metastasis, 83 had the second recurrence in the liver, 29 in the lung, 12 in both liver and lung and 52 in the other organs. Sixteen of the 29 patients with pulmonary recurrence and one of the 12 patients with both hepatic and pulmonary recurrences were treated surgically. Two patients had undergone resections for both hepatic and pulmonary recurrences after more than two hepatic metastasectomies. In the remaining 90 patients who had undergone pulmonary resection as the first treatment for colorectal metastasis, three had the second recurrence in the liver, 27 in the lung, four in both liver and lung and 16 in other organs. All three patients with hepatic recurrence were treated surgically. However, all four patients with both hepatic and pulmonary recurrences underwent systemic chemotherapy as the second treatment.

As a result, 30 patients underwent both hepatic and pulmonary resections for colorectal metastasis. The patients consisted of 19 men and 11 women, ranging in age from 24 to 75 years with a mean of 59 years. Two of the patients had received adjuvant chemotherapy (tegafur/uracil and 5-fluorouracil/leucovorin) after primary colorectal resection and one patient had received preoperative chemoradiation for rectal cancer.

The criteria for hepatectomy were as follows: (1) metastatic lesions are confined to the liver and technically resectable, (2) no extrahepatic metastases except resectable pulmonary metastasis are detected, and (3) liver function is equal to complete resection of all hepatic tumors. The criteria for pulmonary resection were as follows: (1) metastatic lesions are confined to the lung and technically resectable, (2) no extrathoracic metastases except resectable hepatic metastasis are detected, and (3) cardiorespiratory function is equal to complete resection of all pulmonary tumors. The timing of the detection of hepatic and pulmonary metastases or the number of prior resections for metastases did not affect these criteria, so the selection criteria for further resections for recurrences after hepatic and pulmonary resections are the same as above.

At hepatectomy, intraoperative ultrasonography was performed to confirm tumor location and size of the lesions in all patients, and all of the resections were ultrasound-guided procedures. Hepatic resection was performed by the forceps fracture method under inflow occlusion (Pringle's maneuver). At pulmonary resection, hilar or mediastinal lymph node dissection was used to sample lymph nodes of most patients who had a lobectomy.

When hepatic and pulmonary metastases were detected simultaneously, hepatic resection was carried out first, followed by pulmonary resection.

No patient received adjuvant chemotherapy after hepatectomy or pulmonary resection.

After hepatic or pulmonary resection, patients were closely followed with diagnostic imaging [chest X-ray and abdominal computed tomography (CT)] and measurement of serum carcinoembryonic antigen (CEA) levels every 3 months; they also underwent an annual colonoscopy to detect any tumor recurrence. The median follow-up of survivors was 53 months.

MORPHOLOGICAL INVESTIGATIONS

The resected specimens of colon or rectum, liver and lung were fixed in 10% phosphate-buffered formalin, cut at intervals of 5 mm and embedded in paraffin. Serial sections of 3-μm thickness were stained with hematoxylin and eosin for morphological examination. Each case was histologically classified according to the histological type, tumor size, location, number of metastases, presence of serosal invasion, nodal status and margin status. Histological diagnosis was performed according to the World Health Organization intestinal tumor classification (15).

STATISTICAL ANALYSIS

The student t-test was used to compare data between subgroups by the location of the primary tumor. The Mann–Whitney's U test was used to compare serum CEA levels between subgroups. Analyses of survival rates were performed using the Kaplan–Meier method (16) and differences between the curves were tested using the log-rank test. Factors related to survival were analyzed with the Cox proportional hazards regression model (17). A P value of less than 0.05 was considered to denote significance.

RESULTS

CLINICOPATHOLOGICAL FEATURES OF PRIMARY AND METASTATIC TUMORS

The primary tumors were staged as I ($n = 1$), II ($n = 10$), III ($n = 15$) and IV ($n = 4$) according to TNM classification (Table 1). All patients at stage IV had hepatic metastasis at resection of the primary tumor.

At the initial hepatectomy, the average number of hepatic tumors was 2.1 (range, 1–12), the average maximum size was 3.2 cm (range, 0.3–9 cm) and the average preoperative CEA level was 19.9 ng/ml (range, 0.8–68.5 ng/ml). In all hepatectomies, the average number of hepatic tumors was 2.8 and the average maximum size was 3.3 cm. Lymph node metastasis at the hepatoduodenal ligament was shown in one patient.

Regarding pulmonary metastases, the average number of pulmonary tumors was 1.8 (range, 1–5), the average maximum size was 2.2 cm (range, 0.7–6.7 cm) and the average prethoracotomy CEA level was 12.4 ng/ml (range, 1.0–66.7 ng/ml) at initial pulmonary resection. In all pulmonary resections, the average number of pulmonary tumors was 2.1 and the average maximum size was 2.5 cm. Hilar lymph node metastasis of the lung was shown in two patients.

SURGICAL RESECTIONS FOR HEPATIC AND PULMONARY METASTASES

Forty-five hepatectomies (30 partial resections, four subsegmentectomies, seven segmentectomies and four lobectomies

Table 1. Correlation between clinicopathologic factors and overall survival in patients with resected hepatic and pulmonary metastases from colorectal cancer

	No.	Median survival (mo)	P value		No.	Median survival (mo)	P value
Primary colorectal lesion				**Pulmonary metastases**			
Location				*First pulmonary resection*			
rectum	13	52.7	0.03	Number of tumors			
colon	17	38.6		1	18	47.9	0.31
TNM classification				≥2	12	27.1	
I	1	88.9	0.02*	Maximum size of the tumor (cm)			
II	10	48.9		<3	21	34.8	0.69
III	15	38.8		≥3	9	38.8	
IV	4	14.6		Distribution of metastases			
Lymph node metastasis				unilobar	24	42.1	0.68
absent	11	54.8	0.64	bilobar	6	27.1	
present	19	32.8		Hilar or mediastinal lymph node			
Histological type of adenocarcinoma				negative	28	36.7	0.89
well or moderately differentiated	28	38.7	0.77	positive	2	43.6	
poorly differentiated and others	2	41.7		*All pulmonary resections*			
				Number of tumors			
Hepatic metastases				<3	22	38.7	0.92
First hepatectomy				≥3	8	44.8	
Number of tumors				Maximum size of the tumor (cm)			
1	18	40.8	0.26	<3	19	34.8	0.93
≥2	12	36.8		≥3	11	38.8	
Maximum size of the tumor (cm)				Distribution of metastases			
<3	14	40.0	0.03	unilobar	21	41.1	0.97
≥3	16	35.8		bilobar	9	30.8	
Distribution of metastases							
unilobar	20	40.8	0.36				
bilobar	10	36.8		CEA level at initial recurrence (ng/ml)			
Lymph node of hepatoduodenal ligament				<50	25	38.7	0.34
negative	29	38.8	0.02	≥50	5	33.0	
positive	1	13.9		Disease-free interval from resection of primary tumor			
All hepatectomies				<1 year	19	38.8	0.23
Total number of tumors				≥1 year	11	38.6	
<3	19	38.6	0.79	Simultaneous detection of hepatic and pulmonary recurrences			
≥3	11	38.8		yes	11	34.8	0.35
Maximum size of the tumor (cm)				no	19	38.8	
<3	13	38.8	0.08	Initial metastasis in the lung			
≥3	17	38.6		yes	3	54.8	0.72
Distribution of metastases				no	27	38.6	
unilobar	17	43.0	0.49	Total number of liver and lung resections			
bilobar	13	34.8		2	13	33.0	0.50
				≥3	17	54.3	

CEA, carcinoembryonic antigen.
*Stage I, II or III versus Stage IV.

according to Couinaud's anatomical classification (18)) and 40 pulmonary resections (32 partial resections, seven lobectomies and one pneumonectomy) were performed on the 30 patients. The average number of operations performed for hepatic or pulmonary metastases per patient was 2.8. Three operations were performed on 11 patients, four operations on four patients each and five operations on two patients each.

There was no perioperative mortality. Five complications were observed: two cases of biliary leak and one case each of portal vein thrombosis after hepatectomy, wound infection and air leak after pulmonary resection.

The location of initial metastasis was lung in three patients, liver in 19, and both liver and lung in eight. Eleven patients experienced hepatic and pulmonary metastases detected simultaneously.

RECURRENCE AFTER SURGICAL RESECTIONS FOR HEPATIC AND PULMONARY METASTASES

Among 30 patients who underwent surgical resections for hepatic and pulmonary metastases, 25 developed recurrences when recurrence was defined as the first recurrent disease after at least one resection each for hepatic and pulmonary metastases. Locations of recurrences were as follows: lung in 11 patients, liver and lymph node in four each, both liver and lung in three, peritoneum, local recurrence and brain in one each. Re-resection could be performed in 15 of the 25 patients. Of the remaining 10 patients, eight received systemic chemotherapy, one each received radiation therapy and best supportive care.

