Table 2. Operative and postoperative results of patients who underwent laparoscopic resection

	Transverse/descending group (n = 89)		Other group (n = 366)		p value
	median	range	median	range	
Operative time, min	220	95–615	195	95–400	0.0135
Blood loss, ml	42	2–365	25	2–753	0.0165
Liquid intake, days	1	1–13	1	1–4	0.5552
Solid food, days	3	2–14	3	2–7	0.8111
Hospital stay, days	8	5–20	8	5–28	0.6824

Table 3. Morbidities and mortality in patients who underwent laparoscopic resection (within 30 days)

	Transverse/descending group (n = 89)		Other group (n = 366)	
	n	%	n	%
Mortality	0	0	0	0
Morbidity				
Wound sepsis	5	6	22	6
Bowel obstruction	5	6	4	1
Pneumonia	1	1	2	0.5
Perforation of duodenal ulcer	1	1	0	0
Pulmonary embolism	1	1	0	0
Urinary tract infection	0	0	7	2
Anastomotic bleeding	0	0	2	0.5
Anastomotic leakage	0	0	1	0.3
Gastric ulcer bleeding	0	0	1	0.3
Pneumothorax	0	0	1	0.3
Enterocolitis	0	0	1	0.3
Subcutaneous hematoma	0	0	1	0.3
Total complications	13	15	42	11
Total patients with complication*	13	15	40	11

* p = 0.3571.

firmation of the safety of the laparoscopic approach will require further accumulation of patients.

The most significant technical issue in laparoscopic surgery for transverse colon and descending colon carcinoma may be the division of supplying arteries and drainage veins. Tumor-supplying vessels differ depending on the location of the tumor. Moreover, special attention is necessary to cope with the wide variations of these vessels, especially middle colic arteries and veins [14, 15]. Initially, supplying vessels were routinely divided after mobilization of the colon by laparoscopic surgery in our department; however, we currently use a median-to-lateral approach, in which the supply vessels are ligated first [11]. This approach enables easier division of blood vessels in many cases and may reduce the spillage of isolated tumor cells into the blood stream, although there is no clear evidence for this. However, the division of middle colic vessels before the mobilization of hepatic or splenic flexure is still a technically demanding procedure in laparoscopic surgery for transverse colon carcinoma, and it may be better to ligate these vessels when it can be done most easily, regardless of the timing with respect to mobilization.

Fortunately, the complication rates and postoperative course were similar in the two groups in the present study, but the incidence of postoperative bowel obstruction in the transverse/descending group (5/89, 6%) was higher than in the other group (4/366, 1%). Although a successful conservative treatment was performed in all 5 patients in the dransverse/descending group, one patient in the other group required laparoscopic division of an adhesive band for a postoperative small bowel obstruction. Interestingly, all 5 patients who developed postoperative bowel obstruction in the transverse/descending group were patients with transverse colon carcinoma, and right hemi-colectomy was conducted in two and partial resection in three. In previous studies, the incidence of postoperative bowel obstruction after laparoscopic surgery in transverse colon carcinoma has been found to be 2- to 3-fold higher than in other colon carcinomas [9, 10]. Regarding this aspect, data collection from more patients is essential before making decisions; however, the possibility of increased postoperative bowel obstruction should always be kept in mind after laparoscopic surgery for transverse colon carcinoma.

The mean operative time in the present study was slightly longer than in previous studies of laparoscopic surgery. This may have been partly due to an increased proportion of patients in relatively advanced stages, and also because, in many cases, trainee doctors performed

part or all of the surgical procedures under the guidance of staff doctors. Our hospital is an educational institution and the rate of laparoscopic surgery for colon carcinoma conducted by trainee doctors has been increasing as laparoscopic surgery has become more common in Japan; however, the results of the present study indicate that the quality of our surgical procedures has not been lowered.

In conclusion, laparoscopic surgery for transverse colon and descending colon carcinoma can be performed safely without increased morbidity or mortality, and shows short-term benefits comparable to those after laparoscopic surgery for other colon carcinomas. Considering that conducting a new randomized clinical trial targeting these patients is virtually difficult, the safety of this procedure requires confirmation through the accumulation of more patients prospectively.

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REVIEW ARTICLE

Laparoscopic colorectal cancer surgery: Japanese experience

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Abstract

In Japan, laparoscopic colectomy for cancer started in 1992. A national survey has revealed that, since that time, the number of cases that have undergone this procedure has steadily increased, and by 2007, there were over 9000 cases. This figure includes an increase in the percentage of more advanced cases, which has occurred due to technical improvements in lymph node dissection.

A Japanese randomized controlled trial comparing laparoscopic to open surgery started in November 2004, with enrollment ending in April 2009 with 1050 cases. For this study, preoperative stage T3 and T4 cases were selected for inclusion, and D3 dissection was required.

To assess the technical skill of surgeons, the Japan Society of Endoscopic Surgery established the Endoscopic Surgical Skill Qualification System to encourage high-level surgical techniques. Assessment is conducted by reviewing unedited videos. The success rate for colon and rectal surgeries has ranged between 37%–40%. The Endoscopic Surgical Skill Qualification System has contributed to the establishment of standard technical skills in laparoscopic surgery, the development of an educational system for laparoscopic surgeons, and a reduction in the number complications. Technical difficulties still exist in laparoscopic rectal cancer surgery, but with the technical progress in laparoscopic colorectal surgery, the number of laparoscopic rectal cancer surgeries has been gradually increasing in number.

A multicentric phase II study on the feasibility and long-term outcome for stage I and II rectal cancer started in 2008. In this study, the short-term outcomes including anastomotic leakage rate and long-term survival, will be clarified.
Combined with continuously improved technologies, training techniques and surgical standards, laparoscopic colorectal surgery is steadily progressing in Japan.

Introduction

Laparoscopic surgery has been performed for various diseases of the digestive organs. The benefits of laparoscopic surgery include a reduced likelihood of postoperative ileus, shorter hospital stays, decreased postoperative pain and a smaller incision resulting in good cosmesis. In the field of laparoscopic colorectal surgery such benefits have also been reported both in randomized and non-randomized studies (1–3). Laparoscopic cholecystectomy for gallstone diseases became common in the mid-1990s because of the simplicity of the procedure. While laparoscopic surgery has become a standard treatment for diseases of a benign nature such as gallstone diseases, it has yet to become the established surgery to treat cancer of the digestive organs. However, laparoscopic colectomy for cancer is the most well-developed technique among other laparoscopic procedures for cancer of the digestive organs.

In 1991, Jacobs *et al.* were the first to report their experiences with laparoscopic-assisted colectomy for benign as well as malignant diseases (4). Due to immense improvements in technique since that time, laparoscopic-assisted colectomy (LAC) for colorectal cancer slowly became the treatment of choice both in Japan and overseas. However, these developments in laparoscopic

