

Original articles

Hepatic resections for bilobar liver metastases from colorectal cancer

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Abstract The present study was performed to assess survival benefits in patients who underwent a hepatic resection for isolated bilobar liver metastases from colorectal cancer. Thirty-eight patients underwent a curative hepatic resection for isolated colorectal liver metastasis. Among them, 11 patients had bilobar liver metastases and 19 had a solitary metastasis. The remaining 8 patients had unilobar multiple lesions. We investigated survival in two groups those with bilobar and those with solitary metastatic tumors. Survival and disease-free survival were 36% and 18% at 5 years, respectively, in the patients with bilobar liver metastases, while these survivals were 43% and 34% in the patients with solitary liver metastasis. In the 38 patients, repeated hepatic resections were performed in 15 patients with recurrent liver disease. The 5-year survival and disease-free survival rates for these patients were 38% and 27%, respectively, after the second hepatic resections. Of the 11 patients with bilobar liver metastases, 5 underwent a repeated hepatic resection, and they all survived for over 42 months. Based on our observations, a hepatic resection was thus found to be effective even in selected patients with either bilobar nodules or recurrence in the remnant liver.

Key words Bilobar liver metastasis · Colorectal cancer · Hepatic resection

Introduction

Hepatic metastases from colorectal cancer are noted in from 20%–30% of patients during their clinical course,¹ while involvement of only the liver is seen in about 10%.² Regional chemotherapy is one of the effective strategies for patients with colorectal liver metastases. However, the mean survival period achieved after such

treatment ranges from 13 to 16 months.^{3,4} Hepatectomy for patients with liver metastases has been performed safely in the past decade.^{5–11} From these studies, the 5-year survival has been reported to range from 31% to 49%. Hepatic resection for selected patients with isolated liver metastases from colorectal cancer is currently acceptable.^{12–15} However, bilobar liver metastases may be one of the prognostic factors, and the hepatic surgery for such patients may not always be easy. Recurrence in the remnant liver after a hepatic resection is not rare, and it tends to develop in 35%–50% of all patients.^{2,16,17} Recently, repeat hepatectomy has become the treatment of choice in some patients, and the surgical results have been favorable.^{2,18–21} In the present study, we evaluated the surgical results in patients who underwent a hepatic resection for colorectal liver metastases, and paid special attention to the clinical significance of a hepatic resection in patients with either bilobar metastatic nodules in the liver or recurrence in the remnant liver after a hepatic resection.

Methods

Patients

From 1981 to 1997 in our department, 579 patients were operated on for colorectal cancer, and 64 (11.1%) patients underwent a hepatic resection for colorectal liver metastases. Of these 64 patients, 26 underwent a palliative resection (8 patients had non-curative resections for primary colorectal cancer, 7 had extrahepatic disease, 8 had residual tumors after hepatic resection because of multiple liver nodules, and 3 had microscopic cancer cells at the surgical liver margin). These 26 patients were therefore excluded from this study.

The remaining 38 patients with isolated liver metastases, who underwent a curative resection, were the subjects of the present study. There were 26 men and 12 women. The mean age of the 38 patients at the time of

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the initial surgery was 60 years (range, 39 to 80 years). Liver metastases were noted preoperatively by hepatic imaging in 34 patients and intraoperatively in 4 patients. Liver metastases were present unilaterally in 27 patients. Among these 27, a solitary nodule was found in 19, while in 8 patients, there were multiple nodules. In addition, 11 patients had bilobar liver metastases. All data were examined at the time liver metastases were diagnosed. The survival rates were calculated after each operation. In patients with synchronous metastases, resections of the primary tumor and liver metastases were performed during the same operation. In the patients who underwent repeated hepatic resections, the disease-free interval after the first hepatic resection represents the total number of months after the first, second, and third hepatic surgeries.

All 38 patients were followed up until either December 1, 1998, or death. The mean follow-up time was 47 months after the first hepatic resection (range, 7–126 months) and 48 months after the second hepatic resection (range, 6–112 months).

Statistics

Both the survival and disease-free survival rates were calculated according to the methods of Kaplan and Meier. Mean values (estimated values) for survival time and the SD were calculated, using Stat View 5 software (SAS Institute, Cary, NC, USA).

Results

Clinical features of the 38 patients with liver metastases from colorectal cancer

In the 38 patients, 26 had metastatic disease from colon cancer and 12 had metastasis from rectal cancer. In terms of disease stage, 12 were Dukes A, 2 were Dukes B, and the remaining 24 were Dukes C. The liver metastases were found at the same time as the diagnosis of colorectal cancer was made in 23 patients (synchronous metastasis), and were detected later on in 15 patients (metachronous metastasis). No hospital mortality was observed in these patients.