SURVIVAL

Survival time was calculated from the date of the first metastasectomy for the second organ metastasized (liver or lung).

Actuarial overall survival was 58% at 5 years with a median survival of 39 months (Fig. 1). Disease-free survival was 56% at 1 year and 8% at 3 years, with a median recurrence-free survival of 13 months. Nine 5-year survivors were observed and eight of the nine patients are still alive without disease. Of the nine 5-year survivors, six had undergone three operations and one had undergone four operations.

When survival time was calculated from the date of the first metastasectomy for the first organ, actuarial overall survival was 70% at 5 years with a median survival of 60 months.

CORRELATION BETWEEN CLINICOPATHOLOGIC FACTORS AND OVERALL SURVIVAL

To find prognostic factors for survival after resection of hepatic and pulmonary metastases, clinicopathologic factors and overall survival calculated from the date of the first metastasectomy for the second organ were analyzed in 30 patients (Table 1). Primary colon carcinoma ($P = 0.03$),
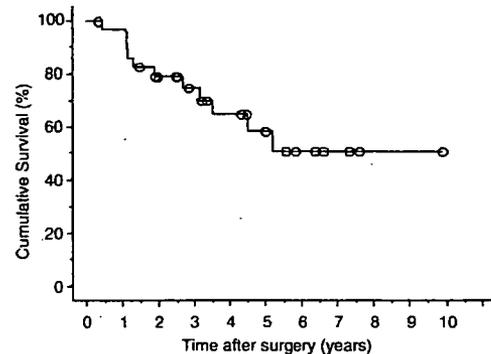

Figure 1. Cumulative survival curves for 30 patients who underwent resections for both hepatic and pulmonary metastases of colorectal cancer.

stage IV in TNM classification ($P = 0.02$), maximum size of hepatic tumor >3 cm at initial hepatectomy ($P = 0.03$), and lymph node metastasis of the hepatoduodenal ligament ($P = 0.02$) were significantly associated with poor overall survival. Whether hepatic and pulmonary metastases were detected simultaneously or sequentially was not correlated with survival ($P = 0.35$). Neither a disease-free interval of less than 1 year from resection of the primary tumor nor initial metastasis in the lung affected survival.

We examined the independent predictive value of the aforementioned factors on overall survival (Table 2). Lymph node metastasis of the hepatoduodenal ligament was excluded from the analysis because only one of the 30 patients had the factor. Primary colon carcinoma (Fig. 2A), stage IV in TNM classification (Fig. 2B), and maximum size of hepatic tumor >3 cm at initial hepatectomy (Fig. 2C) had predictive value for decreased overall survival after resection of hepatic and pulmonary metastases from colorectal cancer.

Comparing clinicopathological factors of patients with primary colon carcinoma and those of patients with primary rectal carcinoma, maximum size of pulmonary tumors (2.6 ± 1.6 cm versus 1.7 ± 0.7 cm) was significantly larger and prethoracotomy CEA level (18.2 ± 23.8 ng/ml versus 5.3 ± 5.4 ng/ml) was significantly higher in patients with primary colon carcinoma. The interval from primary resection to the first pulmonary resection tended to be longer in patients with primary colon carcinoma than in patients with primary rectal carcinoma (25.7 months versus 17.1 months, median).

DISCUSSION

Results of this study indicate that aggressive multiple resections for hepatic and pulmonary metastases of colorectal carcinoma are safe and contribute to long-term survival in some patients.

Hepatic and pulmonary metastases may be detected sequentially or simultaneously in patients with colorectal carcinoma. Although two distant organs are affected by the

Table 2. Multivariate analyses of factors affecting overall survival in patients with resected hepatic and pulmonary metastases from colorectal cancer

	Hazard ratio (95% CI)	*P* value
Location of primary tumor		
Rectum	—	0.01
Colon	8.74 (1.53—49.91)	
TNM classification of primary tumor		
I, II, III	—	0.03
IV	11.37 (1.34—96.53)	
Maximum size of tumor at first hepatectomy (cm)		
<3	—	<0.01
≥3	14.47 (2.33–89.85)	

CI, confidence interval; CEA, carcinoembryonic antigen.

disease, several studies have demonstrated the efficacy of resections for both hepatic and pulmonary metastases (2–14). However, because of the frequent recurrences after resections, the best selection criteria for resection have not been established.

Lenhart *et al.* reported a disease-free survival of only 24% at 2 years in patients who underwent sequential hepatic and pulmonary resections for colorectal metastases (9). In the present study, the 2-year disease-free survival rate after the first metastasectomy for the second organ was also 24% with a median disease-free survival of only 13 months. The best treatment strategy for the recurrences after hepatic and pulmonary resections is obscure. However, only surgical removal of metastases offers a chance of cure. Aggressive repeat metastasectomy has been applied for recurrences after hepatic and pulmonary resections in our institution.

For the 30 patients of the present study, 45 hepatectomies and 40 pulmonary resections were performed and 17 patients received three or more resections with a maximum of five resections. Overall survival after the first metastasectomy for the second organ was 58% and nine 5-year survivors were observed. Surprisingly, seven of the nine 5-year survivors had undergone three or more resections. When survival time was calculated from the date of the first metastasectomy for the first metastasized organ, overall survival reached 70% at 5 years with a median survival of 60 months in the present study. Little is available on the result of repeat metastasectomy for recurrences after hepatic and pulmonary resections. Our results of long-term survival after hepatic and pulmonary resections in spite of frequent recurrences support the view that patients who can undergo resections for both hepatic and pulmonary metastases of colorectal cancer are in a selected population but can sometimes survive a long time with multiple metastasectomies. Interestingly, a recent study by Shah *et al.* also reported 74% 5-year survival rate after
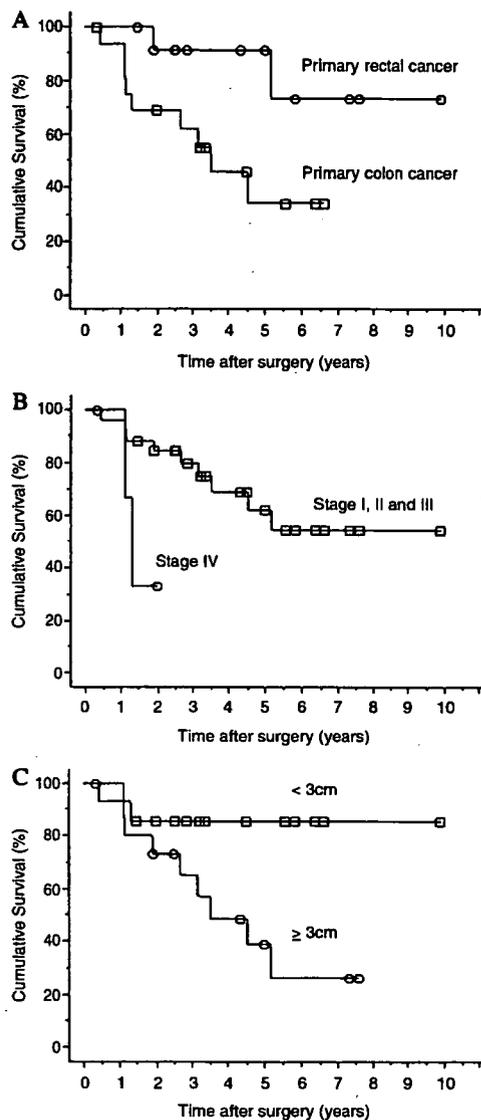

Figure 2. Cumulative survival curves after resections for hepatic and pulmonary metastases of colorectal cancer according to (A) location of primary tumor, (B) stage in TNM classification, and (C) maximum size of hepatic tumor at initial.

multidisciplinary surgical metastasectomies for colorectal cancer (19). The strategy and results of Shah *et al.* were similar to ours. However, while a majority of the patients received adjuvant chemotherapy after metastasectomies in Shah's study, no patient underwent adjuvant chemotherapy in the present study. These results indicate that the strategy of aggressive multiple metastasectomies count more than postoperative chemotherapies in the treatment for very restricted population of patients.

We found three factors for poor prognosis: size of hepatic tumor >3 cm at the first hepatectomy, primary colon carcinoma and stage IV tumor.

Maximum size of the hepatic tumor has been reported to be one of the important prognostic factors after hepatic resections for colorectal hepatic metastasis (20,21). This factor could affect prognosis in this population.