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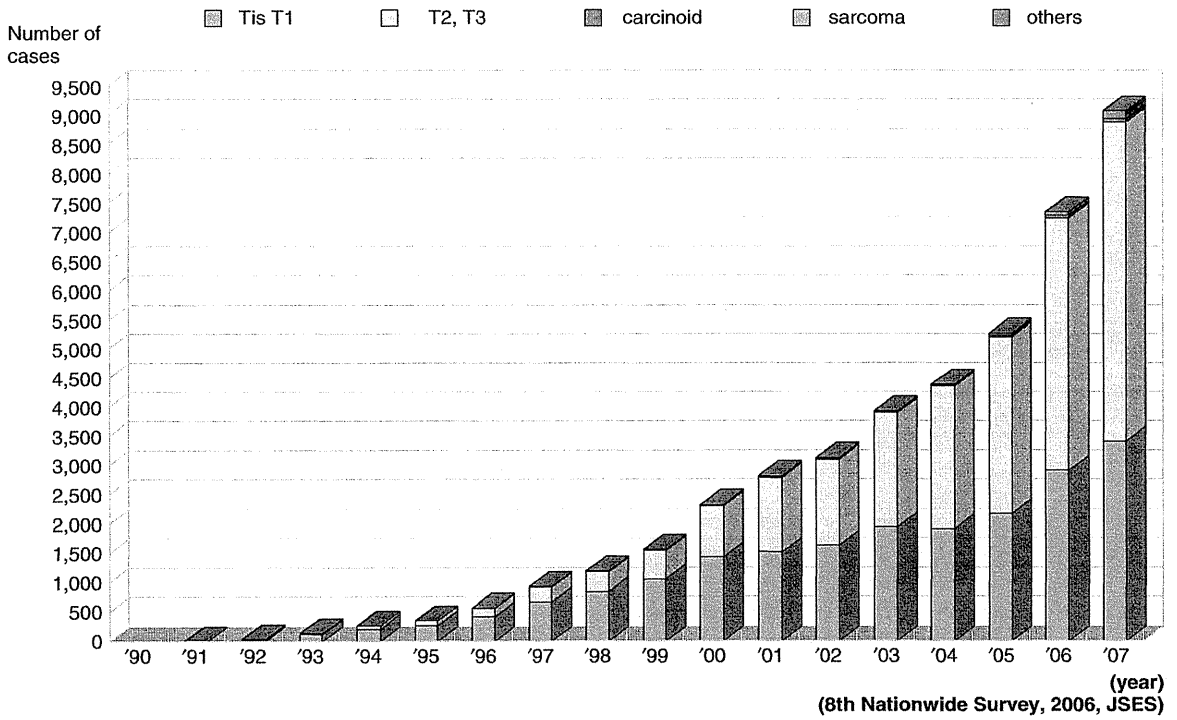

Figure 1 Nationwide survey of laparoscopic colectomy cases for malignant tumors. There is a rapidly increasing tendency in the numbers each year. There were over 9000 cases in 2007. The percentage of more advanced stage cancer cases has been increasing due to the technical advancement in lymph node dissection.

surgery for colorectal cancer occurred at a relatively slow pace primarily because it is a difficult technique and the long-term oncological results are uncertain. According to the surgeons who worked on developing this procedure, the curability of colorectal carcinoma treated with LAC is considered to be as good as that treated with open surgery (5–7). Despite this, the long-term results of LAC for cancer in comparison to open surgery are still controversial. Opinions differ due to uncertainties about the adequacy of resection margin and lymph node dissection and due to the possibility of cancer cell dissemination in the peritoneal cavity and/or to the port sites.

The development of laparoscopic colorectal cancer surgery in Japan

Laparoscopic colectomy for cancer was first performed in Japan in 1992 – 1 year after Jacobs *et al.* reported on their treatment of benign disease with LAC in the USA. The initial cases were report by Watanabe *et al.* (8). Initially, LAC was considered as an intermediate procedure between colonoscopic resection and open bowel resection. Although a laparoscopic simple segmental resection for early stage cancer was considered feasible, it was not known whether an adequate extent of lymph node dissection for more advanced cases could be done in laparoscopoic procedures (9). According to the national survey conducted by the Japanese Society of Endoscopic Surgery (committee chaired by Seigo Kitano), the number of cases that undergoing this procedure has steadily increased since it was first introduced, and there were over 9000 cases per year by 2007 (Figure 1) (10). During the early part of the 4 year study (which was conducted between 1994 and 1997), early cancers (Tis and T1) constituted 85%–100% of all the cases. However, during the later part of the study, the percentage of more advanced cancer (T2 or higher) increased to 50%. The increase in the percentage of more advanced cases was due to technical improvements in lymph node dissection (D2, D3 dissection).

For colorectal cancer surgery, three grades of lymph node dissection have been practiced in Japan according to the preoperative and/or intraoperative T staging of the tumor. Provided curative resection is to be performed, D1 dissection is suited for Tis and some T1 stage tumors, D2 dissection is suited for T2 stage tumors, and D3 dissection

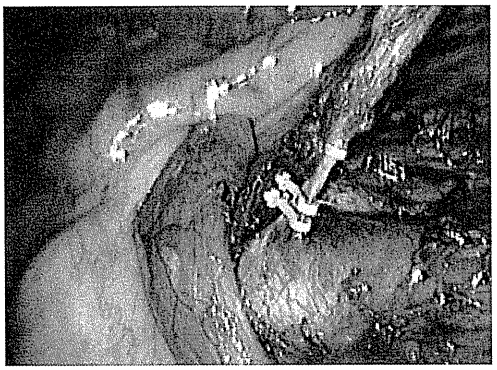

Figure 2 Three grades of lymph node dissection that are practiced in Japanese colorectal cancer surgery. An appropriate grade of dissection is selected according to the preoperative or intraoperative T staging.

is suited for T3 and T4 tumors. The differences in these three grades of lymph node dissection are presented in Figure 2 (11). Konishi *et al.* first reported laparoscopic D3 dissection in both right-sided and sigmoid colon cancer cases, and have shown that the laparoscopic dissection of lymph nodes around the origins of the mesenteric artery branches, such as ileocolic artery or inferior mesenteric artery, is technically feasible and safe (12).

In 1998, the Japanese Society for Cancer of the Colon and Rectum started a working group, the Clinical Research Group of Laparoscopic Colectomy (CRGLC) (chaired by Fumio Konishi; succeeded by Masahiko Watanabe), in order to establish a laparoscopic surgical technique to treat colorectal cancer (13). The clinical research group developed a standardized technique, organized regular training courses in Japan using pigs, and also worked on the retrospective multicentric data analyses of the laparoscopic colectomy cases for colorectal cancer. A standardized technique for both right-sided and left-sided (mainly sigmoid) colon resection for cancer was established by meticulously reviewing videos of study group participants over the course of 4 years (1998–2001). The details of the technique were published in a book entitled *Laparoscopic Colectomy – Approach and Standard Technique* (14). Training courses on laparoscopic colectomy using pigs organized by CRGLC have been held three to four times a year since. It is 1 day course consisting of lectures and hands-on pig surgery. There are approximately 30 participants each time. The details of the training courses held from 1998 to 2001 were reported by Yamada *et al.* in 2002 (15). The multicenter data analysis by the CRGLC covered 1784 cases that were operated on between 1993 and 2000, of which 1692 had sufficient data to be analyzed for long-term outcome. The number of cases in stage II and III was 492 in this series. The 5 year overall survival rate of curatively operated cases was 98.9% for Stage 0, 98.5% for Stage I, 94.5% for Stage II, 85.9% for Stage IIIa, and 74.6% for Stage IIIb (16). The percentage of port-site recurrence was 0.03%. These retrospectively analyzed data were encouraging but not entirely dependable due to the selection bias in the data collection.

Randomized controlled trials – Japanese Trial: JCOG 0404

Although non-randomized comparisons between laparoscopic and open surgery in Japan were favorable towards laparoscopic colectomy with regard to the long-term outcome of colorectal cancer surgery (5,6), there was only one small-scale randomized study (17). On the other hand, in other countries there have been several randomized controlled trials (RCT) comparing laparoscopic surgery to conventional colectomy for colorectal cancers (Table 1). The first reported RCT was a trial in Spain and involved a single institution. The results showed that there was no difference between the two procedures in stage II cases, and that LAC was associated with a significantly reduced risk of tumor relapse and death from cancer in stage III cases (18). In 2008, a long-term follow-up of the same trial showed better survival rates in the laparoscopic groups (19). A National Cancer Institute-sponsored trial in the USA [Clinical Outcomes of Surgical Therapy (COST)] found that there were no differences in the survival rate between laparoscopic and open surgery for both stage II and III colon cancer (20,21). A Colon Cancer Laparoscopic or Open Resection (COLOR) trial in northern Europe was closed for accrual, but the long-term results have yet to be reported (22). A Conventional versus Laparoscopic-Assisted Surgery in Colorectal Cancer (CLASICC) study in the UK reported that there were no differences between laparoscopic and open surgery on both the colon and the rectum (23). Furthermore, a meta-analysis that included COST, COLOR and CLASICC cases, covering a total of 1536 cases, again showed that there were no differences in the long-term outcome between laparoscopic and open surgery (24). Regarding RCT for colon cancer in Asian countries, a small-scale RCT was reported from Taiwan, and the results were similar to those from Western countries (25). While the results of those RCT were encouraging, we still need to have the results of our own RCT in Japan.