Patients with bilobar metastatic liver tumors

In the 11 patients with bilobar liver metastases, 2 were Dukes A and 9 were Dukes C for the primary lesion, while the time that liver metastases were diagnosed was synchronous in 5 patients and metachronous in 6 patients. The background of these patients is summarized in Table 1. The average number of nodules found at the first hepatic resection was 3.8 ± 2.3 (mean value \pm SD) and the mean diameter of the largest liver metastasis

Table 1. Patients with bilobar metastatic liver tumors from colorectal cancer

Patient no.	Age (years)/Sex	First hepatic resection			Second hepatic resection			Survival				
		Nodules	Size (cm)	Operation	DFI-1 (months)	Nodules	Size (cm)	Operation	DFI-2 (months)	DFI-1+2	Time (months)	Status
1	72/M	4	10	Ex. lobe	1			1		7	DOD	
2	52/M	4	1.5	Ex. lobe	6			6		15	DOD	
3	42/M	2	6	Ex. lobe	15			15		20	DOD	
4	50/F	3	2.5	Lobe + seg	20			20		27	DOD	
5	55/M	2	3.8	Wedge	12			12		42	DOD	
6	60/M	6	2.2	Ex. lobe + wedge	5	2	2.8	Wedge	25	30	42 (34)	DOD
7	39/M	10	2.6	Lobe + seg + wedge	0	2	2.7	Wedge	6		45 (40)	DOD
8	69/F	3	3.4	Seg + wedge	23	2 ^a	4.4 ^a	Wedge ^a	6	12	64 (40)	DOD
9	63/M	4	3	Seg + wedge	17	1	2.4	Wedge	0	23	66 (27)	DOD
10	56/M	2	3	Seg + wedge	82	1	7	Ex. lobe	12	29	82	ADF
11	58/F	2	4	Wedge	12	1	2	Wedge	101	113	117 (101)	ADF

Figures in parentheses indicate survival after second hepatic resection

Wedge, Wedge resection; seg, segmentectomy; lobe, lobectomy; Ex., extended; DFI-1, disease-free interval after first hepatic resection; DFI-2, DFI after second hepatic resection; DOD, dead of disease; ADF, alive disease free

^aThird hepatic resection

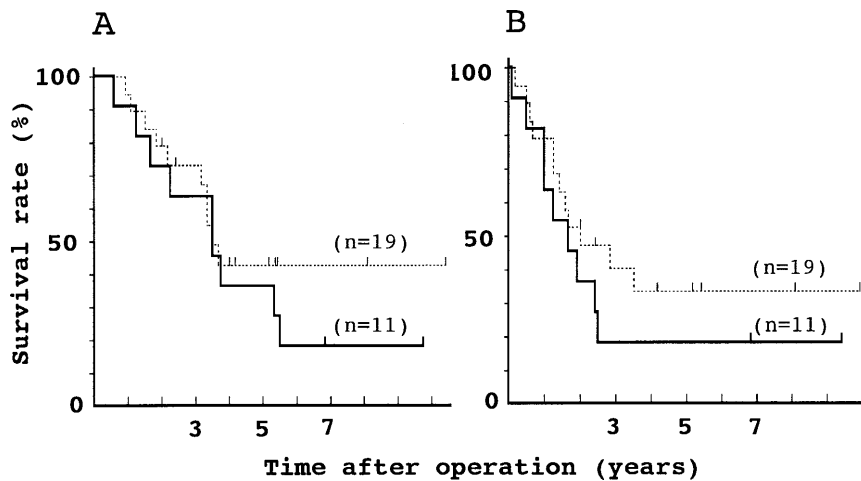


Fig. 1. **A** Survival and **B** disease-free survival for patients with bilobar liver metastases (solid line; $n = 11$) and those with solitary liver metastasis (dotted line; $n = 19$) after first hepatic resection

was 3.8 ± 2.3 cm. Surgical therapy consisted of two wedge resections, three segmentectomies plus wedge resections, one lobectomy plus segmentectomy, one lobectomy plus segmentectomy plus wedge resection, three extended lobectomies and one extended lobectomy plus wedge resection. The data for the 19 patients with solitary liver metastasis are shown in Table 2. Of these patients, 8 were Dukes A, 1 was Dukes B, and the remaining 10 were Dukes C. Twelve patients had synchronous metastases, and 7 had metachronous metastases. As shown in Fig. 1A, the 3-, 5-, and 7-year survival rates were 64%, 36%, and 19%, respectively, in the patients with bilobar metastases (estimated survival time \pm SD; 41.8 ± 6.7 months), whereas these rates were 73%, 43%, and 43%, respectively, in the patients with a solitary metastatic nodule in the liver (estimated survival time; 36.1 ± 2.8 months). The disease-free survival rates were 18% at 3 years and at 5 years in the patients with bilobar metastases (estimated disease-free survival time \pm SD; 18.9 ± 3.2 months) and 41% at 3 years and 34% at 5 years in patients with solitary metastasis (estimated disease-free survival, 26.4 ± 3.5 months) (Fig. 1B).

Table 3 shows the data on the eight patients with unilobar multiple liver metastases. Four patients survived for over 4 years and three of them had no recurrent disease after the first or second hepatic resection.