The reason for poor prognosis in patients with primary colon cancer is unknown. Patients with primary colon cancer had larger pulmonary tumors, higher CEA levels at the first pulmonary resection and relatively longer intervals from primary resection to the first pulmonary resection than patients with primary rectal cancer. A higher prethoracotomy CEA level was a factor of poor prognosis after hepatic and pulmonary resections in several studies (6,11). However, the reason why patients with primary colon cancer had more advanced pulmonary tumors than those with primary rectal cancer was unclear. A 'cascade' hypothesis based on the anatomy of the draining veins from the colon and rectum suggests that pulmonary metastasis in patients with primary colon carcinoma might come from hepatic metastasis with progressive site-induced change; however, pulmonary metastasis in patients with primary rectal carcinoma might come directly from the primary tumor, which seemed to be compatible with our results (22–24). However, the prognostic power of primary tumor location has not been demonstrated yet in patients with resected colorectal pulmonary metastasis (25–27); further examinations are needed to verify the hypothesis.

Neither the large size of the hepatic tumor nor primary colon carcinoma might influence the selection criteria for hepatic and pulmonary resections, because several long-term survivors were observed, even among patients with those factors.

Patients with stage IV disease had a poorer prognosis and showed no long-term survival. However, stage IV itself should not be considered as a contraindication for resections because the follow-up duration of patients with stage IV was short and the poor prognosis in stage IV was not consistent with the result that the disease-free interval from primary resection showed no correlation with prognosis.

Other factors such as synchronous metastasis (5), bilateral or multiple lung metastases (5,7), multiple liver metastases (8), short disease-free interval (8), simultaneous liver and lung metastases (10), mediastinal nodes involvement (11), primary histology (12) and high levels of both CEA and CA19-9 before metastasectomy (13) have been reported as prognostic factors after hepatic and pulmonary metastasectomy of colorectal cancer. Among those factors, whether the timing of the detection of hepatic and pulmonary metastases influences prognosis after resections has been an issue. In the present study, none of the aforementioned factors, including the timing of the detection of the metastases, showed any prognostic value. Based on our results, no single factor that contraindicated resections for hepatic and pulmonary metastases of colorectal cancer was identified.

Thus, surgical resections might be the best option when both hepatic and pulmonary metastases are resectable in colorectal cancer. However, treatment for patients with several poor prognostic factors for multiple resections is still unknown.

The reason for the high survival rate 5 years after resections for hepatic and pulmonary metastases in our study might be partly explained by precise intrathoracic and abdominal examinations using helical computed tomography (28,29). However, it can not be denied that patients who can undergo both hepatic and pulmonary metastasectomy for colon cancer might have unique characteristics in some factors. For example, there may be some unique host-tumor interaction, considering the rare possibility of both hepatic and pulmonary resections for colorectal metastases and the surprisingly high survival rate after the metastasecomies in spite of multiple, multiphase and multi-organ metastases. The aforementioned hypothesis is supported by the fact that excellent survival in the present study was achieved, unexpectedly, without any help of adjuvant chemotherapy, although adjuvant chemotherapy after pulmonary or hepatic metastasectomy is a potential treatment for improving the prognosis of patients with colorectal cancer. Further investigation to clarify the reason for the good prognosis of this population might elucidate the mechanisms of metastases in colorectal cancer.

A limitation of our study is the relatively small population, because patients who can undergo resections for both hepatic and pulmonary metastases of colorectal carcinoma are rare. There is some possibility that correlations between several clinicopathological factors such as positive lymph nodes of the hepatoduodenal ligament, hilus pulmonis, or mediastinum and survival after resections could not be sufficiently validated because of the small cohort. A large multi-institutional study is recommended to verify the correlation.

In conclusion, multiple resections for hepatic and pulmonary metastases of colorectal cancer are safe and effective. Surgical resections could be the best option for resectable hepatic and pulmonary metastases in colorectal cancer.

Acknowledgments

Conflict of interest statement
None declared.

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and Other Interventional Techniques

Laparoscopy-assisted hepatic lobectomy using hilar Glissonean pedicle transection

A. Cho,[1] T. Asano,[1] H. Yamamoto,[1] M. Nagata,[1] N. Takiguchi,[1] O. Kainuma,[1] H. Souda,[1] H. Gunji,[1] A. Miyazaki,[1] H. Nojima,[1] A. Ikeda,[1] I. Matsumoto,[1] M. Ryu,[1] H. Makino,[2] S. Okazumi[3]

[1] Department of Gastroenterological Surgery, Chiba Cancer Center Hospital, 666-2 Nitonachou, Chuouku, Chiba 260-8717, Japan
[2] Department of Surgery, Shimotsuga General Hospital, Chuouku, Chiba, 260-8717, Japan
[3] Department of Surgery, Chiba University of Medicine, 666-2 Nitonachou, Chuouku, Chiba 260-8717, Japan

Abstract

Although many reports have described laparoscopic minor liver resections, major hepatic resection, including right or left lobectomy, has not been widely developed because of technical difficulties. This article describes a new technique for performing laparoscopy-assisted right or left hepatic lobectomy using hilar Glissonean pedicle transection. Laparoscopic mobilization of the right or left hepatic lobe is performed, including dissection of the round, faliciform, triangular, and coronary ligaments. The right or left Glissonean pedicle is encircled and divided laparoscopically. A parenchymal dissection is then performed though the upper median or right subcostal incision, through which the resected liver is removed. We successfully performed this procedure in 6 patients without blood transfusion or serious complications. Laparoscopy-assisted hepatic lobectomy using hilar Glissonean pedicle transection can be feasible and safe in highly selected patients.

Key words: Laparoscopy — Hepatic lobectomy — Glissonean pedicle

Laparoscopy for liver resection is a highly specialized field, as laparoscopic liver surgery presents severe technical difficulties. However, the recent rapid development of technological innovations, improvements in surgical skills, and the accumulation of extensive experience by surgeons have improved the feasibility and safety of a laparoscopic approach for properly selected patients. Since the first report of laparoscopic anatomical left lateral segmentectomy in 1996 [1], a limited number of laparoscopic anatomical liver resections have been described [2–6, 9, 12]. During open right or left hepatic

Correspondence to: A. Cho

lobectomy, the right or left Glissonean pedicle is often ligated and divided en bloc extrahepatically before parenchymal dissection [10, 11]. Herein we describe our experience with laparoscopic encircling and dividing the right or left Glissonean pedicle during laparoscopy-assisted right or left hepatic lobectomy, representing the first description of this laparoscopic technique.

Surgical procedure

The patient is placed in a supine position when left lobectomy is performed, and in a left semi-lateral decubitus position for right lobectomy. A 12-mm trocar is placed 1 cm below the umbilicus, through which CO_2 gas is delivered. Pneumoperitoneum is controlled electronically at a pressure of 10 mmHg. The other three trocars are located as shown in Figure 1. The round ligament is transected using laparoscopic coagulation shears (LCS; Ethicon Endo Surgery Industries, Cincinnati, OH, USA), and the falciform and coronary ligaments are then dissected to expose the suprahepatic inferior vena cava (IVC). The lesser omentum is sectioned and the hepatoduodenal ligament is encircled by a tape to be used as a tourniquet for complete interruption of blood inflow to the liver only if necessary. For left lobectomy, the left triangular and coronary ligaments are divided to expose the left hepatic vein, so that the left lateral segment can be mobilized. The ligamentum venosum is then divided with LCS while the lateral segment is retracted. Dissection of the porta hepatis is performed with laparoscopic scissors between the hepatic parenchyma and the left Glissonean pedicle, which is then encircled using the Endo Retract Maxi (ERM; United Surgical, a division of Tyco Healthcare group LP; Norwalk, CT, USA) at the hepatic hilum (Fig. 2). The left Glissonean pedicle is divided with a Linear Cutter (Ethicon Endo Surgery Industries, Cincinnati, OH, USA). Next, an upper median incision approximately 6 cm long is made and covered with a Lap Protector (Hakko Shoji, Tokyo, Japan). Parenchymal dissection is performed through the upper median incision to prevent gas embolism, and is continued to the left hepatic vein, which is not meticulously dissected to reduce the risk of tearing. The left hepatic vein is sectioned using a Linear Cutter. The left lobe is then delivered through the upper median incision. For right lobectomy, the right lobe is mobilized by dividing, with laparoscopic scissors and LCS, the hepato-renal, right triangular, and right coronary ligaments, as well as the lateral attachments of the right lobe. The right Glissonean pedicle is encircled using the ERM at the bifurcation in the hepatic hilum (Fig. 3). A little dissection of the hepatic parenchyma covering
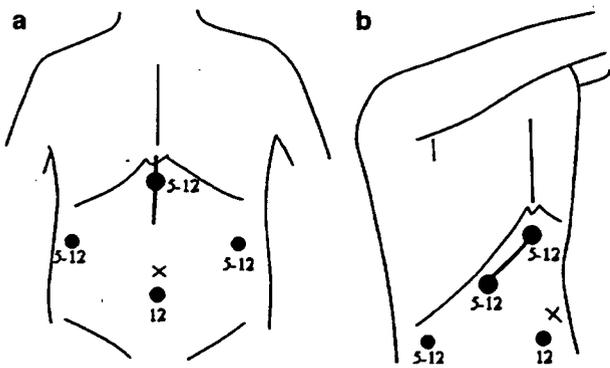
Fig. 1. Diagrams of typical trocar placement for laparoscopy-assisted hepatic lobectomy. A. Left lobectomy. Patient is supine with lower limbs apart, and the surgeon stands between the legs. B. Right lobectomy. The surgeon is on the left side.

