemic chemotherapy are shown in Table 5. No clinical response was observed in any of the 17 evaluable patients.

### Survival

With a 16.5-month median follow-up, the median survival time of all 26 patients after the first treatment was 19.4 months (Fig. 1).

## DISCUSSION

Prospective, randomized studies of patients with unresectable liver metastases from colorectal cancer have shown significantly higher response rates for HAI than for systemic chemotherapy without impact on the overall survival. In Japan, HAI of 5-FU for liver metastases from colorectal cancer has been

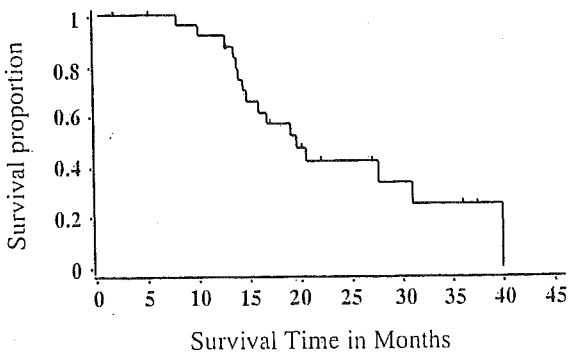


**Figure 1.** Overall survival curve ($n = 26$).

widely performed. It has been reported that weekly HAI of 5-FU has demonstrated a high response rate of 78% and a median survival duration of 25.8 months in 32 patients. Furthermore, it caused no serious toxicities and no decrease in the patients' quality of life (12). The current study demonstrated a response rate of 46% (consisting of two complete responses and 12 partial responses among 26 cases) similar to most other randomized HAI studies (6–11). Although direct comparison of results from this study with the phase II study reported by Arai et al. (12) is difficult, given that the studies differ with respect to population characteristics, our study failed to reproduce the response rate to weekly HAI of 5-FU reported by Arai et al. One of the reasons for this might be complications associated with the HAI catheter system. Great care should be taken to prevent or quickly detect any disorders resulting from technical factors and if necessary, an adequate countermeasure should be taken as described by Arai et al.

No definite survival advantage due to the development of extrahepatic progression has been demonstrated. In this study, extrahepatic progression was observed in one-third of the patients with termination of HAI. Further attempts, such as a combination with systemic chemotherapy to prevent extrahepatic progression, are needed to prolong overall survival.

There have been few reports about the impact of second-line systemic chemotherapy in patients refractory to HAI. In the present study, the efficacy of second-line chemotherapy after termination of HAI was evaluated. Irinotecan is active in patients with advanced colorectal cancer as second-line therapy after failure of first-line 5-FU-based treatment (15). We reported previously that an MTX plus 5-FU regimen and protracted venous infusion of 5-FU produced relatively high response rates, 25% in both regimens, in pretreated patients with advanced colorectal cancer (16,17). However, in the present study, 17 cases with liver metastases or extrahepatic metastases failed to respond to second-line systemic chemotherapy including irinotecan. This might be due to prior exposure to the intensive treatment with high-dose 5-FU. The small number of patients, however, precludes any further conclusions as far as second-line chemotherapy is concerned.

In conclusion, this study showed an average response rate similar to those in most other randomized HAI studies and a median survival time of 19.4 months, which appears to be better than that of regional therapies reported previously. However, extrahepatic progression was observed in one-third of patients on termination of HAI and a response to second-line chemotherapy was not demonstrated. Regional treatment with systemic chemotherapy should be conducted to achieve good results in terms of survival. To this end, the Japan Clinical Oncology Group (JCOG) is now preparing a phase I/II study of weekly HAI of 5-FU with concurrent systemic irinotecan in patients with liver metastases from colorectal cancer.

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SURGICAL ENDOSCOPY
and Other Interventional Techniques

# A comparison of the complication rates between laparoscopic colectomy and laparoscopic low anterior resection

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**Abstract**
*Background:* This study compared the short-term outcomes, including the complication rate and minimum surgical invasiveness, between patients with colon and rectal carcinomas, who underwent laparoscopic surgery.
*Methods:* A review evaluated 151 patients who underwent laparoscopic colectomy (Lap-colectomy; $n = 120$) and laparoscopic low anterior resection (Lap-LAR; $n = 31$) between July 2001 and December 2003. The short-term outcomes were compared between the two groups.
*Results:* The mean operative time and blood loss were significantly greater in the Lap-LAR group. However, the complication rates and postoperative course between the two approaches were similar, and no anastomotic leakage was observed. There was no significant difference in the serum C-reactive protein level and white blood cell count between the two groups in the early postoperative period.
*Conclusions:* Lap-LAR for rectal carcinoma can be performed safely without increased morbidity or mortality, and its short-term benefits are comparable with those conferred by Lap-colectomy.

**Key words:** Laparoscopic colectomy — Laparoscopic low anterior resection — Complication — Colorectal cancer — Short-term outcome

More than 10 years have passed since laparoscopic surgery became the approach of choice for colorectal cancer, but its value still remains unestablished. One of the reasons for this is that oncologic safety, which is the most important factor in a cancer surgery, has not been well confirmed for LS as it has for conventional open surgery. Oncologic outcome is not compromised by the laparoscopic approach, at least in the short term [6, 7, 9, 19]. According to some reports, the treatment outcome for laparoscopec surgery is not inferior to that for open surgery in terms of 5-year survival. However, the safety of laparoscopic surgery should be evaluated and confirmed in prospective randomized controlled trials [8, 15].

Unfortunately, laparoscopic surgery as an approach to rectal cancer is a very difficult surgery from a technical standpoint. Consequently, many trials have excluded patients with middle and lower rectal carcinomas. Laparoscopic low anterior resection (Lap-LAR) reportedly involves a high rate of anastomotic leakage (5.7–21%), and some authors have recommended covering ileostomy routinely in Lap-LAR cases, a step that is not required in some open surgery cases [1, 3, 5, 10, 13, 20]. Technical difficulties may be overcome by the surgeon's proficiency, and by the improvement and development of instruments, but because of the high complication rate, it currently is controversial whether Lap-LAR can be regarded as a minimum invasive surgery for rectal cancer.

Since our first laparoscopic colectomy for colorectal carcinoma in 1993, approximately 280 laparoscopic resections for colorectal malignancies have been performed at our institution. In June 2001, we unified our surgical and postoperative management procedures, and began to expand the use of laparoscopic surgery to include middle and lower rectal carcinomas. As a consequence, the complication rate and mean length of hospitalization have been reduced at our institution.

In the current study, short-term outcomes, including the complication rate and minimum surgical invasiveness, were compared selected patients with colon carcinoma and those with rectal carcinoma who underwent laparoscopic surgery at our hospital after June 2001 to evaluate whether Lap-LAR is a surgical technique with benefits similar to those for laparoscopic colectomy (Lap-colectomy).

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## Patients and methods

### *Patients*

Between June 2001 and December 2003, we performed 151 continuous laparoscopic resections for selected patients with colorectal carcinoma. Because the safety of laparoscopic surgery patients with cancer remains to be established, candidates for radical surgery were patients who had a preoperative diagnosis of T1 or T2. Additionally, laparoscopic surgery cases also included patients with a preoperative diagnosis of T3 who nevertheless wished to undergo laparoscopic surgery and those with colon or upper rectal carcinoma for which palliative resection was considered necessary. We excluded the following groups of patients from laparoscopic resection: patients with tumors larger than 6 cm, patients with a history of extensive adhesions, patients with severe obesity (body mass index exceeding 32 kg/m2), patients with intestinal obstruction, and patients who did not consent to laparoscopic surgery.