Because of the CRGLC's efforts, group members became highly adept at performing laparoscopic colectomies and by the early 2000s a uniform standard was achieved. Despite this, the rate of conversion from open surgery to laparoscopic colectomy in Japanese institutions is generally much lower than that in the previously done RCT in other parts of the world. In 2004, we felt that it was the

Table 1 Randomized trials of laparoscopic vs open surgery for long-term results

	COST 2007 Lap vs Open	CLASICC 2007 Lap vs Open	Liang *et al.* 2007(6) Lap vs Open	Lacy *et al.* 2008(7) Lap vs Open
n	435:428	273:140	135:134	106:102
Year	1994–2001	1996–2002	2000–2004	1993–1998
Age	70:69	69:69	64:64	68:71
Exclusion	TNM: T4 and M1, transverse colon	TNM: M1 transverse colon	TNM: T4, right and proximal transverse colon, AJCC Stage I and IV	TNM: T4 and M1, transverse colon
AJCC stage				
I	35%:26%	16.7%:16.4%	0:0	25.4%:17.6%
II	31%:34%	34.6%:36.9%	50.4%:47.8%	39.6%:47.1%
III	26%:28%	36.1%:34.7%	49.6%:52.8%	34.9%:35.3%
IV	4%:2%	Not reported	0:0	4.7:5.9%
Conversion	21%	25%	3%	11%
Median follow-up	7 years	36.8 months	40 months	95 months
Cancer outcomes				
Overall recurrence	19.4%:21.8%	—	17.0%:21.6%	18%:28%
Cancer related mortality	11.0%:14.3% (2004 data)	22.7%:19.3%	—	16%:27%
Overall mortality	23.6%:25.4%	28.8%:32.2%	—	36%:49%

AJCC, American Joint Committee on Cancer; CLASICC, Conventional versus Laparoscopic-Assisted Surgery in Colorectal Cancer; COLOR, Colon Cancer Laparoscopic or Open Resection; COST, Clinical Outcomes of Surgical Therapy; TNN, tumor metastasis (lymph) node.

right time to start RCT in Japan, and we began to design the RCT comparing laparoscopic versus open surgery. The study was designed by laparoscopic colorectal surgeons from over 20 institutions (members of CRGLC), in collaboration with the Japanese Clinical Oncology Group (JCOG), an organization of the National Cancer Center, Japan. The Japanese Ministry of Health Welfare and Labor funded the study. The study's aim was to enroll 842 cases in 2–3 years, and it sought to prove that the survival rate of LAC is not lower than open colectomy by 7.5% for T3 and T4 tumors. This was a non-inferiority trial in which we intended to prove that the long-term outcome of the two kinds of treatment was equal (26). The inclusion criteria were as follows: (1) patients aged 25–75; (2) patients without associated malignancies; (3) tumors in the cecum, ascending colon, sigmoid colon or in the recto-sigmoid; (4) tumors preoperatively staged as T3 or T4 by preoperative examinations; (5) tumors measuring < 8 cm on preoperative examinations; and (6) tumors that are not causing bowel obstruction. In all cases, D3 lymph node dissection was a required procedure (Figure 3). The Japanese trial started in November 2004 and completed in 2009. Because the interim short-term survival rate was higher than expected by 2007, the number of case accruals was increased to 1050 in order to have a sufficient number for statistical analysis. The case accrual went smoothly and finished in April 2009, with a final enrollment of over 1050 cases. The short-term outcomes will be analyzed in the near future, and we continue to wait for the long-term outcome results.

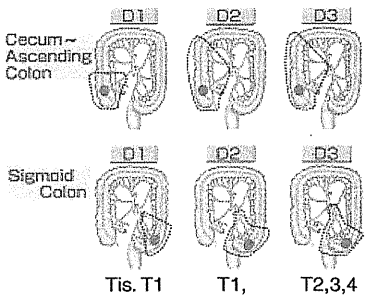

Figure 3 A case of upper rectal cancer in which D3 lymph node dissection was done. The lymph nodes around the origin of the inferior mesenteric artery were dissected.

Qualification system of laparoscopic surgical skill in Japan

Laparoscopic colorectal cancer surgery is one of the more difficult procedures in laparoscopic surgery. It has been 17 years since laparoscopic colorectal surgery was introduced in Japan in 1992. Technical difficulties, including the limited number of training institutions and the difficulty surgeons have in mastering the technique, are still the reasons for the limited usage of the laparoscopic technique for colorectal surgery.

Training involves a variety of teaching methods to ensure that surgeons master laparoscopic technique. Firstly, teaching courses with animal laboratory surgery are useful ways to learn the technique. Virtual training

devices are also useful, but the availability of such devices is limited. Additionally, visiting and observing clinical cases of laparoscopic colorectal surgery in institutions is very helpful before starting and also during the learning period. Thirdly, hands-on learning with experienced surgeons is the most significant form of training. In our experience, a trainee can become independent to carry out standard uncomplicated laparoscopic colorectal surgery after having operated on at least 20 cases under the guidance of an experienced trainer. During the initial period of hands-on learning, stepwise progress in instruction – beginning with the simpler aspects of the procedure and building to the more complex – is often most effective. Throughout training, it is also extremely important to have a good team of laparoscopic colorectal surgeons overseeing and guiding the process to good progress and successful results.

In 2004, the Japan Society of Endoscopic Surgery (JSES) established the Endoscopic Surgical Skill Qualification System (ESSQS) (chaired by Dr Taizo Kimura) for the purpose of encouraging high-level techniques and safe endoscopic surgical procedures. Those who succeed in getting the qualification have both the ability to safely perform endoscopic operations independently and to teach trainees. This is the first technical credential system in the world for laparoscopic surgery. Assessment is conducted by reviewing unedited videos of the applicants performing laparoscopic surgery in one of the sub-classified fields such as biliary tract, esophagus, stomach and colon. Applicants are then assessed on a scale of 100, with 60 marks allocated to "Common Criteria" to evaluate basic endoscopic surgical techniques and 40 marks for "Organ-specific Criteria" to evaluate special surgical techniques. Each applicant has participated either in at least 45 laparoscopic cholecystectomies in addition to five other higher-grade procedures, or in at least 20 or more advanced procedures such as laparoscopic colectomies. Two assessors carefully review identical unedited videos submitted by the applicants. During the first 3 years of ESSQS, there were changes to the types of laparoscopic colorectal surgery approved for video submission as well as changes in the assessment criteria. Due these changes and the higher level of standards, the equitable judgment of the technique became possible (12). As a result, the success rate in the field of colorectal laparoscopic surgery ranged from 37% to 40% (2004–2008) without significant variability. The relatively low success rate is considered adequate because the purpose of the ESSQS is to accredit the technique level with which one can conduct a safe and sufficient operation as well as teach trainees. Kappa Values of Inter-rater Agreement ranged from 0.38 to 0.40 (2004–2008), which can be considered as acceptable to fair. The preoperative complication rate was significantly lower for successful surgeons than for unsuccessful ones.

The ESSQS continues to be the assessment body for endoscopoic surgeons in Japan. It contributes to the establishment of standard technical skills in laparoscopic surgery, the development of educational system and the reduction in complications.

Cost problems of laparoscopic colorectal cancer surgery

Although laparoscopic colorectal surgery is considered beneficial for patients because of its minimal invasiveness, it does create financial problems due to the need for disposable instruments and longer operation time. Changes in reimbursement rates by Japanese public health insurance in 2008 increased the reimbursement rate for laparoscopic colectomy for cancer rose by 90,000 yen (approximately US$937), or to 417,000 yen (US$4344) per operation. Similarly, reimbursement for laparoscopic rectal resection for cancer rose by 92,000 yen (US$958), to 534,000 yen (US$5562) per operation. In addition to these reimbursements, public health insurance pays 30,000 yen (US$312) for the cost of laparosonic coagulating shears and up to 100,000 yen (US$1041) for stapling devices. However, the reimbursements for these disposable instruments are insufficient because hospitals pay more than these amounts to suppliers. Additionally, insurance does not cover certain other disposable instruments, such as trocars and clips. Under the Japanese public health insurance system, hospitals are not allowed to claim for the extra costs related the instruments. Likewise, the extra cost for the longer operation is not paid for by the insurance, and the shorter hospital stay for laparoscopic colectomy patients is not enough to compensate for the excess spending. Therefore, under the Japanese public health care system, hospitals may lose money if surgeons perform laparoscopic colorectal cancer surgeries. To solve such problems, we should make strenuous negotiations with the Ministry of Health and Labor to raise the reimbursement rates. On the other hand, surgeons should consider decreasing the number of disposable instruments used in the operations, which can be replaced by reusable instruments.