Fig. 3. The right Glissonean pedicle is encircled with the ERM.

Fig. 2. The left Glissonean pedicle is encircled with the Endo Retract Maxi (ERM) (A) and divided by the Linear Cutter (B).
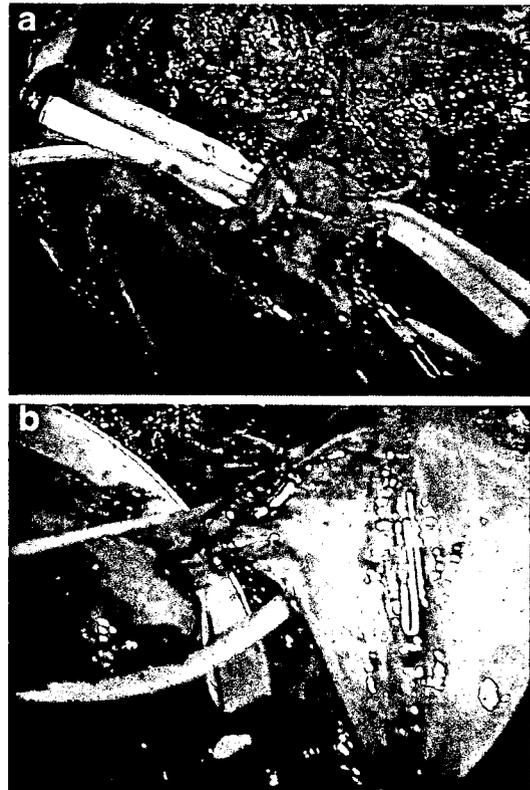

Fig. 4. The right anterior (A) and posterior (B) Glissonean pedicles are encircled with the ERM.

the bifurcation of the right anterior and posterior Glissonean pedicles facilitates encircling these structures. The right anterior and posterior Glissonean pedicles are encircled with the ERM (Fig. 4) and divided with the Linear Cutter. Next, a right subcostal incision approximately 8 cm long is made and covered with a Lap Protector. A tape is passed between the anterior surface of the IVC and the posterior surface of the caudate lobe for the liver-hanging maneuver through the right subcostal incision, after which parenchymal dissection proceeds from the liver surface to the tape through the right subcostal incision. After liver transaction, the short hepatic veins are divided with endoscopic vascular clips (Ethicon Endo Surgery Industries, Cincinnati, OH, USA), and finally the right hepatic vein is sectioned with the Linear Cutter. The right lobe is then delivered through the right subcostal incision.

Results

We successfully performed laparoscopy-assisted left lobectomy in 4 patients and laparoscopy-assisted right lobectomy in 2 patients, as planned. No procedures were converted to open hepatectomy. Mean operative time was 175 min (range, 95–330 min). Mean blood loss was 370 mg (range, 80–1250 mg). No patient required blood transfusion and no serious complications were encountered. Mean duration of hospitalization was 9 days (range, 4–14 days). Underlying

pathology was hepatocellular carcinoma ($n = 2$), intrahepatic stones ($n = 2$), metastatic liver tumor ($n = 1$), and benign liver tumor ($n = 1$). All lesions were well clear of surgical margins.

Discussion

Laparoscopic liver surgery was initially limited for partial resections because of the technical difficulties involved [7, 13]. Recent technological developments and improved endoscopic procedures have spread application of laparoscopic liver resection widely. However, only a few laparoscopic hepatic lobectomies have been reported. The hepatic artery, portal vein, and bile duct, together with connective tissue, are sheathed by the peritoneum to form a fibroid bundle. This portal triad continues from the hepatoduodenal ligament to the intrahepatic portion as the Glissonean pedicle. The entire length of the primary branches of the Glissonean pedicle and the origin of its secondary branches are located outside the liver, and the trunks of the secondary and more peripheral branches run inside the liver [10]. The right or left Glissonean pedicle can thus be ligated and divided en bloc extrahepatically before parenchymal dissection during open hepatic lobectomy [10, 11]. We successfully performed laparoscopic encircling and dividing the right or left Glissonean pedicles extrahepatically before parenchymal dissection in all 6 patients in whom this approach was attempted. Thanks to meticulous and sufficient dissection between hepatic parenchyma and the Glissonean pedicle at the hepatic hilum and encircling the Glissonean pedicle with the ERM, little bleeding was encountered during hilar procedures.

Although a similar laparoscopic technique in which the Glissonean pedicle is encircled has been reported for hemihepatic ischemia, hilar Glissonean pedicle transection and lobectomy were not performed [8]. Previous reports relating to laparoscopic or laparoscopy-assisted right lobectomies have described the right hepatic artery, duct, and portal vein as being dissected and divided separately [9], or the right Glissonean pedicle being transected through the midline incision [5]. We believe

that the present procedure can reduce operation time and the size of the additional incision. Although our experience is limited and appropriate indications must await future studies, we believe that laparoscopy-assisted hepatic lobectomy using hilar Glissonean pedicle transwction can be feasible and safe in highly selected patients and offers the usual benefits of laparoscopic surgery, such as reduced invasiveness.

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原　著

CT colonography による大腸癌術前深達度評価

早 田 浩 明*1　舩 津 宏 之*2　滝 口 伸 浩*1　山 本　　宏*1

永 田 松 夫*1　貝 沼　　修*1　趙　　明 浩*1　郡 司　　久*1

宮 崎 彰 成*1　浅 野 武 秀*1

　Multislice CT (MSCT) による CT colonography (CTC) の大腸癌術前深達度診断能を評価した．CT は原則大腸内視鏡直後に 16 列 MSCT で撮影，Multiplanar reformation, virtual endoscopy, CT enema 像で検討した．70 症例 76 病変を解析した．早期癌 11 病変，進行癌 65 病変の壁深達度の感受性は Tis：20%，T1：71%，T2：83%，T3：85%，T4：60%であり，進行癌での正診性は注腸造影に匹敵する．正診群と非正診群との比較では非正診群で腫瘍径が有意に小さかった．小病変が多い早期癌での精度が悪かったが，評価数が少なく今後も検討を要する．

■キー・ワード：大腸癌，CT colonography，術前診断

Evaluation of the Preoperative Diagnostic Ability of CT Colonography for the Invasion Depth of Colorectal Cancer: Soda H*1, Funatsu H*2, Takiguchi N*1, Yamamoto H*1, Nagata M*1, Kainuma O*1, Cho A*1, Gunnji H*1, Miyazaki A*1 and Asano T*1 (*1Department of Digestive Surgery, *2Department of Diagnostic Radiology, Chiba Cancer Center)

　The preoperative diagnostic ability of multislice CT (MSCT) colonography was evaluated for the invasion depth of colorectal cancer. CT scans were performed immediately after colonoscopy using 16–low MSCT, and multiplanar reformation, virtual endoscopy, and CT enema images were analyzed in 76 lesions in 70 patients. The sensitivities of CT colonography (CTC) for depth of invasion in 11 early and 65 advanced cancer lesions were 20%, 71%, 83%, 85%, and 60% in Tis, T1, T2, T3, and T4, respectively. The diagnostic accuracy of CTC was comparable to that of contrast enema. The diameter of tumors was significantly smaller in the misdiagnosed group. Thus, the diagnostic accuracy was poor for early cancers, which are frequently small. However, the number of patients studied was small, and further studies are needed.