All the patients were evaluated before surgery by clinical investigation including barium enema, total colonoscopy, chest x-ray, abdominal ultrasonography, and computed tomography. For the patients with rectal carcinoma, a primary rectal carcinoma was defined according to its distance from the anal verge, as determined by colonoscopy. The tumors were grouped into lower rectum (0–7 cm), middle rectum (7.1–12 cm), and upper rectum (12.1–17 cm). We defined conversion to open surgery as any incision larger than 7 cm, excluding cases in which the incision was enlarged because of a large specimen that could not be removed through a 7-cm incision.

### *Laparoscopic technique*

The techniques of laparoscopic resections have previously been described thoroughly [6, 19, 20]. For right-sided lesions, the right colon was mobilized initially, and the vascular pedicles were divided at their origin, together with the draining lymph nodes intracorporeally. For patients with a preoperative diagnosis of T2–T3 lesions, the laparoscopic no-touch isolation technique was performed [12]. With this technique, after early proximal ligation of the tumor-feeding vessels and resection of the mesentery intracorporeally, mobilization of the right colon was performed. The bowel loop was delivered under a wound protector through a small incision. The division of the marginal vessels and the anastomosis were performed extracorporeally.

For transversecolon lesions, mobilization of hepatic, splenic, or both flexures was performed according to the tumor location. Proximal ligation of the right, left, or both branches of the middle colic vessels at their origins was performed intracorporeally or extracorporeally. The bowel loop was delivered, and anastomosis was performed in the same way.

For the descending colon and the proximal sigmoid colon lesions for which extracorporeal anastomosis was considered possible, the left colon was mobilized initially. After mobilization of the splenic flexure, intracorporeal ligation of the tumor-feeding vessels (left colic artery, sigmoid arteries, inferior mesenteric vessels) at their origins was performed. The bowel loop was delivered through a small incision, and the division of the mesenterium was performed extracorporeally, followed by extracorporeal anastomosis.

For the distal sigmoid colon and rectal lesions, after mobilization of the left colon and splenic flexure, if necessary, intracorporeal high ligation of the inferior mesenteric vessels followed by mobilization of the rectum and mesorectum was performed. For higher lesions, mesorectal tissue down to 5 cm below the tumor was excised routinely. Middle and lower rectal tumors were treated by total mesorectal excision. Rectal transection was performed with endolinear staplers (Endo GIA Universal; Auto Suture, U.S. Surgical Corp., Norwalk, CT, USA). A 4-cm incision then was made over the mid-lower port site, and the bowel was exteriorized under wound protection. The anastomosis was performed by the double stapling technique. For patients with lesions located within 2 cm of the dentate line, laparoscopic intersphincteric rectal resection and handsewn coloanal anastomosis were performed. This surgical technique has been described previously [18].

### *Study parameters*

The parameters analyzed included gender, age, body mass index (BMI), prior abdominal surgery, operative time, operative blood loss, conversion rate, days to resume diet, length of postoperative hospital stay, and both intraoperative and postoperative complications within 30 days of surgery. Pathologic staging was performed according to Dukes' stage. White blood cell (WBC) count and C-reactive protein (CRP) in serum were measured preoperatively and on postoperative day 1 routinely, and on postoperative days 2, 3, and 4, if necessary.

### *Statistical analysis*

Statistical analysis was performed using Student's $t$ test, Fisher's exact test, and the chi-square test as appropriate. A $p$ value less than 0.05 was considered significant.

## Results

The patient demographics are summarized in Table 1. No significant differences were observed in baseline characteristics between the two groups, with the exception that mean BMI was significantly greater in the Lap-LAR group ($p = 0.0438$). In the Lap-LAR group, two patients underwent laparoscopic handsewn coloanal anastomosis, and a transverse-coloplasty pouch was constructed for two patients. All the patients with covering ileostomy underwent ileostomy closure. With regard to simultaneously performed surgical techniques, the Lap-colectomy group had two patients who underwent combined surgery: one had a laparoscopic cholecystectomy and the other had resection of a benign submandibular gland tumor. In the Lap-LAR group, two patients underwent concurrent laparoscopic cholecystectomy. Data on these combined surgical techniques all were included in the analyses of the colorectal cancer surgeries.

Operative and postoperative results are shown in Table 2. All the operations were completed laparoscopically in this study. The mean operative time and blood loss were significantly greater in the Lap-LAR group. We did not experience accidental intestinal perforation at or near the tumor site. Liquid and solid foods were started on median postoperative days 1 and 3 in both groups. The median length of postoperative hospitalization was 8 days in both groups. No significant differences were observed in the postoperative course between the two groups. All the patients were discharged to home.

The postoperative complications are listed in Table 3. There were no perioperative mortalities. The morbidity rate was 13.3% (16/120) in the Lap-colectomy group and 16.1% (5/31) in the Lap-LAR group. However, no anastomotic leakage occurred in this study. Reoperation of the laparoscopic division of an adhesive band for a postoperative small bowel obstruction was necessary for one patient in the Lap-colectomy group (0.8%). No significant differences in complication rates were observed between the two groups. No significant differences were found between the two groups in terms of CRP and WBC levels after surgery (Fig. 1). At the end of the study period, only one patient in the Lap-

**Table 1.** Patient's characteristics

| | Lap-colectomy | Lap-LAR | *p* Value |
|---|---|---|---|
| Number of patients | 120 | 31 | |
| Sex ratio (male:female) | 71:49 | 18:13 | 1.0000 |
| Age(years) *n* (range) | 61 (30–88) | 59 (37–76) | 0.3693 |
| Body mass index (kg/m2) *n* (range) | 22.7 (14.9–29.6) | 23.8 (17.5–32.4) | 0.0438 |
| Prior abdominal surgery *n* (%) | 28 (23.3) | 14 (45.1) | 0.3545 |
| Dukes' stage (*n*) | | | |
| A | 94 | 23 | 0.5248 |
| B | 5 | 0 | |
| C | 16 | 6 | |
| D | 5 | 2 | |
| Follow-up (months) *n* (range) | 13 (2–33) | 14 (2–33) | 0.8472 |
| Location (*n*) | | | |
| Cecum | 15 | | |
| Ascending colon | 21 | | |
| Transverse colon | 16 | | |
| Descending colon | 12 | | |
| Sigmoid colon | 56 | | |
| Rectosigmoid/upper rectum | | 6 | |
| Middle rectum | | 6 | |
| Lower rectum | | 19 | |
| Laparoscopic colorectal procedures (*n*) | | | |
| Ileocecal resection | 15 | | |
| Right hemicolectomy | 27 | | |
| Transverse colectomy | 5 | | |
| Left hemicolectomy | 2 | | |
| Descending colectomy | 10 | | |
| Sigmoid colectomy | 49 | | |
| Partial resection | 12 | | |
| Anterior resection with DST | | 29 | |
| Anterior resection with ISR-CAA | | 2 | |
| Transverse coloplasty pouch | | 2 | |
| Covering ileostomy | | 6 | |

Values are means (range)
Lap, laparoscopic; LAR, low anterior resection; DST, double-stapling technique; ISR-CAA, intersphincteric rectal resection and handsewn coloanal anastomosis