Future directions of laparoscopic colorectal surgery in Japan

Laparoscopic rectal cancer surgery is not as simple as laparoscopic colectomy because of its anatomical complexities. Particularly, the dissection and the division of the rectum in the deep part of the pelvic cavity sometimes involve complications. In addition to complications, the lateral pelvic node dissection for T3, T4 lower rectum tumors is

Table 2 Randomized trials comparing laparoscopic and open surgery for rectosigmoid and rectal tumors

	Leung *et al.* 2004(1) Rectosigmoid Lap vs Open	CLASICC 2007 Lap vs Open	Zhou *et al.* 2004 (26) Lap vs Open
n	203:200	253:128	82:89
Year	1993–2002	1996–2002	2001–2002
Age	67:67	69:69	44:45
TME	NA	79%:67%	100%
Site in rectum	NA	Not reported	1.5–8 cm from dentate line
AJCC stage			
I	15.3%:14.0%	16.7%:16.4%	6.1%:6.7%
II	35.5%:36.5%	34.6%:36.9%	11.2%:9.0%
III	31.5%:34.5%	36.1%:34.7%	76.8%:76.4%
IV	17.7%:15.0%	Not reported	4.9%:8.5%
Conversion	23.2%	34%	Not reported
30 day mortality	0.6%:2.4%	4%:5%	0%:0%
Median follow-up	52.7 months	36.8 months	Range 1–16 months
Cancer Outcomes			
Locoregional recurrence	6.6%:4.1%	9.9%:9.4%	0%:3.4%
Distant recurrence	18.0%:15.3%	18.6%:16.4%	0%:0%
Cancer related mortality	15.6%:11.8%	12.6%:18.0%	0%:0%
Overall mortality	22.8%:23.5%	Not specifically reported	0%:0%

AJCC, American Joint Committee on Cancer; CLASICC, Conventional versus Laparoscopic-Assisted Surgery in Colorectal Cancer; TME, total mesorectal excision.

technically challenging if it is to be performed laparoscopically. At the moment, laparoscopic lateral node dissection is still in the experimental stage and conducting a trial on laparoscopic resection of advanced low rectal cancers remains extremely difficult in Japan.

Globally, there have been few good quality studies comparing laparoscopic surgery to open surgery for rectal cancers. There are only three randomized studies available in the world (Table 2) (3,23,27). Of these trials, the study from Hong Kong is only on rectosigmoid lesions, and the results were similar to colon cancer surgery. Of the other trials on rectal cancer, the CLASICC trial is the only one that presented dependable results, but there was a relatively high conversion and morbidity rate in this study (23). In the study by Zhou *et al*, (27), the methodology of the study was unclear and the follow-up period was very short. Therefore, long-term outcomes of laparoscopic rectal cancer surgery as compared to open surgery remain unclear. In the future, COLOR II and LAPKON II trials may provide good information regarding the long-term outcome of laparoscopic rectal cancer surgery compared to open surgery.

In Japan, retrospective multicentric data collection and the analysis of laparoscopic rectal cancer surgery were done by the Japan Society of Laparoscopic Colorectal Surgery (previously named the CRGLC). The results of this study were reported by Miyajima *et al.* (28). Of the 1011 curatively treated patients in their series, the 3 year disease-free survival rate was 100% in stage 0, 94.6% in stage I, 82.1% in stage II, and 79.7% in stage III. These rates were similar to the results of open surgery. A phase II prospective, non-randomized trial on the feasibility of laparoscopic rectal resections for early stage rectal cancers is currently being conducted under the direction of the Japan Society of Laparoscopic Colorectal Surgery. The sample size is 350. The short-term outcome is mainly focused on the anastomotic leakage rate while the long-term measure is disease-free survival (29).

Conclusions

Laparoscopic colorectal cancer surgery in Japan developed more or less in parallel to Western and other Asian countries. However, in Japan, similar to open colorectal cancer surgery, lymph node dissection has been meticulously done in laparoscopic surgery. The high-level technique of laparoscopic D3 dissection is a special skill in our practice. Our randomized controlled trial started after the technique was established. Considering the very low conversion to open rate in Japan, our multi-centric prospective trials may produce new results that are different from those in Western and other Asian countries.

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Timing of Relapse and Outcome after Curative Resection for Colorectal Cancer: A Japanese Multicenter Study

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Key Words
Colorectal cancer · Treatment for relapse · Curative resection · Time to relapse · Recurrence

Abstract
Background: The aim of this multicenter study was to clarify the influence of timing of relapse after curative resection for colorectal cancer on prognosis. ***Methods:*** We enrolled 5,230 consecutive patients who underwent curative resection for colorectal cancer at 14 hospitals from 1991 to 1996. All patients were intensively followed up. Time to relapse (TR) was classified into three groups as follows: group A, TR ≤1 year; group B, TR >1 year and ≤3 years, and group C, TR >3 years. The prognoses after relapse were compared among the three groups. ***Results:*** Of the 5,230 patients, 906 experienced relapse (17.3%). The curative resection rates for recurrent tumors were 35.2% in group A, 46.6% in group B, and 45.1% in group C ($p = 0.0045$). There were significant differences in the prognoses after relapse among the three TR groups in patients with relapse to the liver ($p = 0.0175$) and in those with local relapses ($p = 0.0021$), but not in those with pulmonary or anastomotic recurrence. There were no differences in prognoses after relapse in any recurrence site among the three groups in patients who underwent curative resection for relapse. ***Conclusion:*** If patients can undergo curative resection for relapse, they receive a survival benefit regardless of the timing of relapse.

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Introduction

Colorectal cancer is the second most common cause of cancer death in both the USA and Japan, and is one of the most rapidly expanding diseases in Japan [1, 2]. Although the most promising treatment for colorectal cancer is curative resection, some of the patients with curative resection for colorectal cancer develop relapse [3]. Therefore, it is important to improve the outcome of treatment for relapse of colorectal cancer.

Recent remarkable advances of multiagent chemotherapies, including those using molecular target drugs, have improved the prognosis of metastatic colorectal cancer [4–6]. However, the complete resection of metastatic tumors is still the best treatment for this disease. There have been many studies investigating the outcome of resection for metastatic tumors of colorectal cancer. The 5-year survival rates after resection for hepatic and pulmonary metastases ranged from 27 to 58% and from 29 to 64%, respectively [7–17]. Most of the relapses occur within 5 years after curative resection for colorectal cancer [3]. However, it remains uncertain whether there is an association between the timing of relapse and the outcome. Kornprat et al. [18] demonstrated that the disease-free interval from colorectal surgery to liver metastases was not associated with the prognosis after hepatectomy. On the other hand, it has been reported that the disease-free survival after hepatectomy in patients with metachronous liver metastasis is better than that in patients with synchronous liver metastasis [19].

The relationship between the time to relapse (TR) and the rate of resection after relapse remains unclear. Further, the association between the outcome in patients treated with resection for relapse and the TR is also obscure.

The aim of this retrospective multicenter study was to clarify the association between TR after resection for colorectal cancer and prognosis after relapse.