Key words: Colon cancer, CT colonography, Preoperative diagnosis
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はじめに

　近年の画像診断技術の進歩は目覚しく，特にコンピューターを駆使したデジタル画像は電子カルテの普及とともに飛躍的に進化している．マルチスライス CT (MSCT) の情報から構築された CT colonography (CTC) は新しい大腸画像診断

として注目され[1,2]，欧米では検診診断としても研究が進められている[3,4]．わが国では欧米とは大腸癌発生に対する認識の違い[5]，大腸内視鏡 (CF) 技術の熟練から CTC の使用目的がはっきりとしてはいない．現在，大腸癌の術前検査では大腸内視鏡 (CF)，注腸造影，CT をルーチンとしている施設が一般的だが[6]，マルチスライス CT (MSCT) による CT colonography (CTC) の有用性を報告するものも多くなってきた[7~9]．今回，われわれは CTC を行うことで術前検査で

*1 千葉県がんセンター消化器外科

*2 千葉県がんセンター画像診断科

の注腸造影を省略することを念頭に，CTC の大腸癌診断能を検討した．

1.　対象および方法

1) 対象症例

大腸癌と診断または疑診され，千葉県がんセンターを受診し CTC 検査を行った症例の内，2005年6月から2006年12月までの虫垂癌を除く大腸癌切除例70症例76病変を対象とした．

2) 方　法

撮影日は原則的に大腸内視鏡（CF）検査当日とし，前日に低残渣食，液状下剤服用し，当日は腸管洗浄液を服用処置した．CF 直前または直後に経肛門的に送気，非イオン性造影剤を自動注入器にて急速静注して仰臥位と腹臥位の二体位で撮影した．16列 MSCT で撮影し，画像データをワークステーションに転送後，Virtual Place advance PLUS を使用し，Multiplanar reformation（MPR），virtual colonoscopy（VC）（図1d），CT enema（CTE）像（図1c）を作成し評価検討した．読影は放射線科医師が行い，術前診断を記載した．読影医には主病変占拠部位は知らせていた．術後診断は新鮮手術標本での肉眼型，腫瘍径，ホルマリン固定後での組織診断での壁深達度（TNM 分類第6版による）を記載した．術前診断と術後診断とを比較検討した．図1に直腸癌症例の注腸2重造影像，CF 所見，CTE 画像，VC 画像と切除標本写真を示す．

2.　結　果

1) 腫瘍占居部位

腫瘍占居部位は表1に示すように右側結腸（横行結腸含む）20病変，左側結腸38病変，直腸18病変であった．

2) 腫瘍肉眼型

新鮮切除標本での肉眼型は表在型11病変，1型7病変，2型57病変，5型1病変であった（表1）．

3) CTC での病変描出，肉眼型診断

対象76病変中73病変（96.%）が描出されていた．進行癌はすべて描出されており（描出率100%），描出されなかった3病変はすべて早期癌表在型であった（描出率73%）．肉眼型診断は5型の1病変を除き正診であった．腫瘍主座での描出能に差はなかった．

4) CTC での深達度診断

CTC による術前深達度診断能を切除標本組織学的診断での T 分類別に比較した（表2）．T2，T3 では感受性は良好であるが，Tis，T1 での感受性は良好とは言えなかった．Tis では描出されない3病変と多かった．CTC による深達度の正診性と腫瘍径との関係を解析した（図2）．正診した腫瘍の最大径の平均値は47.5 mm，正診できなかった腫瘍の最大径の平均値は33.1 mm で正診群と非正診群間には有意差を認め（p＝0.003），さらに描出されなかった病変の平均腫瘍径は16.6 mm であった．

3.　考　察

MSCT による大腸の3次元表示を米国では CT colonography（CTC）と総称され，その有用性が多数報告されている[1~3,10]．注腸二重造影の熟練した技術，診断能を持つ医師が多いわが国でも CTC の報告が近年多く見られてきた[7~9]．注腸二重造影では側面変形像の解析から深達度診断が行われ[11]，術前検査とひとつとして定着している[6]．しかし，被曝量や前処置，体位変換の苦痛を伴うことと，検者の技量，病変部位に正診率が左右されることは否めない．われわれは術前検査の注腸造影を省略することを目標に CTC の診断能評価を行った．

今回の検討では，CTC での大腸癌描出能は96%，特に進行癌での描出率は100%で良好であった．T2，T3 での感受性は85%以上であり，注腸造影の診断に匹敵すると思われる．しかし，Tis，T1 での感受性が低かった．Tis では検出できなかった病変が5例中3例あった．いずれも小病変で，内2例は同時性多発大腸癌症例で，狭窄の強い病変による腸管内残渣の停滞が描出の不可に影響していると思われた．残り1例は10 mm の隆起の低い 0-IIa 病変であった．今回われわれは腸管内残渣により，小病変が水没してしまうことを考慮し，仰臥位と腹臥位の二体位で撮影，CT colonography で解析し小病変の描出に努め

図1　下部直腸癌2型 pT2(MP) 症例の各画像所見
a：注腸二重造影像．⇦に明瞭な周提と浅い陥凹病変．
b：下部消化管内視鏡所見．腫瘍に対し接線方向のみの観察像．
c：CTE 画像．▷に弧状変形の腫瘍側面像．
d：VC 画像．腫瘍正面からの観察像．
e：切除標本写真．16×16 mm の2型腫瘍，pT2(MP) 病変．

た．諸家の報告では 0-I 型は描出されやすく，ポリープ型早期癌では検出率は高く，平坦型 0-II 型は描出が難しいとされている[12]．一方 5 mm 以上の隆起性病変なら検出率は良好との報告もある[13]．また，前処置法の違いによっても小病変の検出率は左右される[14]．今回の検討では腫瘍径が小さい早期癌の病変数が少なく，今後も検討を要すると思われる．

CTC における深達度診断では牛尾ら[11]の注腸造影所見での深達度診断を応用し，側面像での所見を重要視した（図1c）．角状変形は T1 (SM)，弧状変形は T2 (MP)，台形状変形は T3 (SS, SE) 以深と判定基準にした．この CTC による側面像の描出能は非常に良好であり，特に注腸造影では腸管が重なり合い診断し難い病変でも容易にかつ正確に描出でき，有用であった．また検者の

表1　解析した病変の主座と肉眼型の病変数

肉眼型	右側結腸	左側結腸	直腸	計
0-Ip		1	1	2
0-Isp	1			1
0-Is	1	1	2	4
0-IIa	1	1	1	3
0-IIa+c			1	1
1型	1	1	5	7
2型	15	19	23	57
5型	1			1
計	20	38	18	76

右側結腸は盲腸，上行，横行結腸を示す．
左側結腸は下行，S状結腸を示す．直腸は直腸S状部，上部，下部直腸を示す．

表2　CTC での術前深達度診断能評価

			最終診断		
		Tis	T1	T2	T3	T4
術前診断 Tis	1(20%)				
T1	1	5(71%)	1	1	
T2		2	10(83%)	6	
T3			1	40(85%)	2
T4					3(60%)
非描出	3				

T分類別に病変数と切除標本組織学的診断での最終診断との一致率（感受性）を表で示す．CTC で指摘されなかった病変は非描出として示す．

技量に左右されず，大腸癌術前検査として注腸造影以上の有用性があると思われた．図1のような大腸内視鏡では腫瘍に対し接線方向からしか観察できない場合でも，VC 画像では腫瘍正面からの観察像を描出でき，病巣の把握に非常に有用であった．

MPR 像での解析は壁外浸潤をよく描出でき有用である[9]と期待されたが，壁外浸潤T4の感受性は予想に反して低かった．これは大腸癌では炎症を伴うことが多いが，今回は微小な壁外浸潤を結腸周囲への炎症と評価し過小評価したためと思われた．しかし，特異度は100%と良好でT3病
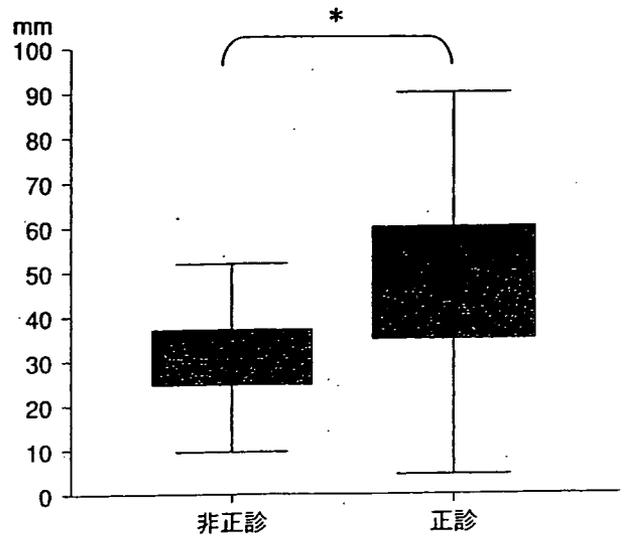