**Table 2.** Operative and postoperative results

| | Lap-colectomy *n* (range) | Lap-LAR *n* (range) | *p* Value |
|---|---|---|---|
| Operative time (min) | 200 (115–348) | 250 (190–472) | < 0.0001 |
| Blood loss (ml) | 32 (5–248) | 60 (10–265) | 0.0011 |
| Conversion | 0 | 0 | |
| Liquid intake (days) | 1 (1–3) | 1 (1–3) | 0.9562 |
| Solid food (days) | 3 (2–5) | 3 (2–4) | 0.8291 |
| Hospital stay (days) | 8 (7–20) | 8 (7–17) | 0.2520 |

Values are medians (range)
Lap, laparoscopic; LAR, low anterior resection

**Table 3.** Morbidities and mortality

| | Lap-colectomy (*n*) | Lap-LAR (*n*) | *p* value |
|---|---|---|---|
| Mortality | 0 | 0 | |
| Morbidity | | | |
| Wound sepsis | 4 | 2 | 0.4007 |
| Bowel obstruction | 6 | 1 | 1.0000 |
| Urinary tract infection | 3 | 0 | 1.0000 |
| Anastomotic leakage | 0 | 0 | 1.0000 |
| Abscess | 0 | 1 | 1.0000 |
| Pneumonia | 1 | 0 | 1.0000 |
| Pneumothorax | 1 | 0 | 1.0000 |
| Pulmonay embolism | 1 | 0 | 1.0000 |
| Enterocolitis | 1 | 0 | 1.0000 |
| Neurogenic bladder | 0 | 1 | 0.2053 |
| Total | 17(16[a]) | 5 | 0.7711 |

Lap, laparoscopic; LAR, low anterior resection
[a] Number of patients

colectomy group experienced a recurrence (hepatic metastases).

## Discussion

In the current study, short-term outcomes were compared between patients with colon cancer and patients with rectal cancer who underwent laparoscopic surgery. In the Lap-LAR group, the mean BMI was found to be significantly greater. In addition, there was significantly more blood loss, and the mean operative time was significantly longer. However, the complication rates and postoperative course between the two approaches were similar, and no anastomotic leakage was observed. The observed safety of Lap-LAR may have been attributable to improved instruments and the surgeon's proficiency.

Historically, conventional open LAR has resulted in higher complication rates, and is considered to be an

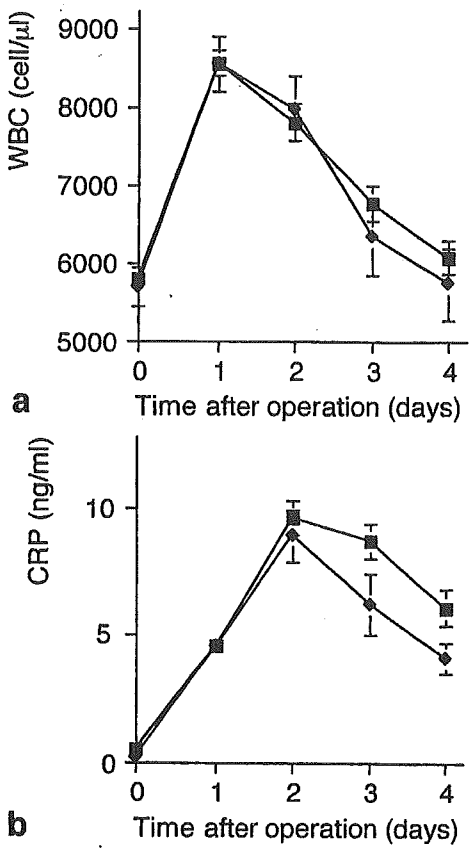


**Fig. 1.** Changes in white blood cell (WBC) count (**a**) and serum C-reactive protein (CRP) (**b**) levels in patients after laparoscopic colectomy (■) and laparoscopic low anterior resection (◇). The difference between the two groups was not significant. Each bar represents the mean ± standard error.

approach of greater invasiveness than open colectomy [2]. In our study, patients were selected appropriately and cautiously. Consequently the conversion rate was 0% in the 151 cases. As a result, in the Lap-LAR group, laparoscopic surgery achieved a minimum invasiveness comparable with that of the Lap-colectomy group. Moreover, when we compared CRP and WBC as objective markers of surgical stress in the early postoperative period, there were no significant differences in either of these markers between the two groups. Instead of expanding the use of laparoscopic surgery without limit, it is necessary to set appropriate criteria for selection, and then to perform laparoscopic surgery while monitoring the safety of the procedure in properly selected patients who can benefit from the advantages of laparoscopic surgery.

This study demonstrated that laparoscopic approaches to rectal carcinoma do not compromise early postoperative recovery such as days to oral feeding and length of hospitalization. Although we did not experience anastomotic leakage, previous studies have reported an anastomotic leakage rate of 5.7% to 21% for patients who underwent Lap-LAR, and some authors have recommended a covering stoma as a routine step in Lap-LAR [1, 3, 5, 10, 13, 20]. For patients who are to have a covering stoma, a surgery for stoma closure also is needed as a matter of course. If a covering stoma, which is not required for open surgery cases, becomes indispensable for Lap-LAR cases, the patient's burden will increase. Currently, with regard to LAR, patients are required to make a choice themselves as to whether they will undergo open or laparoscopic surgery after they have been given sufficient information.

Recently, laparoscopic handsewn coloanal anastomosis has been reported for patients with lesions located in the lower rectum that have more than 2 cm of distal free margin to the dentate line [14, 18]. This technique allows a sufficient distal margin to be obtained under direct vision to preserve the sphincter and avoid abdominal perineal resection. However, further investigation is needed regarding the oncologic and functional safeties of this novel surgical technique.

Despite many successful reports of laparoscopic resection for advanced lower rectal carcinoma in Western countries, advanced lower rectal carcinoma is seldom treated laparoscopically in Japan. Lateral pelvic lymph node dissection combined with total mesorectal excision remains the standard surgical procedure for patients with advanced lower rectal carcinoma in Japan, and lateral lymph node dissection by laparoscopy still is an unexplored frontier.

We believe that the incidence of lateral lymph node involvement for lower rectal cancer (13–16%) is not negligible, and that a 5-year survival rate of 15% to 40 % for patients with lateral lymph node involvement demonstrates that some patients may be cured by extended surgery [4, 11, 16]. In our institution, lateral lymph node dissection by conventional open methods is performed for tumors located in the lower rectum if the preoperative tumor penetration is T3 or T4, despite perirectal lymph node status, or even T2 if perirectal lymph nodes appear to be positive. Therefore, most lesions of the lower rectum treated laparoscopically are T1 or node negative T2 or T3.

In this study, days to the resumption of diet after surgery and length of postoperative hospital stay were compared between the two groups. However, these numeric values are less objective because they are influenced by social factors such as judgment of the physician in charge, clinical pass, manners, and customs. Therefore, it should be noted that these values cannot be indicators of minimum invasiveness. Previous reports on laparoscopic surgery indicate that patients in Japan tend to remain in hospital longer than patients in Western countries [17]. The results of the current study in terms of postoperative stay after laparoscopic surgery for colorectal cancer are among the shortest reported in Japan. However, as compared with data from Western institutions, the mean length of hospital stay was, in fact, 1 to 2 days longer. This may be attributable to the fact the 70% of the medical costs are covered by public health insurance for every patient in Japan. Moreover, many Japanese patients have private health insurance that pays the patient a specified amount of money per day of hospitalization. In some types of insurance contract, the longer the patient stays in hospital, the more the insurance payment is, thereby yielding greater "earnings." Under these circumstances, patients do not need to leave the

hospital in a hurry. Obviously, this situation in Japan is wasting medical funds. It goes without saying that the situation must be improved.