Patients and Methods

The study group of the Japanese Society for Cancer of the Colon and Rectum (JSCCR) on postsurgical surveillance of colorectal cancer collected data on 5,230 consecutive patients who underwent curative resection at 14 member institutions from January 1991 to December 1996. The patients with T1 cancers which were removed by endoscopical or transanal resection were excluded from this study. The patients with cancers associated with familial adenomatous polyposis, ulcerative colitis or Crohn's disease were also excluded. Treatment of recurrent tumors was decided according to the criteria of each institution. The local ethics committee of each institution approved this study. Recurrence sites were classified into liver, lung, local, anastomosis, and others. Other recurrence sites consisted of bone, brain, ovary, distant lymph node, and so on. Peritoneal carcinomatosis was also classified into others.

Table 1. A Cox proportional hazards model for prognosis after relapse

	n	p value	Hazard ratio	95% CI
Age				
<63 years	456	NS	1	
≥63 years	450		1.15	0.99–1.33
Histologic grade				
Well- or moderately differentiated adenocarcinoma	835	0.012	1	
Poorly differentiated adenocarcinoma or mucinous carcinoma	70		1.40	1.08–1.82
Unknown	1			
Direct invasion of the primary tumor to other organs				
Absent	840	0.0010	1	
Present	65		1.58	1.20–2.07
Unknown	1			
TNM stage				
Stage I	51	NS	1.14	0.81–1.60
Stage II	255		0.85	0.72–1.01
Stage III	600		1	
Time to relapse (TR)				
A	358	NS	1.16	0.93–1.46
B	395		1.07	0.86–1.34
C	153		1	
Resection for relapse with curative intent				
Absent	527	<0.0001	1	
Present	379		0.26	0.22–0.31

CI = Confidence interval. A = TR ≤ 1 year; B = 1 year < TR ≤ 3 years; C = 3 years < TR.

Follow-Up Examination

All patients had intensive prospective follow-up after surgery according to the follow-up protocols of each institution. Most institutions established a follow-up examination period of 5–10 years. The standard follow-up protocol was as follows: measurement of a serum tumor marker and hepatic imaging (ultrasonography and/or computed tomography) every 3 months for the first 3 years and every 6 months for the next 2 years, and chest X-ray every 6 months, pelvic CT for rectal cancer every year, and colonoscopy every 1–2 years.

Timing of Relapse

Patients were classified into three groups according to the TR: group A, TR ≤ 1 year; group B, 1 year < TR ≤ 3 years, and group C, 3 years < TR. The prognosis after relapse was compared among the three groups, and between group A and a combined group including groups B and C. The resection rates for metastatic tumors were also compared among the three groups.

Table 2. Characteristics of patients

	Patients with relapse	Patients without relapse	p value
Gender			
Male	559 (18.0)	2,546 (82.0)	NS
Female	347 (16.3)	1,778 (83.7)	
Age	62 ± 11	63 ± 11	NS
Primary tumor site			
Colon	506 (14.1)	3,077 (85.9)	<0.0001
Rectum	400 (24.3)	1,247 (75.7)	
TNM stage			
Stage I	51 (3.7)	1,316 (96.3)	<0.0001
Stage II	255 (13.3)	1,657 (86.7)	
Stage III	600 (30.8)	1,351 (69.2)	
First recurrence site			
Liver	373		
Lung	250		
Local	209		
Anastomosis	22		
Others	199		
Follow-up period	3.5 ± 2.9	7.1 ± 3.1	<0.0001

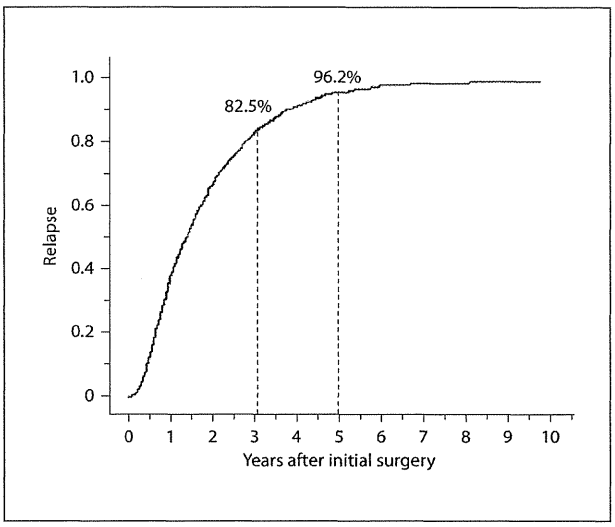

Fig. 1. Curve showing the accumulated relapse rate of patients who underwent curative resection for colorectal cancer. More than 80% of the relapses occurred within 3 years, and 96.2% occurred within 5 years after curative resection for colorectal cancer.

Prognostic Factors after Relapse

Age, gender, location of tumor, histologic grade, direct invasion of the primary tumor to other organs, TNM staging, lymphatic invasion, venous invasion, TR, and resection for relapse with curative intent were analyzed as risk factors for overall survival after relapse (table 1).

Statistical Analysis

Statistical analysis was performed with the StatView statistical package (StatView 5.0; Abacus Concepts, Inc., Berkeley, Calif., USA). All data are expressed as the median ± SD. The χ^2 test for independence was used to investigate the frequency of resection in relapsed cases for each of the three TR groups. We used the Kaplan-Meier method to calculate the actuarial survival of patients. Overall survival rates for each of the three patient groups were assessed by log-rank test. A Cox proportional hazards model was used to determine which risk factors had an independent effect on survival after relapse. Differences in results were considered significant at $p < 0.05$.

Results

Relapse

Of the 5,230 patients, 906 (17.3%) had relapse after curative resection for colorectal cancer during the median follow-up time of 6.6 ± 3.1 years. Among them, 39.5% developed recurrence within 1 year (group A), 82.5% within 3 years, and 96.2% within 5 years (fig. 1). There were no differences in gender or age between patients with relapse and those without (table 2). Relapse was significantly more frequent in patients with rectal cancer than in those with colon cancer. The more advanced the stage, the more frequent the relapse. The most common recurrence site was the liver, followed in order by the lungs and local recurrence sites.

Overall Survival after Initial Colorectal Surgery according to Timing of Relapse

There was a significant difference in overall survival after colorectal surgery in patients with liver, lung, and local relapse, but not in those with anastomotic relapse (table 3). The later the relapse occurred, the better the prognosis was after initial colorectal surgery.

Overall Survival after Relapse according to the Timing of Relapse

There was a significant difference in overall survival after relapse in patients with liver or local relapse (table 3) according to the timing of relapse ($p = 0.0175$ and $p = 0.021$, respectively). The survival after relapse in group A patients with liver metastasis was worse than that in group B or group C patients, but there was no difference