図2　腫瘍径と深達度診断正診性の関係
CTC での深達度診断で正診群と非正診群での腫瘍径を比較した．正診群の平均腫瘍径は 44.7 mm に対し非正診群の平均腫瘍径は 33.1 mm と正診群の腫瘍径より有意に小さかった（＊：p＝0.003）．

変をT4と術前診断する過大評価がなかった．

検査を行うタイミングについては大腸内視鏡の直後に CTC 検査を行うことで，腸管内残渣を極力少なくでき，描出能を上げていると考えられた．また術前検査に必要な日数を短縮でき，かつ下剤処置を改めて行う必要がなく被検者への負担も軽減でき効率的であり，大腸内視鏡直後に CTC を行うことは術前検査でのゴールドスタンダードと思われた．

まとめ

CT colonography は進行癌では大腸癌切除を前提とした注腸造影検査と同等以上の術前診断能と判断するが，微小病変の多い早期癌では今後も検討を要する．

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Clinicopathological Features of Skip Metastasis in Colorectal Cancer

Original Paper

Manabu Shiozawa[1], Makoto Akaike[1], Roppei Yamada[1], Teni Godai[1], Naoto Yamamoto[1]
Hiroshige Saito[1], Yukio Sugimasa[1], Shoji Takemiya[1], Yasushi Rino[2], Toshio Imada[3]

[1]Department of Gastrointestinal Surgery, Kanagawa Cancer Center
[2]First Department of Surgery, Yokohama City University School of Medicine, and
[3]Department of Gastroenterological Center, Yokohama City University Medical Center, Yokohama, Japan
Corresponding Author: Manabu Shiozawa MD, Department of Gastrointestinal Surgery, Kanagawa
Cancer Center, 1-1-2 Nakao, Asahi-ku, Yokohama, 241-0815, Japan
Tel: +81 45 391 5761, Fax: +81 45 361 4692, E-mail: shiozawam@kcch.jp

ABSTRACT

Background/Aims: Japanese general rules for the staging of colorectal cancer conventionally classify lymph node metastasis into three groups according to location with respect to the primary tumor. Skip metastasis, in which distant nodes are positive but regional nodes are negative, is often encountered but poorly understood. We studied the clinicopathological features of skip metastasis in colorectal cancer. **Methodology:** The location of positive nodes was classified in 323 patients with Dukes' stage C colorectal cancer. Skip n2 lymph node metastasis was defined as positive N2 metastasis without negative N1 or N3 metastasis. Clinicopathological findings and survival were compared between the patients with skip n2 metastasis (skip n2 group) and those with n1 (n1 group) or n2 metastasis (n2 group). **Results:** There were 211 patients in the n1 group, 91 in the n2 group, and 21 in the skip n2 group. Pathological examination showed that the skip n2 group had fewer positive nodes than the n1 and n2 groups, but was positioned between these groups with respect to the degree of lymphatic invasion. Cumulative survival was significantly poorer in the n2 group than in the skip n2 group ($p=0.039$ by log-rank test). Survival was similar in the skip n2 group and n1 group. There was also no difference in survival between patients in the skip n2 group and patients with one, two, or three N1 metastases. **Conclusions:** Lymph nodes with skip n2 metastasis are most likely sentinel nodes of the primary tumor in patients with colorectal cancer. The prognosis of patients with skip n2 metastasis is therefore better than that of patients with n2 metastasis and similar to that of patients with n1 metastasis.

INTRODUCTION

Although various prognostic factors have been proposed in colorectal cancer, lymph node metastasis and the depth of tumor invasion remain the most reliable predictors of outcome. The presence of lymph node metastasis has been used in many staging systems since the establishment of Dukes' classification (1). The numbers or locations of lymph node metastases are included as staging factors for lymph node metastasis in Dukes' stage C disease (2-5).

In Japan, lymph node metastasis is classified according to the General Rules for Clinical and Pathological Studies on Cancer of the Colon, Rectum and Anus (6). Information on the number of positive nodes and the location of lymph node metastasis is thereby provided. Skip metastasis, in which distant nodes are positive but regional nodes are negative, is often encountered but poorly understood. The presence of skip metastasis can increase the risks associated with laparoscopic surgery or other minimally invasive procedures. Failure to diagnosis skip metastasis can also lead to selection of ineffective regimens for chemotherapy. To gain a better understanding of the

status and implications of skip metastasis, we studied the clinicopathological features of skip metastasis in patients with Dukes' stage C colorectal cancer.

METHODOLOGY

Patients and Methods

From February 1990 through August 2002, we studied 323 patients with Dukes' stage C colorectal cancer who underwent curative resection at Kanagawa Cancer Center. Patients with multiple advanced cancers or mucinous or signet-ring-cell carcinomas were excluded.
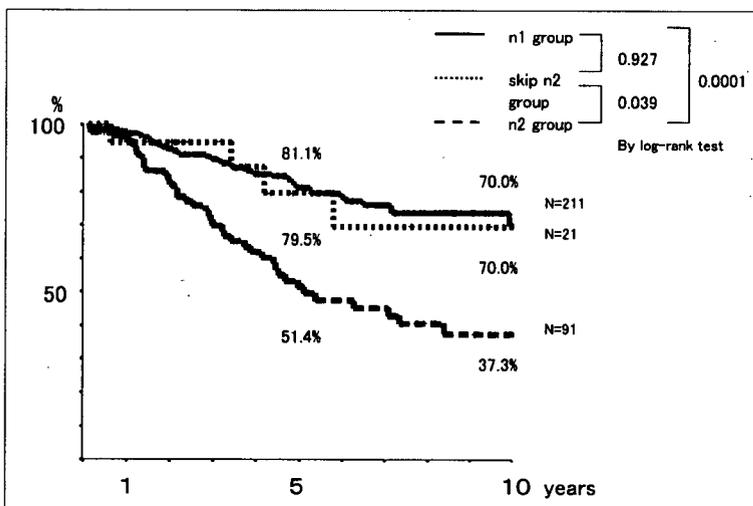
During operation, the distance from the tumor margin was measured and marked on the mesentery at 5-cm intervals to determine lymph-node location. The mesentery was separated from the resected specimen and fixed in 10% formalin solution. All removed lymph nodes were embedded in paraffin, stained with hematoxylin and eosin (HE), and examined histopathologically to determine metastatic status. The resected nodes were histologically examined by two pathologists. We evaluated the numbers of positive nodes and the locations of lymph node metastases and classified

TABLE 1 The Number of Cases with Skipping Nodal Metastasis of n2 according to the Location of the Tumor

	Location	n1	Skip n2	n2	Total cases	Skip %
Colon	Cecum	7	1	4	12	8.3%
	Ascending	24	1	9	34	2.9%
	Transverse	14	1	3	18	5.6%
	Descending	10	2	4	16	12.5%
	Sigmoid	63	5	26	94	5.3%
Rectum	Rectosigmoid	35	1	10	46	2.2%
	Rectum above peritoneal reflection	17	5	7	29	17.2%
	Rectum below peritoneal reflection	39	5	27	71	7.0%

TABLE 2 Number of the Cases in Three Directions of the Skip n2 Metastasis according to the Location of the Tumor

	Location	Main nodes	Paracolorectal nodes	Lateral nodes	Total cases
Colon	Cecum	1			1
	Ascending	1			1
	Transverse		1		1
	Descending	1	1		2
	Sigmoid	5			5
Rectum	Rectosigmoid	1			1
	Rectum above peritoneal reflection	5			5
	Rectum below peritoneal reflection	3		2	5
		17	2	2	21

FIGURE 1 Overall survival rates of patients with n1, skip n2, and n2 lymph nodes metastasis.

nal iliac arteries. The paracolorectal nodes located within 5cm from the tumor margin are classified as N1 nodes, and those between 5 and 10cm from the tumor margin are classified as N2 nodes. The N2 nodes also include the main nodes, with the exception of the N3 nodes, around the origin of the main vessel. The patients were classified as having n1, n2, or n3 lymph node metastasis according to the level of the most distant, microscopically positive nodes. These categories are defined as follows: n1 metastasis means positive nodes only in the N1 region; n2 metastasis indicates positive nodes in the N1 and N2 regions and negative nodes in the N3 region; and skip n2 metastasis means positive nodes in the N2 region, but negative nodes in the N1 and N3 regions. In addition, cases with positive lateral pelvic nodes, but negative paracolorectal nodes and main nodes were also considered positive for skip n2 metastasis.

Clinicopathological findings and survival were compared between the skip n2 group and the n1 or n2 group. The chi-square test and unpaired t-test were used for statistical analysis of two unpaired samples. Cumulative 5-year survival rates were calculated by the Kaplan-Meier method. The log-rank test was used to compare survival curves. All tests were two-tailed, and $p < 0.05$ was considered to indicate statistical significance.