The mean operative time in the current study was a little longer than in previously reported studies. This may be attributable to the fact that at our institution, trainee doctors perform part or all of a surgical procedure under the guidance of staff doctors in many cases. Also, we are unable to make a laparoscopic team. However, it is evident from results of this study that the quality of our operations has not been lowered.

In conclusion, the current study demonstrates that Lap-LAR can be performed safely without increased morbidity or mortality, and that it offers benefits in terms of faster recovery of bowel motility and shorter hospital stay comparable with patients who undergo Lap-colectomy. With improvements in technology and surgeons' experience, we believe that the use of this procedure will expand. Analysis of long-term oncologic outcomes for patients with colon and upper rectal carcinoma will take place in a few years time. It remains unclear, however, whether laparoscopic resection for middle and lower rectal carcinoma is equivalent to conventional open surgery in terms of oncologic outcome, and this can determined only by evaluation of multiple randomized studies.

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# Safety of Laparoscopic Intracorporeal Rectal Transection With Double-Stapling Technique Anastomosis

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**Abstract:** To assess the feasibility and analyze the short-term outcomes of laparoscopic intracorporeal rectal transection with double-stapling technique anastomosis, a review was performed of a prospective registry of 67 patients who underwent laparoscopic sigmoidectomy and anterior resection with intracorporeal rectal transection and double-stapling technique anastomosis between July 2001 and January 2004. Patients were divided into 3 groups: sigmoid colon/rectosigmoid carcinoma, upper rectal carcinoma, and middle/lower rectal carcinoma. A comparison was made of the short-term outcomes among the groups. The number of cartridges required in bowel transection was significantly increased in patients with middle/lower rectal carcinoma, and significant differences were observed in the length of the first stapler cartridge fired for rectal transection. Furthermore, mean operative time and blood loss were also significantly greater in the middle/lower rectum group; however, complication rates and postoperative course were similar among the 3 groups. No anastomotic leakage was observed. Laparoscopic intracorporeal rectal transection with double-stapling technique anastomosis can be performed safely without increased morbidity or mortality.

**Key Words:** laparoscopic low anterior resection, rectal transection, double-stapling technique, complication, colorectal carcinoma

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More than 10 years have passed since the first report of laparoscopic colectomy by Jacobs et al[1] in 1991. With regard to long-term oncological safety, which is the most important concern for laparoscopic surgery (LS) for malignancies, there have been no reports indicating that LS is inferior to conventional open surgery (OS).[2–5] On the other hand, because LS requires surgical techniques that are different from those of OS, even a surgeon with considerable experience in OS cannot readily perform LS.

In particular, LS for rectal carcinoma is very difficult surgery from a technical standpoint, and consequently many randomized, controlled trials have excluded patients with middle/lower rectal carcinoma. This is because of concerns over the safety of the procedure, ie, the risk of complications associated with the laparoscopic procedure and the risk of tumor cell spillage because of traumatic manipulation of the tumor. Previous studies have reported an anastomotic leakage rate of 5.7% to 21% in patients who underwent laparoscopic low anterior resection (Lap-LAR), and some authors have recommended a covering ileostomy as a routine in Lap-LAR cases.[6–12] It remains uncertain which cases of rectal carcinoma are appropriate for laparoscopic surgery.

Since our first laparoscopic colectomy for colorectal carcinoma in 1993, approximately 280 laparoscopic resections for colorectal malignancies have been carried out at our institution. Most of our early experience was confined to early (Tis or T1) colorectal cancer located at the cecum, ascending colon, sigmoid colon, or rectosigmoid due to technical problems and concerns regarding port site and peritoneal recurrences. In June 2001, we unified our surgical and postoperative management procedures and expanded our indications for laparoscopic colectomy to include advanced colorectal cancers (ie, T2 lesions and beyond) located anywhere in the colon and/or rectum.

In 1980, Knight and Griffen[13] described the double-stapling technique (DST), which offered great advantages in that it permitted low rectal anastomoses to be performed with great ease. The aim of the present study was to assess the feasibility and analyze the short-term outcomes of laparoscopic intracorporeal rectal transection with DST anastomosis, one of the most demanding and stressful techniques in laparoscopic colorectal surgery, in selected patients with sigmoid colon and rectal carcinoma, who all underwent LS at our hospital after June 2001.

## PATIENTS AND METHODS

### Patients

At the Division of Colorectal Surgery of the National Cancer Center Hospital in Japan, 156 nonrandomized consecutive patients underwent laparoscopic colorectal resections between July 2001 and January 2004. During this period, 67 patients were treated by laparoscopic sigmoidectomy and anterior resection with DST anastomosis. Because the safety of LS in cancer patients remains to be established, candidates for laparoscopic surgery were patients who were preoperatively diagnosed with T1 or T2. Additionally, LS cases also included patients with sigmoid colon or upper rectal carcinoma who were preoperatively diagnosed with T3 but wished to undergo LS, as well as those for which palliative resection was

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considered necessary. Exclusion criteria for LS were tumors larger than 6 cm, a history of extensive adhesions, severe obesity (body mass index >32 kg/m$^2$), intestinal obstruction, and refusal to undergo LS. The preoperative workup consisted of a clinical investigation, barium enema, total colonoscopy, chest x-ray, abdominal ultrasonography, and computed tomography.

LS was contraindicated for patients with preoperative diagnoses of T3 and T4 tumors in the middle and lower rectum because, with the current instrumentation, it was difficult to perform laparoscopic procedures without grasping and manipulating the bowel or mesorectum near the tumor; our concern was that this would result in accidental tumor spillage. Furthermore, lateral lymph node dissection combined with total mesorectal excision remains the standard surgical procedure for patients with T3 and T4 lower rectal carcinoma in Japan, and lateral lymph node dissection by laparoscopy is still an unexplored frontier.[14–16] As a result, some patients were found to have T3 cancer only after histopathological examination of the surgical specimens. Preoperative or postoperative radiation therapy was not performed in this series because of the low local recurrence rate in patients with T1–T3 lower rectal carcinoma without preoperative radiation.[14,16]

Patients were divided into 3 groups: sigmoid colon/rectosigmoid carcinoma, upper rectal carcinoma, and middle/lower rectal carcinoma. For the patients with rectal carcinoma, a primary rectal carcinoma was defined according to its distance from the anal verge as determined by colonoscopy. The tumors were grouped into lower rectum (0–7 cm), middle rectum (7.1–12 cm), and upper rectum (12.1–17 cm). We combined patients with middle and lower rectal carcinoma as a group because laparoscopic techniques for rectal transection and DST anastomosis were almost same: anastomosis located below peritoneal reflection.[7] Patients with lesions located within 2 cm of the dentate line who underwent laparoscopic intersphincteric rectal resection and hand-sewn coloanal anastomosis were excluded from the present study. This surgical technique has been described previously.[17] Conversion to open surgery was defined as any incision greater than 7 cm, excluding cases in which the incision was enlarged due to a large specimen size that could not be removed with a 7-cm incision.

## Laparoscopic Technique

Laparoscopic resection techniques have previously been described, with minor modifications.[7,17] Initial port placement was performed using the open technique, and pneumoperitoneum was induced using carbon dioxide. Two 5-mm ports were then inserted in the left lower midabdominal and the left lower quadrant regions, and 2 other 12-mm ports were inserted in the mid-lower and the right midabdominal regions under laparoscopic guidance.