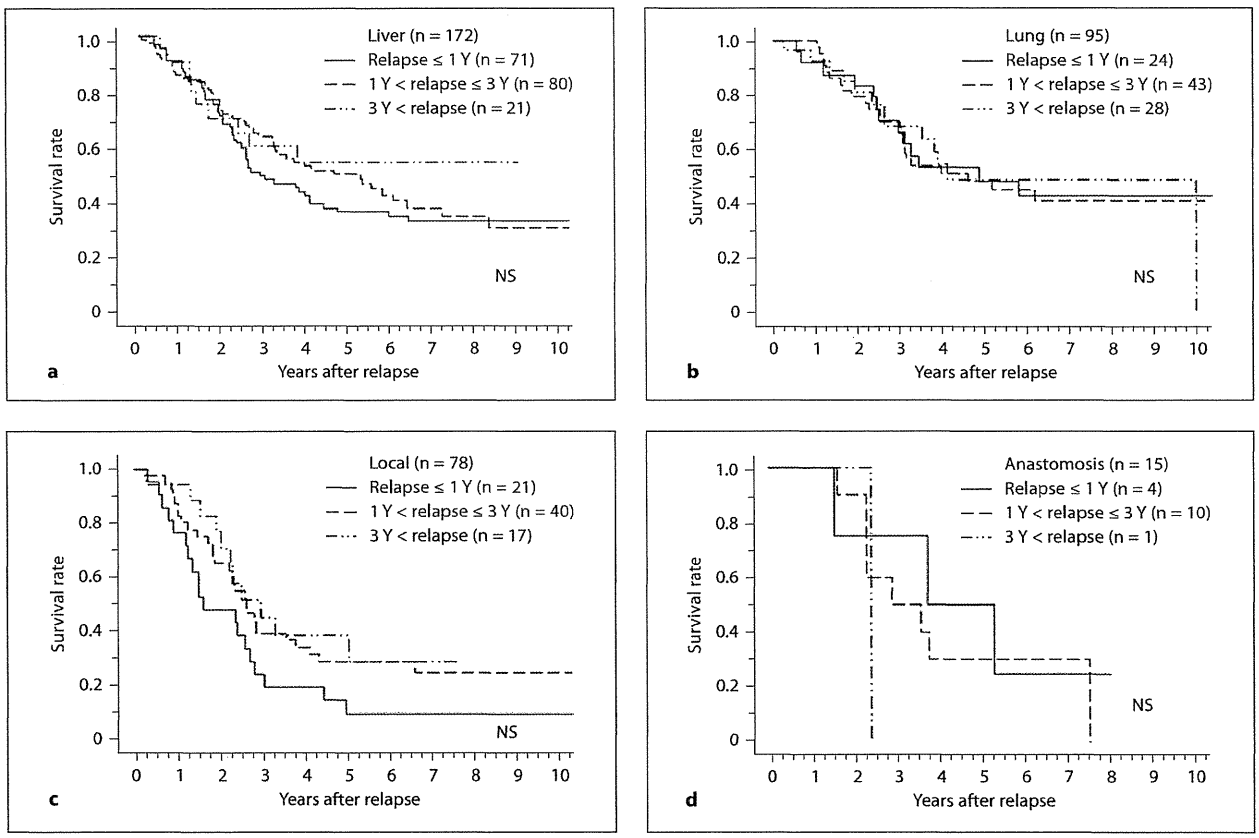

Fig. 2. There were no differences in the prognosis after curative resection for relapse among the three TR groups for patients with (**a**) liver, (**b**) lung, (**c**) local, or (**d**) anastomotic recurrence.

between group B and group C patients. There were no significant differences in survival after relapse among the three TR groups for patients with pulmonary or anastomotic relapse (table 3).

Resection Rate in Relapsed Cases

Curative resection for recurrent tumors was performed in 46.1% of cases of liver metastasis, 38.0% of cases of lung metastasis, 37.3% of cases of local recurrence, and 68.2% of cases of anastomotic recurrence. There were significant differences in the resection rates for the patients with liver ($p = 0.0023$) and pulmonary ($p = 0.038$) relapse among the three TR groups (table 4, while no differences were observed in resection rates for patients with local or anastomotic relapse among the three TR groups. The resection rate for other recurrence sites was 40.2% in total.

Survival after Curative Resection for Recurrent Tumors

Of the 906 patients with relapse, 379 (41.8%) underwent curative resection for recurrent tumors. The 5-year survival rates after resection for recurrent tumors of the liver, lungs, local sites, and anastomotic sites were 45, 48, 27, and 33%, respectively.

There was no difference in survival after relapse in patients who underwent curative resection for any relapse sites according to the timing of relapse (fig. 2). However, group A patients who received resection for local relapse showed significantly worse survival than the combined group of patients from groups B and C who received resection for local relapse ($p = 0.040$). In other recurrence sites, there were no differences in prognosis between group A, group B and C. Of the 379 patients who received resection for recurrent tumors, 240 (63.3%) experienced

Table 3. Overall survival rate after initial colorectal surgery and relapse according to timing of relapse

Recurrent site	TR (patients)	5-Year overall survival rate after initial colorectal surgery, %	p value	5-Year overall survival rate after relapse, %	p value
Liver	A (188)	18	<0.0001	14	0.018
	B (140)	39		31	
	C (45)	69		32	
Lung	A (82)	18	<0.0001	15	0.34
	B (113)	29		21	
	C (55)	72		26	
Local	A (74)	12	<0.0001	9	0.0021
	B (95)	26		16	
	C (40)	83		26	
Anastomosis	A (7)	29	0.22	29	0.95
	B (14)	36		21	
	C (1)	100		0	

A = TR ≤ 1 year; B = 1 year < TR ≤ 3 years; C = 3 years < TR.

re-relapse. Among them, 24 remained disease-free after surgery for re-relapse. Finally, 163 of the 906 patients with relapse (18.0%) remained disease-free.

Prognostic Factors after Relapse

In the 906 patients, age ($p < 0.0001$), histologic grade ($p < 0.0001$), direct invasion of the primary tumor to other organs ($p = 0.0075$), TNM staging of the primary tumor ($p = 0.0014$), timing of relapse ($p = 0.0035$), and the performance of curative resection for relapse ($p < 0.0001$) had effects on survival after relapse based on the log-rank test. Among them, histologic grade ($p = 0.012$), direct invasion of the primary tumor to other organs ($p = 0.0010$), and the performance of curative resection for relapse ($p < 0.0001$) were independent prognostic factors (table 1).

Discussion

This study demonstrated that, in patients who underwent curative resection for relapse of colorectal cancer, the timing of relapse did not affect the survival time after relapse. There were no differences in overall survival after hepatectomy for liver metastases according to timing of relapse in our series. Kornprat et al. [18] reported the outcome after hepatectomy for multiple colorectal metastases. In their study, there was no difference in survival between patients with a disease-free interval after colorectal surgery of <12 months and those with an interval of ≥12 months. On the other hand, Tsai et al. [19] demonstrated that synchronicity of liver metastasis is associated with disease-free survival after hepatectomy. In their study, the disease-free survival after hepatectomy in patients with metachronous liver metastasis was better than that in those with synchronous liver metastasis. Their multivariate analysis revealed that both synchronicity and primary tumor stage were independent prognostic factors that influenced disease-free survival.

In pulmonary metastases, we showed that there were no differences in prognoses after curative metastasectomy among the three different TR groups. That is, the survival curves after pulmonary resection were very similar among the three TR groups in this study. Lee and coworkers [17] demonstrated an association between timing of relapse and prognosis after pulmonary resection for metastases from colorectal cancer. In their study, the prognoses after pulmonary resection did not differ between the patients with a TR of <24 months and those with a TR of >24 months. Our study supports their results. On the other hand, a recent German study [20] showed that a disease-free interval of >36 months was a prognostic factor in a group of 153 patients. A large-scale study will be needed to clarify the association between timing of relapse and survival after pulmonary resection.

As for local relapse, the patients who underwent curative resection for recurrent tumors within 1 year after the initial colorectal resection had worse outcomes after relapse than those who underwent such resection after 1 year. In contrast, Wanebo et al. [21] demonstrated that there was no difference in prognosis between patients undergoing an abdominosacral resection for recurrent rectal cancer within 1 year and those undergoing this procedure after 1 year. One of the reasons for this discrepancy may be the difference in the populations of the two studies. That is, only patients with advanced recurrent rectal cancer were evaluated in the study of Wanebo et al.

In this study, we showed that the curative resection rates differed according to the timing of relapse for patients with liver or lung recurrence, but not for those with local or anastomotic recurrence. In other words, there were significant differences in the resection rates for distant metastases according to the timing of relapse after curative resection for colorectal cancer. In our series, the

Table 4. TR and curative resection rate

Recurrence site	TR	Patients with curative resection for relapse	Patients without resection for relapse	Total number of relapses %	Resection rate, %	p value
Liver		172	201	373 (7.1)	46.1	
	A	71	117	188	37.8	0.0023
	B	80	60	140	57.1	
	C	21	24	45	46.7	
Lung		95	155	250 (4.8)	38.0	
	A	24	58	82	29.3	0.038
	B	43	70	113	38.1	
	C	28	27	55	50.9	
Local		78	131	209 (4.0)	37.3	
	A	21	53	74	28.4	NS (0.14)
	B	40	55	95	42.1	
	C	17	23	40	42.5	
Anastomosis		15	7	22 (0.4)	68.2	
	A	4	3	7	57.1	NS (0.63)
	B	10	4	14	71.4	
	C	1	0	1	100.0	

The total number of patients in this study was 5,230. A = TR ≤ 1 year; B = 1 year < TR ≤ 3 years; C = 3 years < TR.

resection rates for hepatic relapse were 37.8% in group A and 54.6% in the combined group that included groups B and C. In a French population-based study, the curative surgery rate was 7.2% in synchronous liver metastases and 19.8% in metachronous ones [22]. The authors of this previous study indicated that the synchronous presence of liver metastasis with primary colorectal cancer was associated with a lower curative resection rate than metachronous liver metastasis. On the other hand, we could not find any previous study on the association between timing of relapse and the resection rates of lung metastasis from colorectal cancer. As for local relapse, several studies reported that there were no significant associations between timing of relapse and curative resection rate, which are consistent with the findings of the present study [17, 23, 24].