RESULTS

The 323 patients with Dukes' stage C disease were classified according to the location of positive nodes. There were 211 patients in the n1 group and 91 in the n2 group, as compared with only 21 in the skip n2 group.

Skip n2 metastasis was most commonly associated with primary tumors arising in the descending colon and upper rectum as compared with other portions of the colorectum **(Table 1)**. The direction of skip n2 metastasis with respect to the location of the primary tumor was mainly along the main nodes **(Table 2)**. Two of five cases (40%) of lower rectal cancer had skip metastasis to the lateral pelvic nodes.

Clinicopathological examination **(Table 3)** showed that the frequency of well-differentiated adenocarcinoma was higher in the skip n2 group than in the n1 or n2 groups. The degree of lymphatic invasion in the skip n2 group was intermediate between those in the n1 and n2 groups. Other clinicopathological findings did not differ significantly among the three groups.

The mean number of positive nodes in the skip n2 group was significantly lower than those in the n1 and n2 group **(Table 4)**.

Cumulative survival was significantly poorer in the n2 group than in the skip n2 group ($p = 0.039$ by log-rank test). Survival was similar in the skip n2 group and n1 group **(Figure 1)**. There was also no difference in survival between the skip n2 group and patients with one, two, or three N1 metastases **(Figure 2)**.

positive nodes as n1, n2, and n3 according to the Japanese General Rules for Clinical and Pathological Studies on Cancer of the Colon, Rectum and Anus (6).

The Japanese rules propose that colon cancer has two directions of lymph nodes metastasis: along the axis of the bowel (paracolic nodes) and along the origin of the main vessel supplying the primary tumor site (main nodes). Rectal cancer has three types of lymph node metastasis: paracolic nodes, main nodes, and lateral pelvic nodes along the internal and exter-

TABLE 3 Clinicopathological Features of the Three Groups

		n1 group	skip n2 group	n2 group	P value
Gender	male	118	12	58	0.448
	female	93	9	33	
Age		62.0 0.8	66.6±1.8	62.7±1.2	ns***
Diameter	(mm)	47.1±1.3	49.0±2.7	51.3±1.9	ns***
Histological type[a]	wel	65	10	14	
	mod	129	11	69	0.010
	por	17	0	8	
Macroscopic type	1	31	4	9	
	2	146	12	60	
	3	26	5	17	0.414
	4	8	0	5	
Depth of invasion	11	9	1	0	
	12	19	2	5	
	13	108	10	42	0.003
	14	75	8	44	
ly[b]	0	49	5	14	
	1	129	12	45	
	2	27	3	24	0.011
	3	6	0	8	
v[c]	0	87	9	27	
	1	65	5	32	
	2	49	7	27	0.435
	3	9	0	5	

ns*** ; there were no significance between n1, skip n2 and n2 groups.
[a] Histological type-wel: well differentiated adenocarcinoma; mod: moderately differentiated adenocarcinoma;
por: poorly differentiated adenocarcinoma.
[b]ly: lymphatic invasion were classified with degree of amounts of tumor invasion.
[c]v: venous invasion were classified with degree of amounts of tumor invasion.

DISCUSSION

Our study showed that skip n2 metastasis was less common than n1 and n2 metastases. The degree of lymphatic invasion associated with skip n2 metastasis was intermediate between that of n1 and n2 metastases, suggesting that implantation of tumor cells in distant lymph nodes requires a high degree of lymphatic invasion.

Recently, many investigators have reported that sentinel node mapping is useful for staging colorectal cancer (7-9). Marrie et al. (10) found that direct lymphatic drainage to apical anatomic skip lesions occurred in 15% of 26 colon cancers evaluated by keratin 20 reverse transcription polymerase chain reaction. Saha et al. (11) reported skip metastasis in 3.9% of colorectal cancers on hematoxylin and eosin staining. The incidence of skip metastasis in colorectal cancer as assessed by molecular techniques is estimated to be higher than previously estimated (8).

Our study also demonstrated that the survival of patients with skip n2 metastasis was similar to that of patients with one, two, or three N1 metastases. Moreover, the mean number of positive nodes in the skip n2 group was significantly lower than that in the n1 and n2 groups. This finding suggests that most lymph nodes with skip metastasis are sentinel nodes. Lymph node mapping is therefore useful for detecting lymph nodes with skip metastasis and can help to
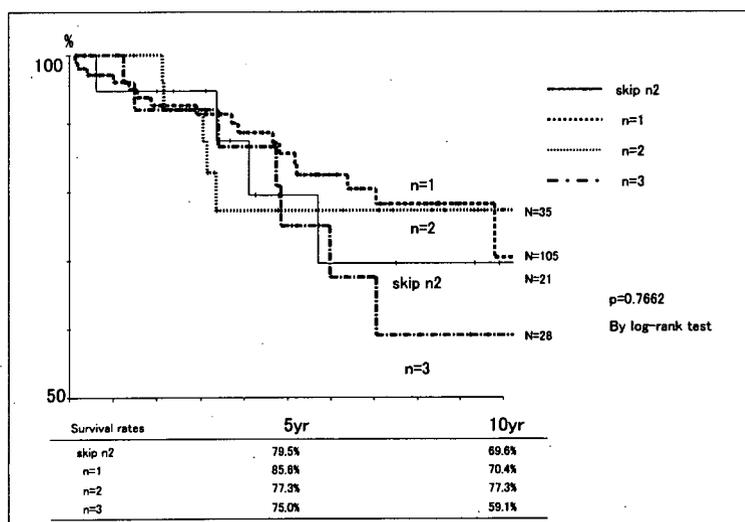

FIGURE 2 Overall survival rates of patients with one, two, three lymph node metastasis in N1 area and skip n2 lymph node metastasis.

ensure that metastatic lymph nodes are completely resected along with the primary tumor.

Yamamoto et al. (12) found that the presence of skip metastasis is associated with better outcomes than the absence of skip metastasis in patients with colorectal cancer. Shida et al. (13) reported that 31.6% of patients with n2 colon cancer have skip metastasis, but

TABLE 4 Comparison of the Number of Lymph Nodes with Metastasis

	Total number of dissected lymph	Number of n1 lymph	Number of n2 lymph nodes with metastasis	Total number of lymph nodes with metastasis
n1 group	29.7±1.2	2.5±0.2	0	2.5±0.2
	$P=0.489$			$P=0.036$
skip n2 group	26.9±3.2 ($P=0.628$)	0 ($P<0.001$)	1.2±0.1	1.3±0.1 ($P<0.001$)
	$P=0.596$		$P=0.010$	$P<0.001$
n2 group	28.7±1.4	4.2±0.4	2.5±0.2	6.8±0.5

(Mean±SE)

found no significant difference between patients with skip metastasis and those without skip metastasis. We found that the outcome of patients with skip n2 metastasis was similar to that of patients with n1 metastasis, but better than that of patients with n2 metastasis. This finding justifies the staging of colorectal cancer according to the number of lymph node metastases, as done in the TNM classification (14). However, an anatomical assessment of lymph node metastasis is useful for deciding the required extent of mesenteric lymph node resection. Moreover, the possibility of skip metastasis should be considered in patients undergoing curative resection for colorectal cancer.

Our results suggest that both the locations and the numbers of lymph node metastases should be incorporated into classification systems for the evaluation of patient prognosis.

In summary, our clinicopathological study showed that n2 skip metastasis was less common than n1 or n2 metastasis. The degree of lymphatic invasion associated with n2 skip metastasis was intermediate between that associated with n1 metastasis and that associated with n2 metastasis. Lymph nodes with skip metastasis were apparently sentinel nodes of the primary tumor. Therefore, the outcome of patients with skip n2 metastasis was similar to that of patients with n1 metastasis, but better than that of patients with n2 metastasis.

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Lateral Lymph Node Dissection for Lower Rectal Cancer

Manabu Shiozawa[1], Makoto Akaike[1], Roppei Yamada[1], Teni Godai[1], Naoto Yamamoto[1]
Hiroshige Saito[1], Yukio Sugimasa[1], Shoji Takemiya[1], Yasushi Rino[2], Toshio Imada
[1]Department of Gastrointestinal Surgery, Kanagawa Cancer Center, [2]The First Department of Surgery and
[3]Department of Gastroenterological Center, Yokohama City University Medical Center, Yokohama, Japan
Corresponding Author: Manabu Shiozawa MD, Department of Gastrointestinal Surgery, Kanagawa Cancer
Center, 1-1-2 Nakao, Asahi-ku, Yokohama, 241-0815, Japan
Tel: +81 45 391 5761, Fax: +81 45 361 4692, E-mail: shiozawam@kcch.jp

ABSTRACT

Background/Aims: This study was conducted to evaluate the effects of lateral lymph node dissection (LLD) on overall survival, disease-free survival, and local recurrence for the patients with lower rectal cancer.