The left colon was initially mobilized laterally to medially until the left ureter and superior hypogastric nerve plexus were identified. The mobilization of splenic flexure was performed if necessary. Usually, Japanese patients have a long sigmoid colon, and if the surgeon preserves 1 or 2 arcades of marginal vessels of sigmoid colon by division of sigmoidal arteries between superior rectal artery and marginal vessels, mobilization of splenic flexure becomes unnecessary; thus, splenic mobilization was performed in only about 20% of our patients. Then, a window was made between the mesocolon containing the arch of the inferior mesenteric vessels and the superior hypogastric nerve plexus, starting at the bifurcation, with support from an assistant holding the sigmoid mesocolon ventrally under traction and to the left using a 5-mm bowel grasper through the left lower quadrant port. After the dissection, proceeding to the origin of inferior mesenteric artery, taking care not to injure the superior hypogastric nerve plexus and the roots of the sympathetic nerves, intracorporeal high ligation of the inferior mesenteric artery was performed. After cutting the inferior mesenteric vein and left colic artery, mobilization of the rectum and mesorectum was performed. The avascular plane between the intact mesorectum anteriorly and the superior hypogastric nerve plexus, right and left hypogastric nerves, and Waldeyer fascia posteriorly was entered by sharp dissection and extended down to the level of the levator muscle for middle and lower rectal carcinomas, taking care to protect the pelvic nerves. For proximal sigmoid colon carcinoma, the mesentery at the promontory was excised routinely using ultrasonic shears (laparoscopic coagulating shears [LCS], Ethicon Endo-Surgery Inc, Cincinnati, OH) or an endolinear stapler (Endo GIA Universal, Tyco Healthcare, Auto Suture Co, US Surgical Corp, Norwalk, CT). For rectosigmoidal and upper rectal lesions, mesorectal tissue extending down to 5 cm below the tumor was excised routinely using LCS. Middle and lower rectal tumors were treated by total mesorectal excision. Immediately before rectal transection, laparoscopic rectal clamping was performed just above the anticipated point of rectal transection, using a bowel clamping device (Fig. 1) introduced through the 12-mm mid-lower port. A distinct advantage of this device is that the bowel clamp at the head of the device can be easily bent intraabdominally without reducing the grasping strength. Rectal washout was performed routinely using 1000 mL of a 5% povidone-iodine solution. Rectal transection was then performed by a multiple-firing technique, using Endo GIA Universal staples, introduced through the 12-mm right midabdominal port.[18] If the rectal transection was not completed after the first cartridge, the stapler line for the second cartridge was carefully positioned on the anal side stapler line of the first cartridge. The third and fourth firings were performed in the same way. A 4- to 5-cm incision was then made over the mid-lower 12-mm port site, and the bowel was exteriorized under wound protection and divided with appropriate proximal clearance. After inserting the anvil head of the circular stapler into the end of the proximal colon, the proximal colon was internalized and the incision was closed. Intracorporeal anastomosis under a laparoscopic view was performed by means of the DST, using a circular stapler (ECS 29 or 33 mm, Ethicon Endo-Surgery Inc). After the insertion of the body of the circular stapler into the anus, the puncturing cone was pushed through the midpoint of the linear staple line. In patients in whom 2 or more linear stapler cartridges were used for rectal transection, the puncturing cone was pushed near the crossing point of the first and second stapler lines.

The anastomotic air leakage test was performed if the "doughnuts" were incomplete. Patients with a low anastomosis within 1 cm from the dentate line and incomplete doughnuts

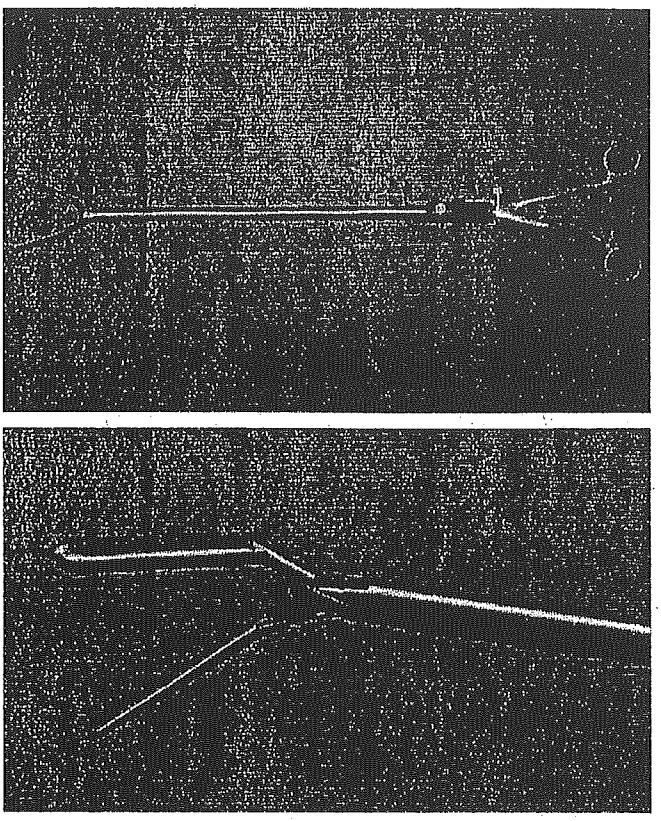

**FIGURE 1.** Bowel clamping device. A distinct advantage of this device is that the bowel clamp at the head of the device can be easily bent intraabdominally without reducing the grasping strength.

underwent a covering ileostomy. However, the decision to perform a protective ileostomy in this series was based on much looser criteria than those used in OS to avoid major anastomosis complications that could lead to a permanent stoma or a fatal outcome, especially in the early LS cases of lower rectal carcinoma.

## Study Parameters

The parameters analyzed included gender, age, body mass index, prior abdominal surgery, operative time, operative blood loss, number of stapler cartridges fired and the length of the first stapler cartridge for rectal transection, conversion rate, days to resume diet, length of postoperative hospital stay, and both intraoperative and postoperative complications within 30 days of surgery. Pathologic staging was performed according to Duke's stage.

## Statistical Analysis

Statistical analysis was performed using the $\chi^2$ test, Kruskal-Wallis test with Bonferroni correction, and repeated-measure analysis of variance (ANOVA) with the Scheffe method when appropriate. A $P$ value of $<0.05$ was considered significant.

## RESULTS

The patient demographics are summarized in Table 1. No significant differences were observed in baseline characteristics among the 3 groups. In the middle/lower rectum group, anastomosis was performed <3 cm from the dentate line in 7 patients and >3 cm but below the peritoneal reflection in 3 patients. We performed an anastomotic air leakage test in 2 patients with lower rectal carcinoma and did not find any sign of air leakage; however, both patients underwent a protective ileostomy, Overall, a protective ileostomy was required in 4 patients, and a transverse coloplasty pouch was created in 1 patient.

The number of patients in relation to the number of stapler cartridges used for rectal transection in each group is shown in Table 2. The number of cartridges required during bowel transection was significantly increased in patients with middle/lower rectal carcinomas compared with the other groups. Similarly, significant differences were observed in the length of the first stapler cartridge fired for rectal transection (Table 3). In patients with middle/lower rectal carcinomas, the length of the first stapler cartridge was 45 or 30 mm, and it was 45 or 60 mm for proximal lesions.

Operative and postoperative results are shown in Table 4. Mean operative time and blood loss were significantly greater in the middle/lower rectum group. All the operations were completed laparoscopically. We did not experience any accidental intestinal perforations at or near the tumor site. Liquid and solid food was started at a median of 1 and 3 postoperative days in all groups. The median length of postoperative hospitalization was 8–9 days. No significant differences were observed in the postoperative course among the 3 groups. All patients were discharged home.