This study also demonstrated that the overall survival after relapse differed according to the timing of relapse in patients with hepatic and local relapse after curative resection for colorectal cancer. One of the reasons for this phenomenon may have been the differences in the resection rate according to the timing of relapse, because the prognoses after the resection with curative intent for relapse did not differ according to the timing of relapse.

At the present time, surgery with curative intent seems to be the only way to achieve the long-term survival of patients with colorectal cancer relapse. During the period of the present study, chemotherapies such as FOLFOX or FOLFIRI were not available in Japan. Chemotherapy for colorectal cancer has improved remarkably in recent years. To cure patients with relapse of colorectal cancer, it is necessary to increase the rate of curative resection for recurrent tumors. Recent studies have demonstrated that neoadjuvant chemotherapy can render nonresectable liver metastases resectable [25, 26]. Therefore, advances in chemotherapy may contribute to the improvement of surgical resection for metastases from colorectal cancer.

In conclusion, the timing of relapse after curative resection for colorectal cancer may affect the rate of curative resection for recurrent tumors. However, if patients can undergo curative resection for recurrent tumors, they may receive a survival benefit regardless of the timing of relapse. Further studies will be needed to validate our results in the era of multiagent chemotherapy.

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Retrospective, Matched Case–Control Study Comparing the Oncologic Outcomes Between Laparoscopic Surgery and Open Surgery in Patients with Right-Sided Colon Cancer

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Abstract

Purpose. The short- and long-term outcomes of laparoscopic surgery for right-sided colon cancer remain largely uninvestigated. This study was undertaken to compare the morbidity and mortality after either a laparoscopic right hemicolectomy (LRHC) or an open right hemicolectomy (ORHC) for this type of tumor.

Methods. The study group included 100 patients who underwent an LRHC and 100 patients who underwent an ORHC for right-sided colon cancer from 1990 through 2004. The two groups were retrospectively well matched with respect to sex, age (±5 years), and pathological tumor-node-metastasis (TNM) stage.

Results. The median follow-up period was 83 months in the LRHC group and 105 months in the ORHC group. The LRHC group had a lower volume of intraoperative bleeding ($P < 0.001$), a lower rate of wound infection ($P = 0.019$) or postoperative intestinal obstruction ($P = 0.013$), and a shorter hospital stay ($P < 0.001$) than the ORHC group. The rate of recurrence did not differ significantly between the LRHC group (19%) and the ORHC group (22%). In patients with TNM stage I or II, the disease-free survival (DFS) rate (94.9% vs 95.1%) and overall survival (OS) rate (95.8% vs 95.0%) did not differ significantly between the two groups. A similar tendency was observed in patients with stage III with the rates for DFS (71.3% vs 60.4%) and OS (73.6% vs 64.1%), respectively.

Conclusions. An LRHC for right-sided colon cancer has the advantage over an ORHC of better short-term outcomes, and both groups have similar long-term oncologic outcomes. An LRHC is thus an acceptable alternative to an ORHC for the treatment of this type cancer.

Key words Right-sided colon cancer · Laparoscopic surgery · Hemicolectomy

Introduction

The indications for laparoscopic surgery have been extended from early colon cancer to advanced cancer.[1,2] This procedure has several distinct advantages in comparison to open surgery, including briefer use of analgesics, earlier return of bowel motility, a shorter hospital stay, and faster perioperative recovery.[2,3] The meta-analysis of the results of 2512 procedures from 12 randomized clinical trials reported improved short-term outcomes for laparoscopic surgery in comparison to conventional open surgery for colorectal cancer.[4] Laparoscopic surgery has also been performed in our hospital on more than 600 patients with colon cancer. Recently, the medium-term outcome of laparoscopic surgery and open surgery for advanced colorectal cancer were assessed in a matched group of patients, revealing that no significant difference was found in the survival or recurrence rate.[5] In addition, our study demonstrated the incidence of wound infections to be significantly lower after a laparoscopic colectomy than after an open procedure.[6] Laparoscopic surgery to a right-sided tumor is technically different from that of a rectosigmoid tumor.[8,9] The previous study, however, did not separate right-sided from left-sided tumors. Few retrospective studies have focused on the safety and efficacy of laparoscopic surgery for right-sided colon cancer.[10–13] The present matched case–control study was thus designed to compare the short- and long-term outcomes between laparoscopic and open surgeries in patients with right-sided colon cancer. Its ultimate goal was to determine whether a laparoscopic resection of this type of tumor is warranted.

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Subjects and Methods

A laparoscopic colectomy was first performed in our hospital in 1996. From 1996 through 1999, laparoscopic surgery was basically indicated for early colon cancer. From 2000, the indication of this procedure was extended to advanced cancer confirmed to have no direct invasion to other organs on preoperative diagnostic imaging studies. All patients underwent a barium enema examination, colonoscopy, abdominal ultrasonography, and computed tomography (CT) of the chest and abdomen before surgery. The procedure for a lymph node dissection was determined based on the depth of tumor invasion on preoperative diagnosis in patients with right-sided colon cancer, who underwent a laparoscopic right hemicolectomy (LRHC) and those that underwent an open right hemicolectomy (ORHC); D2 and D3 lymphadenectomies according to the Japanese Classification of Colorectal Carcinoma[14] were applied for T1 and T2 or deeper tumors, respectively.

From April 1990 through December 2004, a total of 1895 patients underwent surgery for colorectal cancer. During the study period, there were 333 patients with right-sided colon cancers (109 patients for LRHC; 224 for ORHC) of the 1895. A retrospective, matched case–control study of the patients treated with an LRHC and ORHC was carried out; the groups were matched for sex, age (±5 years), and pathological tumor-node-metastasis (TNM) stage. The patients with an intractable intestinal obstruction and patients in whom the LRHC was switched to an ORHC were excluded from the present study.

Finally, 100 patients who underwent an LRHC and 100 who underwent an ORHC were compared (Table 1). The median (range) follow-up period was 83 (36–156) months in the LRHC group (number of

Table 1. Demographic characteristics of the patients

	LRHC (n = 100)	ORHC (n = 100)	P value
Male:female	65:35	65:35	NS
Age (years)[a]	64 (39–89)	65 (39–88)	NS
Location			NS
Cecum	14	21	
Ascending colon	72	62	
Transverse colon	14	17	
BMI (kg/m^2)[a]	22 (15–33)	22 (15–34)	NS
ASA status			NS
I	36	31	
II	55	51	
III	9	18	
Tumor size (cm)[a]	3.5 (0.7–9.4)	4.7 (0.8–14)	NS
No. of lymph nodes removed[a]	14 (10–58)	20 (12–92)	NS
pT category			NS
pT1	19	19	
pT2	11	11	
pT3	70	70	
pN category			NS
pN0	61	61	
pN1	27	27	
pN2	12	12	
Tumor differentiation			NS
Well	51	56	
Moderate	43	38	
Poor	4	3	
Mucinous	2	3	
pTNM			NS
I	29	29	
II	32	32	
III	39	39	
Follow-up period (months)[a]	83 (36–156)[b]	105 (48–216)[c]	NS

LRHC, laparoscopic right hemicolectomy; ORHC, open right hemicolectomy; BMI, body mass index; ASA status, physical status according to the American Society of Anesthesiologists classification; NS, not significant

[a]Values are expressed as median (range)