Methodology: From 1990 through 2000, 169 consecutive patients with T2 (TNM classification) or more advanced, extended lower rectal cancer (located below the peritoneal reflection) underwent curative resection at Kanagawa Cancer Center were reviewed.

One hundred and forty-three patients who underwent LLD and the 26 patients who did not were entered in this study.

Results: Cox's multivariate regression analysis showed T stage (TMN classification), N stage (TNM classification), and LLD were found to be significantly related to the rates of both cumulative survival and disease-free survival. That mean LLD was identified as a significant prognostic factor. But disease-free survival did not differ significantly between the patients who underwent LLD and those who did not undergo LLD in stage I, II, or III disease ($p=0.3681$, $p=0.1815$, and $p=0.0896$, respectively).

The local recurrence rate was similar in patients who received LLD (17.5 percent) and in those who did not receive LLD (23.1 percent; $p=0.498$). But 7 patients with lateral lymph node metastasis (33.3 percent) remained disease free. And these patients had local lateral lymph node metastasis and benefited from LLD.

Conclusions: LLD can substantially improve outcomes in selected patients at high risk for lateral lymph node metastasis. A randomized controlled clinical study is necessary to clarify the role of LLD in the treatment of rectal cancer.

INTRODUCTION

In lower rectal cancer, lymphatic drainage is mainly to the superior rectal artery and inferior mesenteric artery or to the lateral lymph nodes beyond the pelvic nerve plexus (1-3). Lymph node metastasis most frequently occurs along the inferior mesenteric artery, and patients with lateral node metastasis have a poor prognosis (4-6). Lateral lymph node dissection (LLD) has therefore received considerable attention.

In Japan, extended lymphadenectomy has been done to improve outcome in rectal cancer (7-9), but complications associated with auto-nerve resection, such as urinary dysfunction and sexual disturbance, became evident with improved survival (7,10). Subsequently, surgeons in Japan developed a procedure for LLD with auto-nerve preservation (4,11-15). This procedure has improved urinary function, but sexual function remains unsatisfactory (4,11). Lateral lymph node metastasis has been considered systemic disease in patients with rectal cancer (16). However, some patients have only lateral lymph node metastasis, and the lateral lymph nodes have been designated regional lymph nodes (6,17,18). Such patients have had good outcomes after LLD. Available evidence thus suggests

that LLD should be avoided in patients with a low risk of lateral lymph node metastasis or those unlikely to benefit from the procedure, thereby enhancing their postoperative quality of life. On the other hand, LLD should be done patients likely to benefit from the procedure in terms of a lower risk of local recurrence and an improved outcome. In this retrospective study, we evaluated the effects of LLD on overall survival, disease-free survival, and local recurrence.

METHODOLOGY

From 1990 through 2000, 169 consecutive patients with T2 (TNM classification) or more advanced, extended lower rectal cancer (located below the peritoneal reflection) underwent curative resection at Kanagawa Cancer Center. The diagnosis of depth of tumor invasion was due to barium enema, computed tomography, and colonoscopy. Because liver metastasis, peritoneal dissemination, and distant metastasis were considered to have a far stronger impact on outcome than LLD, patients with these conditions were excluded from analysis. Histopathologically, well, moderately, and poorly differentiated adenocarcinomas and mucinous adenocarcinomas were studied.

Clinicopathological data was obtained from clinical chart, retrospectively.

The indication for LLD was originally T2 or more advanced, extended lower rectal cancer. We performed LLD with auto-nerve preservation. This procedure was contained total mesorectal resection. LLD was not done in patients who had cardiovascular complications or respiratory dysfunction, elderly patients, and those not consenting to the procedure. Patients were followed up by computed tomography and measurement of serum tumor makers (CEA and CA19-9) at intervals of 2 to 4 months for the first 2 years and 4 to 6 months thereafter. Median follow-up was 5.6 months. Adjuvant chemotherapy was recommended in all patients, and received by only patients hoped. Radiotherapy was not given.

The statistical significance of differences between groups was evaluated with the chi-square test and t-test. Cumulative survival rate and disease-free survival rate were calculated by the Kaplan-Meier method, and survival curves were compared by the log-rank test. Cox's regression analysis was used for univariate and multivariate analyses. A p value of <0.05 was considered to indicate statistical significance.

RESULTS
Clinicopathological Features of the Patients and Related Factors

The clinicopathological features of the 143 patients who underwent LLD and the 26 patients who did not are shown in **Table 1**. Mean age ($p=0.008$) and preoperative complications ($p=0.008$) differed significantly between these groups.

The overall rates of cumulative survival and disease-free survival at 5 years were 73.3 percent and 61.5 percent, respectively **(Figure 1)**. Cox's univariate regression analysis showed that the cumulative survival rate was significantly related to macroscopic type, T stage (TMN classification), N stage (TNM classification), preoperative levels of CEA and CA19-9 in serum, and LLD **(Table 2)**. In addition to these factors, disease-free survival rate was significantly related to histological type and intraoperative lymph node metastasis **(Table 3)**. T stage (TMN classification), N stage (TNM classification), and LLD were found to be significantly related to the rates of both cumulative survival and disease-free survival **(Tables 4, 5)**. LLD was thus an important prognostic factor for both cumulative and disease-free survival.

Survival Rate of Patients Undergoing LLD and Those Not Undergoing LLD

The disease-free survival rate at 5 years was significantly higher in patients who underwent LLD (65.4 percent) than in those who did not undergo LLD (39.0 percent; $p=0.0182$) **(Figure 2)**. Disease-free survival did not differ significantly between the patients who underwent LLD and those who did not undergo LLD in stage I, II, or III disease ($p=0.3681, p=0.1815$, and $p=0.0896$, respectively) **(Figure 3)**.

|		LLD (N=143)	No LLD (N=26)	P value
Sex	male	102	17	
	female	41	9	0.541
Age (Mean±SE)		60.2±0.9	66.4±1.9	0.008
Macroscopic type	elevated	120	17	
	depressed	23	9	0.088
Tumor diameter (Mean±SE)		53.2±1.7	52.6±5.9	0.902
Pathological type	well	49	10	
	mod	81	14	0.909
	others	13	2	
Depth of invasion	pT2	37	9	
	pT3	91	14	0.613
	pT4	15	3	
Lymph node status	pN0	67	10	
	pN1	35	7	0.72
	pN2	41	9	
Pathological stage (TNM)	I	28	5	
	II	39	5	0.66
	III	76	16	
Adjuvant chemotherapy	(-)	61	16	0.075
	(+)	82	10	
Preoperative serum CEA	normal	115	21	
	high	28	5	0.967
Preoperative serum CA19-9	normal	115	19	
	high	28	7	0.395
Preoperative complications	(-)	112	14	
	(+)	31	12	0.008

TABLE 1 Clinicopathological Features of Patients
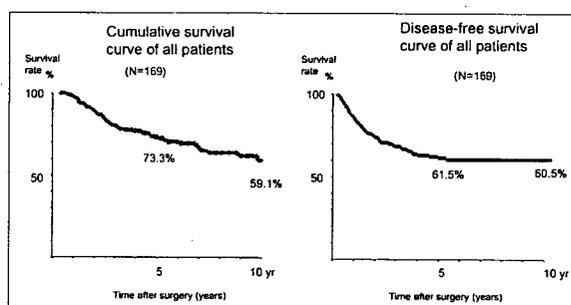
FIGURE 1 Mean observation period was 3390±146 (S.E.) days (95%CI: 3104-3675) after surgery for cumulative survival and 3098±157 (S.E.) days (95%CI:2790-3405) after surgery for disease-free survival.

Lateral Lymph Node Metastasis and Effect of LLD in Stage III Disease

The rate of disease-free survival 5 years after LLD did not differ significantly between patients with stage III disease who had lateral lymph node metastasis (33.3 percent) and those without lateral lymph node metastasis (47.4 percent). The rate of disease-free survival at 5 years was significantly higher in patients with stage III disease without lateral lymph node metastasis who underwent LLD (47.4 percent) than in patients with stage III disease who did not undergo LLD (25.0 percent; $p=0.0449$) **(Figure 4)**. Disease-free survival at 5 years was also analyzed after dividing the patients who underwent LLD into three groups: those without lateral lymph node metastasis, those with only one lateral lymph node metastasis, and those with two or more lateral lymph node metastases. There was no significant difference in disease-