The postoperative complications are listed in Table 5. There were no perioperative mortality and no anastomotic leakage. Reoperation of a laparoscopic division of an adhesive band for a postoperative small bowel obstruction was necessary in 1 patient with sigmoid colon carcinoma. No significant differences were observed in complication rates among the 3 groups.

**TABLE 1.** Patient's Characteristics*

| | Sigmoid Colon/ Rectosigmoid | Upper Rectum | Middle/Lower Rectum |
|---|---|---|---|
| No. of patients | 36 | 21 | 10 |
| Sex ratio (male:female) | 22:14 | 10:11 | 8:2 |
| Age (y) | 59 (30–79) | 59 (37–73) | 60 (47–76) |
| Body mass index (kg/m$^2$) | 23.5 (18.9–29.0) | 24.1 (17.5–32.4) | 23.8 (19.5–26.4) |
| Prior abdominal surgery (%) | 6 (17) | 5 (24) | 5 (50) |
| Duke's stage | | | |
| A | 27 | 16 | 7 |
| B | 1 | 0 | 0 |
| C | 7 | 3 | 3 |
| D | 1 | 2 | 0 |

*Values are means (range), $P > 0.05$.

TABLE 2. Number of Patients in Relation to the Number of Stapler Cartridges Fired for Rectal Transection*

| No. of Stapler Cartridges Fired | Sigmoid Colon/Rectosigmoid† | Upper Rectum† | Middle/Lower Rectum |
|---|---|---|---|
| 1 | 25 | 8 | 0 |
| 2 | 9 | 12 | 2 |
| 3 | 2 | 1 | 6 |
| 4 | 0 | 0 | 2 |

*$P < 0.01$ between groups, Kruskal-Wallis test.
†$P < 0.01$ versus middle, lower rectum/Boneferroni test.

## DISCUSSION

In the present study, short-term outcomes were compared among different tumor sites in patients who underwent laparoscopic intracorporeal rectal transection with double-stapling technique anastomosis. The closer the tumor site was to the anus, the more the number of stapler cartridges needed for rectal transection increased and the use of a longer Endo GIA Universal stapler cartridge was significantly restricted, suggesting that rectal transection for Lap-LAR in patients with middle/lower rectal carcinomas may be a difficult and stressful procedure. In the present study, however, the complication rate did not increase despite lower anastomotic sites. With thorough and careful intracorporeal rectal transection and DST anastomosis, the safety of Lap-LAR may be established.

Minimum invasiveness is often noted as one of the merits of LS in comparison with OS for colorectal cancer.[19–23] But even recently, some studies have reported that minimal or no short-term benefits were found with LS compared with standard OS.[24–26] Reviewing these reports raises a question about the conversion rate. Even granting that LS has a lower surgical invasiveness than OS, there is a possibility that the treatment outcomes of LS will be contaminated by the treatment outcomes of OS, when the conversion cases are included in the LS group, based on the intention-to-treat principle. In the study by Weeks et al,[26] who reported a conversion rate of 25%, LS showed only minimal short-term quality-of-life benefits compared with OS in an intention-to-treat analysis, probably due to the high conversion rate. Moreover, they pointed out that patients assigned to laparoscopy-assisted colectomy who required intraoperative conversion to open colectomy had slightly poorer quality-of-life outcomes than patients who successfully underwent minimally invasive resection, and that the length of postoperative hospital stay in the LS group requiring conversion was longer than that in patients assigned to OS (7.4 vs. 6.4 days), although statistical analysis was not performed regarding these points. If the conversion patients did not show a worse outcome than those undergoing OS, patients who might benefit from LS should be considered as candidates for LS. Further studies are necessary to evaluate postoperative and oncological outcomes of patients assigned to laparoscopy-assisted colectomy who then require intraoperative conversion.

The results of the current study suggested that laparoscopic approaches to middle/lower rectal carcinoma do not compromise early postoperative recovery, such as days to oral feeding and length of hospitalization. Previous studies reported an anastomotic leakage rate of 5.7% to 21% in patients undergoing Lap-LAR.[6–12] Some authors have recommended a covering ileostomy as a routine step in Lap-LAR.[6,10,27] At present, patients with a preoperative diagnosis of T1–T2, middle/lower rectal carcinoma are required to decide whether they prefer to undergo OS or LS, after being given full information at our institution.

TABLE 3. Length of the First Stapler Cartridge Fired for Rectal Transection*

| Length of the First Stapler Cartridge (mm) | Sigmoid Colon/Rectosigmoid† | Upper Rectum† | Middle/Lower Rectum |
|---|---|---|---|
| 60 | 34 | 16 | 0 |
| 45 | 2 | 5 | 7 |
| 30 | 0 | 0 | 3 |

*$P < 0.01$ between groups, Kruskal-Wallis test.
†$P < 0.01$ versus middle/lower rectum, Boneferroni test.

TABLE 4. Operative and Postoperative Results

| | Sigmoid Colon/Rectosigmoid | Upper Rectum | Middle/Lower Rectum |
|---|---|---|---|
| Operative time,* min (range) | 221 (135–348)† | 244 (190–328)‡ | 315 (190–392) |
| Blood loss,* mL (range) | 29 (6–161)† | 24 (10–198)† | 124 (17–265) |
| Conversion | 0 | 0 | 0 |
| Liquid intake, d (range) | 1 (1–4) | 1 (1–3) | 1 (1) |
| Solid food, d (range) | 3 (2–5) | 3 (3–4) | 3 (2–4) |
| Hospital stay, d (range) | 8 (7–12) | 8 (7–11) | 9 (7–17) |

*$P < 0.01$ between groups, repeated-measure analysis of variance.
†$P < 0.01$ versus middle/lower rectum, Scheffe test.
‡$P < 0.05$ middle/lower rectum, Scheffe test.

TABLE 5. Morbidity and Mortality*

| | Sigmoid Colon/ Rectosigmoid | Upper-Rectum | Middle/Lower Rectum |
|---|---|---|---|
| Mortality | 0 | 0 | 0 |
| Morbidity | | | |
| Wound sepsis | 2 | 1 | 0 |
| Bowel obstruction | 1 | 0 | 1 |
| Urinary tract infection | 1 | 0 | 0 |
| Abscess | 0 | 0 | 1 |
| Neurogenic bladder | 0 | 1 | 0 |
| Anastomotic leakage | 0 | 0 | 0 |
| Total | 4 | 2 | 2 |

*$P > 0.05$.

In this study, the authors evaluated the safety of laparoscopic rectal transection using an endolinear stapler, which is one of the most technically difficult procedures in Lap-LAR. To date, we have not observed serious complications, such as anastomotic leakage. However, this surgical procedure remains technically difficult. We consider that this method should not be attempted if it is not performed by a laparoscopic surgical team with sufficient experience in LS. Regarding a surgical procedure that can be placed between OS and Lap-LAR, Vithiananthan et al[28] reported a hybrid method. In their procedure, they mobilized the left-sided colon and completed high ligation of the inferior mesenteric vessels with the use of the pneumoperitoneum, and then, from the inferior midline incision measuring 8 cm or longer, they performed rectal mobilization, mesorectal division, rectal transection, and anastomosis by DST using the OS tools. They noted that the mean incision length was 11.1 cm, which is longer than in Lap-LAR but shorter than in OS and that the patients treated with this method showed a significantly faster postoperative recovery than those treated with OS. Hand-assisted laparoscopic surgery may also be another treatment option.[29] However, compared with the standard Lap-LAR technique evaluated in this study, both of these methods may need a larger incision. With the surgeon's proficiency in the surgical procedure and the improvement in and development of instruments, the safety of standard Lap-LAR will probably be established; however, it is important to remember that this surgical technique cannot be employed at an early stage of the learning curve of laparoscopic surgery.