[b]n (alive at last visit) = 87

[c]n (alive at last visit) = 82

Table 2. Demographic characteristics of the patients in former and latter terms

	Former term (1990–2000)			Latter term (2001–2004)		
	LRHC (n = 45)	ORHC (n = 67)	P value	LRHC (n = 55)	ORHC (n = 33)	P value
Male:female	29:16	48:19	NS	36:19	17:16	NS
Age (years)[a]	62 (39–86)	63 (39–88)	NS	68 (50–89)	66 (53–86)	NS
Location			NS			NS
Cecum	5	12		9	9	
Ascending colon	33	42		39	20	
Transverse colon	7	13		7	4	
BMI (kg/m^2)[a]	22 (15–27)	21 (15–28)	NS	22 (16–33)	23 (18–34)	NS
ASA status			NS			NS
I	22	22		14	9	
II	21	31		34	20	
III	2	14		7	4	
Tumor size (cm)[a]	3.1 (0.7–9.4)	4.5 (0.8–12)	NS	3.5 (1.3–7.5)	5.5 (1–14)	NS
No. of lymph nodes removed[a]	24 (10–58)	29 (5–92)	NS	18 (10–38)	22 (2–42)	NS
pT category			NS			NS
pT1	12	14		7	5	
pT2	9	7		3	4	
pT3	24	46		45	24	
pN category			NS			NS
pN0	33	49		29	15	
pN1	7	15		21	16	
pN2	5	3		5	2	
Tumor differentiation			NS			NS
Well	32	40		19	16	
Moderate	10	22		33	16	
Poor	2	3		2	0	
Mucinous	1	2		1	1	
pTNM			NS			NS
I	21	21		8	7	
II	11	27		21	8	
III	13	19		26	18	
Follow-up period (months)[a]	101 (24–156)	105 (48–216)	NS	63 (12–92)	68 (14–100)	NS

LRHC, laparoscopic right hemicolectomy; ORHC, open right hemicolectomy; BMI, body mass index; ASA status, physical status according to the American Society of Anesthesiologists classification; NS, not significant
[a]Values are expressed as median (range)

patients alive at last visit [n] = 87) and 105 (48–216) months in the ORHC group (n = 82). The demographic characteristics such as age, body mass index, physical status according to the American Society of Anesthesiology (ASA) status, tumor size, the number of dissected lymph nodes, and pathological TNM stage did not differ significantly between the LRHC group and the ORHC group (Table 1). The numbers of subjects who underwent surgery during the following periods were: 1990 through 2000 (former term), 45 patients underwent an LRHC and 67 patients underwent an ORHC; and 2001 through 2004 (latter term), 55 LRHCs and 33 ORHCs. In the former and latter terms, the clinical and pathological data including the number of dissecting lymph nodes did not significantly differ between LRHC and ORHC (Table 2).

The technique for laparoscopic surgery has been described previously;[15] a new method was employed in which the first trocar was inserted after the application of a LAP DISC placed on the upper abdomen. After pneumoperitoneum, an additional four trocars were inserted into abdominal cavity under observation with a 5-mm flexible scope.

The postoperative follow-up examinations included the measurement of serum carcinoembryonic antigen levels (every 3 months to 1 year), CT scans of the chest and abdomen (at 6-month intervals), and colonoscopy, in addition to routine outpatient visits. Recurrent disease was assessed based on the clinical, laboratory, diagnostic imaging, and pathological findings.

A statistical analysis was performed with the Chi-square and Mann–Whitney U-tests. Disease-free survival (DFS) and overall survival (OS) rates were estimated according to the Kaplan–Meier method. The log-rank test was used to compare these survival rates between the groups. P values of less than 0.05 were considered to indicate statistical significance.

Table 3. Operative time, blood loss during operation, hospital stay, and postoperative complications

	LRHC	ORHC	*P* value
Operation time (min)[a]	215 (85–355)	195 (100–332)	NS
Blood loss during operation (ml)[a]	50 (0–400)	120 (0–900)	<0.001
Hospital stay (days)[a]	9 (5–50)	17 (8–57)	<0.001
Wound infection[b]	3	13	0.019
Ileus[b]	7	20	0.013
Postoperative bleeding[b]	1	1	NS

NS, not significant
[a]Values are expressed as median (range)
[b]Values represent number of events

Results

Table 3 shows the short-term outcomes of right-sided colon cancer patients with LRHC and ORHC. The median bleeding volume was significantly lower in the LRHC group (50 ml) than in the ORHC group (120 ml; $P < 0.001$). The median hospital stay after surgery was significantly shorter in the LRHC (9 days) than in the ORHC (17 days; $P < 0.001$). Postoperative complications were significantly less frequent in the LRHC (11%) than in the ORHC (34%; $P = 0.001$); wound infections ($P = 0.019$) and postoperative intestinal obstruction ($P = 0.013$) were significantly less frequent in the former than in the latter. No significant difference was found in the operation time and postoperative bleeding rate. The recurrence rate did not differ significantly between the LRHC (19%) and the ORHC (22%). Liver metastasis was the most common form of recurrence in both groups. No port-site recurrence occurred in the LRHC group. As for the long-term outcomes of patients with TNM stage I or II colon cancer, the DFS rate (94.9% vs 95.1%) and OS rate (95.8% vs 95.0%) did not differ significantly between the LRHC and ORHC groups (Fig. 1a,b). A similar tendency was observed in patients with stage III colon cancer with the rates for DFS (71.3% vs 60.4%) and OS (73.6% vs 64.1%), respectively (Fig. 2a,b).

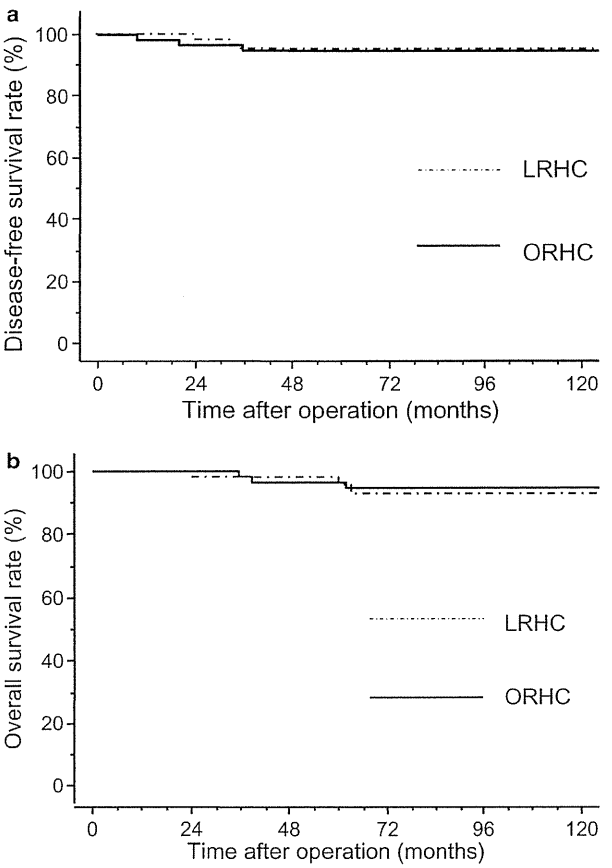

Fig. 1. a Comparison of the disease-free survival rates in patients with stage I or II colon cancer between the laparoscopic right hemicolectomy (*LRHC*) group and the open right hemicolectomy (*ORHC*) group. **b** Comparison of the overall survival rates in patients with stage I or II colon cancer between the LRHC group and the ORHC group

Discussion

An LRHC was associated with a significantly smaller intraoperative bleeding volume, significantly lower rates of wound infection and intestinal obstruction, and a significantly shorter hospital stay than was ORHC in this retrospective, matched case–control study of patients with right-sided colon cancer. There was no significant difference in the recurrence rate, the form of recurrence, or long-term outcomes between the groups. Sex, age, body-mass index, ASA status, tumor size, pathological TNM stage, and the number of dissected lymph nodes were similar in the LRHC group and the ORHC group. The comparison of oncologic outcomes in both groups is therefore considered valid.

A radical lymphadenectomy along the feeding arteries of the tumor is the standard procedure for advanced colorectal cancer. Laparoscopy provides a better, magnified view for surgery,[1,2] but it is not easy to identify