In conclusion, the findings of the present study demonstrate that laparoscopic intracorporeal rectal transection with DST anastomosis can be performed safely without increased morbidity or mortality. Even at present, there are few prospective, randomized trials investigating the short-term and oncological outcomes in patients with middle/lower rectal carcinoma, perhaps mainly because Lap-LAR has not been widely performed compared with LS for colon/upper rectal carcinoma due to the technical difficulties. The radical resection of middle/lower rectal cancers is a procedure that requires advanced technical skills in OS, to say nothing of Lap-LAR; however, we believe that use of Lap-LAR for middle/lower rectal carcinoma will expand with improvements in technology and surgeons' experience in the near future.

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特集 鏡視下手術の適応と限界

# 大腸癌における鏡視下手術の適応と限界

*Laparoscopic-assisted resection for colorectal cancer*

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大腸癌に対する鏡視下手術は，技術的な進歩や手術機器の開発，改良により技術的には開腹手術と同様に行うことができるようになってきた．摘出リンパ節個数，直腸癌の切離断端距離，術後合併症も開腹手術と比べて差がなく，質的にも開腹手術と同様であるという結果が示されている．また，短期QOL，術後自律神経機能，短期予後も差がないが，RCTの結果がないため大腸癌の治療としての鏡視下手術の位置づけが統一されていないのが現状である．

## I. 背 景

大腸の鏡視下手術は1991年に報告され[1]，当初は良性疾患や早期大腸癌に対して行われていたが，手術機器の開発，改良や技術的な進歩も伴い徐々に適応が拡大し，近年では進行大腸癌に対しても行われるようになっている．しかし，良性疾患と悪性疾患に対する鏡視下手術では技術的な問題だけではなく手術の主目的が異なる．良性疾患はQOL，悪性疾患は予後である．したがって，一気に普及した腹腔鏡下胆嚢摘除術とは異なり慎重論も根強く，限られた施設で行われているのが現状である．これはRCT(Randomized Control Study)による長期予後の結果がないことが理由と考えられ，大腸癌の治療として鏡視下手術が適切であるかどうかという根本的な点についてはまだ結論が出ていない．

## II. 手術適応

大腸癌の治療としての鏡視下手術の位置づけに統一した見解が得られていないため，手術の適応も各施設が独自に設定した適応に基づいて行われているのが現状である．しかし，一般的に術前診断にて他臓器浸潤，大きな腫瘍，閉塞を伴う腫瘍は手技的理由から適応外としている施設が多い．他臓器浸潤がある場合はen blocかつsurgical marginを確保して切除することが困難であること，腫瘤径が10 cm近くもある大きな腫瘍は視野の妨げになることや，腫瘍を腹腔内から取り出す際の皮膚切開が大きくなるため整容面のメリットがないこと，閉塞を伴う症例では口側腸管の拡張があり視野の妨げになることが理由である．また，鏡視下手術を試みた場合でも強度の癒着，腸管の拡張，高度の肥満などの要因により視野がと

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れないときには思わぬ出血や他臓器の損傷を起こす可能性が高く，これらの損傷を起こすと鏡視下操作では修復できないこともあるので術中判断で開腹手術に変更とすべきであると考えられる[2)-5)]．当科の適応は，結腸癌，Rs 直腸癌では早期癌および環周率50%までの進行癌，Ra 直腸癌は早期癌，Rb 直腸癌は適応外としている(表1)．深達度については，$CO_2$ ガスの腫瘍に対する影響が解決していないことや，体位変換および手術操作中に腫瘍が鉗子や他部位に触れてしまう可能性があるため，現状では深達度 ss までが適当と考えている．しかし，術前画像診断にて SS' と SE' を正確に区別することは困難である．そこで，当科における過去の内視鏡所見を検討したところ，環周率50%までであれば深達度 se の症例がなかったことから，内視鏡検査所見で環周率50%までを適応としている(図1)．鏡視下の側方郭清はごく限られた施設において行われているが，側方郭清の意義および適応については開腹手術においても議論されていてまだ結論が出ていないため，当科では Ra 進行癌と Rb 直腸癌を鏡視下手術の適応から除外している．

## III. 手　　術

### 1．手術の安全性

コントロールがつかない出血や他臓器の損傷の近年の報告例は0～2例であり，術者の技術が熟練したことや超音波凝固切開をはじめとする手術機器の開発改良などにより，鏡視下手術の安全性は高まっている．開腹手術と比較して learning curve は長いが，鉗子操作などの基本手技や手術の手順をきちんと習得すれば，前述のように視野がとれない症例に無理をして施行しないかぎり，出血や他臓器の損傷はほとんどない[6)7)]．

### 2．剝離と郭清

手術の手順には内側アプローチと外側アプローチがあるが，手術手順は鏡視下手術も開腹手術も統一すべきと考えており，当科では開腹手術と同様の外側アプローチで行っている．結腸の授動は，解剖学的な構造を理解して腎筋膜前葉を残す層で行えば，開腹手術と同様に電気メスおよび鈍的剝離のみで出血なく行うことができる．出血したら

表1　鏡視下手術の適応

| |
|---|
| 1　盲腸，結腸癌，Rs 直腸癌：SS 以浅<br>内視鏡検査で環周率≦1/2 |
| 2　Ra 直腸癌：早期癌 |

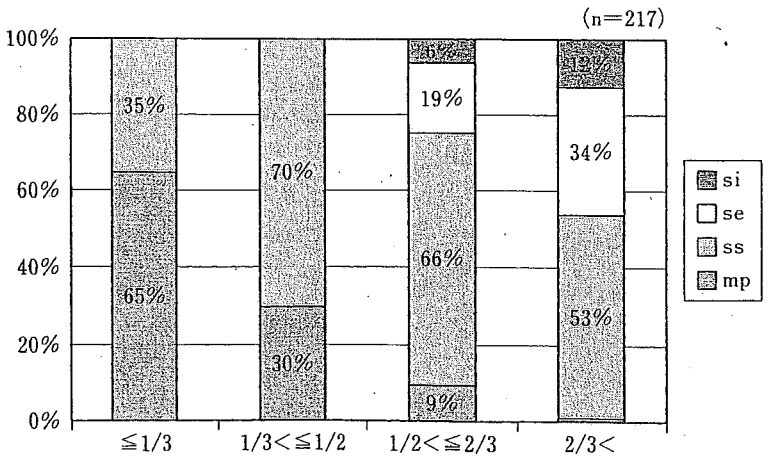


図1　内視鏡環周率と深達度(結腸癌＋Rs 直腸癌)

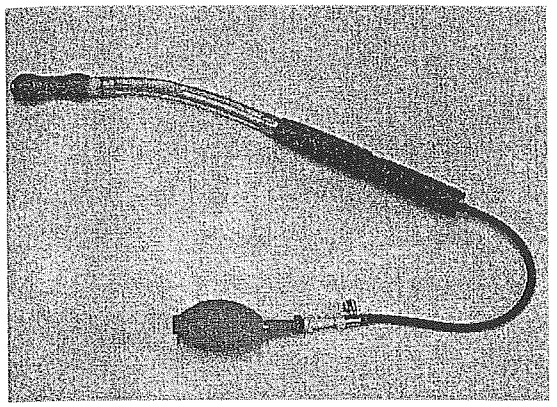

図2　経肛門リトラクター
先端がダブルバルーンになっている

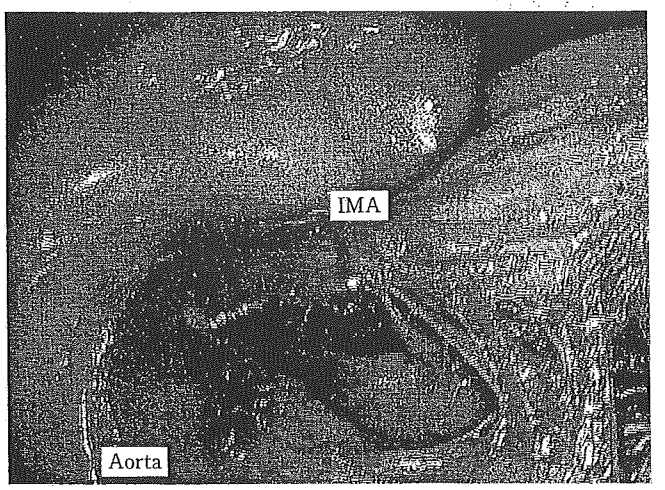


図3　下腸間膜動脈根部

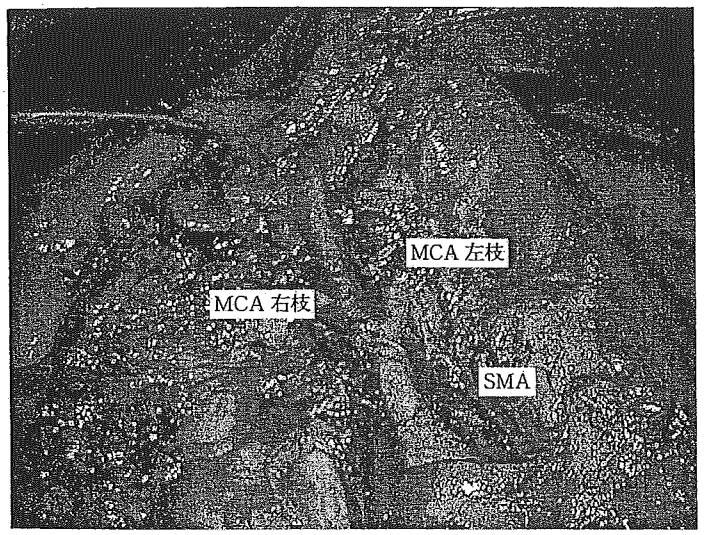


図4　中結腸動脈根部

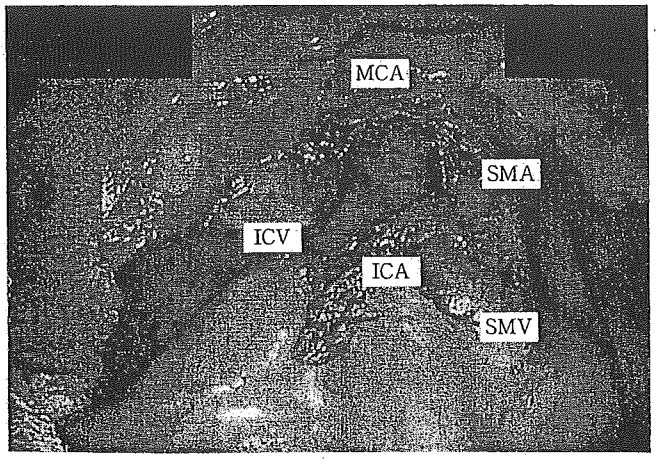


図5　回結腸動脈根部
回結腸動脈が静脈の前面を走行

層が深いことが多いので注意が必要である．また，回盲部およびS状結腸は生理的な癒着が強く，深い層に入りやすいので，右側結腸の授動は肝彎曲部から，左結腸の授動は下行結腸の肛門側寄りから行うと正しい層に入りやすい．剝離の途中で精巣(卵巣)動静脈，尿管などが背側に温存されることが目印となる．骨盤内の剝離操作は，開腹手術と同様に直腸後壁，側壁，前壁の順に剝離するが，骨盤深部になるにしたがい剝離が困難となる．そこで，症例によっては当科で考案した経肛門的リトラクターを使用している(図2)．このリトラクターにより，直腸が進展された状態で前後左右に牽引できるために，挙筋上腔までの剝離が容易にできる．

上方向の郭清については，すべての部位の癌において第3群のリンパ節までの郭清が可能である(図3～5)．リンパ節転移陽性症例もあるので，pedicleを把持するのはバブコック鉗子などを使用し，血管周囲を直接把持してリンパ節を潰さない注意が必要である．主幹動脈根部郭清の際の基本は，剝離鉗子を用いて血管周囲を丁寧に剝離し，剝離した組織をLCSで切離することである．これを繰り返すことで出血なく安全に行うことができる．No. 223郭清はやや煩雑であるが，ゆっくり時間をかけて慎重に行えば安全に行うことができる．

### 3．直腸の切離

鏡視下に直腸を切離する場合，45度屈曲可能なENDO GIA UNIVERSAL™を用いる．装着するカートリッジは45 mmと60 mmが用意されているが，直腸低位での腸管切離が困難なことがある．また，切離可能な場合でも1回では切離できずに，カートリッジを2回あるいは3回追加して切離しなければならないことが多い．これは，切離断端の強度やコストからみて問題であると考えられる．鏡視下で直腸を先に切離した場合は，小開腹して腸管および腸間膜を体外に誘導するときにシングルループになるため，脂肪量にもよるが皮膚切開は約4 cmである．一方，剝離までを鏡視下で行い切離を体外で行った場合，体外に誘導する腸管がダブルループになるため皮膚切開は5～6 cm必要となる．ダブルループの腸管を体外に誘導後，先にS状結腸を切離予定線で切離後にアンビルを装着して腹腔内に戻すとシングルループとなり視野がよくなる．開腹手術で使用する鉤，直角鉗子，TL30などの直腸切離に必要な器具が使用可能となる．当科ではケースバイケースで使い分けているが，1～2 cmの皮膚切開の大きさの違いにこだわらなければ，開腹手術に習熟している外科医ならばストレスなく直腸の切離を行うことができる．また，コストの面でも保険点数内で行うことができるメリットがある．

### 4．手術のquality

手術のqualityを示すため2000年1月～2002年1月までの症例について摘出リンパ節個数と直腸癌の切離断端距離に関して鏡視下手術と開腹手術を比較検討した．その結果，有意差はなく鏡視下手術が癌の手術として受け入れられる可能性を示している(表2，3)．また，他の報告でも同様の結果となっている[8)9)]．

表2 郭清リンパ節個数

| | LAC | OC | |
|---|---|---|---|
| D2 | 9.1±6.9 (6-21) | 12.4±7.1 (7-33) | p=0.15 |
| D3 | 13.9±6.6 (7-28) | 16.1±9.3 (7-39) | p=0.61 |

Mann-Whitney's U test

表3 直腸癌：肛門側断端距離

| | LAC(n=13) | OC(n=27) | |
|---|---|---|---|
| AR | 2.5±0.8(n=5) (1.7-3.2) | 2.9±1.2(n=11) (1.5-4.5) | p=0.72 |
| LAR | 1.8±0.8(n=8) (0.7-3.2) | 1.9±1.0(n=16) (0.3-4.2) | p=0.92 |

AR：anterior resection LAR：low anterior resection

Mann-Whitney's U test