Second hepatic resection

All 38 patients were examined and the clinical features of the 15 patients who underwent repeated hepatic resection were reviewed. The mean disease-free interval between the first and second hepatic resections was 11 months (range, 2–26 months). Of these 15 patients, 14 (93%) had recurrent disease of the liver within 2 years after the first hepatic resection. The number of nodules

was less than three, and the maximum diameter of the largest nodule at the second hepatic resection was less than 7 cm. The surgical therapy consisted of 11 wedge resections, 3 lobectomies, and 1 extended lobectomy. Two patients underwent a third hepatic resection. No death directly related to the repeated hepatic surgery was experienced. As shown in Fig. 2A, the 5-year survival and disease-free survival rates were 38% (estimated survival time; 30.4 ± 3.5 months) and 27% (estimated disease-free survival time; 12.7 ± 2.6 months), respectively, after the second hepatic resection. In the 38 patients in the study, these survival times were 40% (42.9 ± 3.6 months) and 30% (23.5 ± 2.5 months), respectively, after the first hepatic resection (Fig. 2B).

Discussion

Hepatic resection is currently considered to be an acceptable therapy for selected patients with liver metastases from colorectal cancer. The 5-year cumulative survival rates have been reported to be about 40%,^{2,9,10} while the disease-free survival rate is 20%.^{14,17,19} However, the role of hepatic surgery for bilobar metastatic liver tumors is less certain. It was reported that the distribution of the intrahepatic tumors did not make any significant difference to survival.^{9,10,15} However, some investigators^{22–24} have shown that the distribution, or the number, of liver metastases did influence survival. When we compared survival in the groups with bilobar and solitary metastatic lesions, there was no significant difference between the groups, but this may be due to the small number of patients. In our series of 38 patients, those with metastases consisting of more than four nodules ($n = 7$) and those with nodules greater than 6 cm in size ($n = 11$) showed a very poor prognosis (5-year cumulative survival rates were 14% and 0%,

Table 2. Patients with solitary metastatic liver tumor from colorectal cancer

Patient no.	Age (years)/Sex	First hepatic resection			Second hepatic resection			Survival				
		Nodules	Size (cm)	Operation	DFI-1 (months)	Nodules	Size (cm)	Operation	DFI-2 (months)	DFI-1 + 2	Time (months)	Status
1	49/M	1	4.5	Ex. lobe	6	1		6		6	11	DOD
2	58/F	1	10	Wedge	8					8	13	DOD
3	75/F	1	12	Lobe	12	2	Wedge	3		15	18 (8)	DOD
4	56/M	1	6	Wedge	2					2	22	DOD
5	46/M	1	10	Lobe	18	1	Wedge	2		20	26 (7)	DOD
6	59/M	1	6	Wedge	8	1	Lobe	7		15	38 (25)	DOD
7	69/M	1	7.4	Wedge	19					19	40	DOD
8	67/M	1	12	Wedge	9	1	Lobe	8		17	40 (30)	DOD
9	66/M	1	0.4	Wedge	34					34	42	DOD
10	73/F	1	5	Seg	24					24	44	DOD
11	43/M	1	3	Seg	2	2	Lobe	5		7	48 (44)	AWD
12	72/M	1	1	Wedge	26	3	Wedge	16		42	65 (33)	AWD
13	70/M	1	2	Lobe	24					24	24	ADF
14	51/M	1	3.1	Lobe	29					29	29	ADF
15	61/F	1	2	Tri-seg	50					50	50	ADF
16	62/M	1	0.5	Wedge	62					62	62	ADF
17	42/F	1	1	Wedge	65					65	65	ADF
18	57/F	1	1.2	Lobe	97					97	97	ADF
19	68/M	1	2	Wedge	19	1	Wedge	47		125	102	ADF
						1*	Wedge ^a	53		119		ADF

Figures in parentheses indicate survival after second hepatic resection

Wedge, Wedge resection; seg, segmentectomy; lobe, lobectomy; Ex., extended; DFI-1, disease-free interval after first hepatic resection; DFI-2, DFI after a second hepatic resection; DOD, dead of disease; AWD, alive with disease; ADF, alive disease free

^aThird hepatic resection

Table 3. Patients with unilateral multiple metastatic liver tumors from colorectal cancer

Patient no.	Age (years)/Sex	First hepatic resection			Second hepatic resection			Survival				
		Nodules	Size (cm)	Operation	DFI-1 (months)	Nodules	Size (cm)	Operation	DFI-2 (months)	DFI-1 + 2	Time (months)	Status
1	76/M	5	10	Lobe	2	2				2	9	DOD
2	53/M	2	6	Lobe	4					4	14	DOD
3	60/F	3	1.5	Lobe	3					3	17	DOD
4	78/M	7	1.5	Lobe	3	2	Wedge	0		3	18 (6)	DOD
5	62/M	2	2.4	Wedge	24					24	51	DOD
6	57/F	2	1	Lobe	50					50	50	ADF
7	73/F	2	2.5	Wedge	5	1	Wedge	112		117	112	ADF
8	57/M	3	2.5	Lobe	6	2	Wedge	110		116	126 (110)	ADF

Figures in parentheses indicate survival time after second hepatic resection

Wedge, Wedge resection; lobe, lobectomy; DFI-1, disease-free interval after first hepatic resection; DFI-2, DFI after second hepatic resection; DOD, dead of disease; ADF, alive disease free

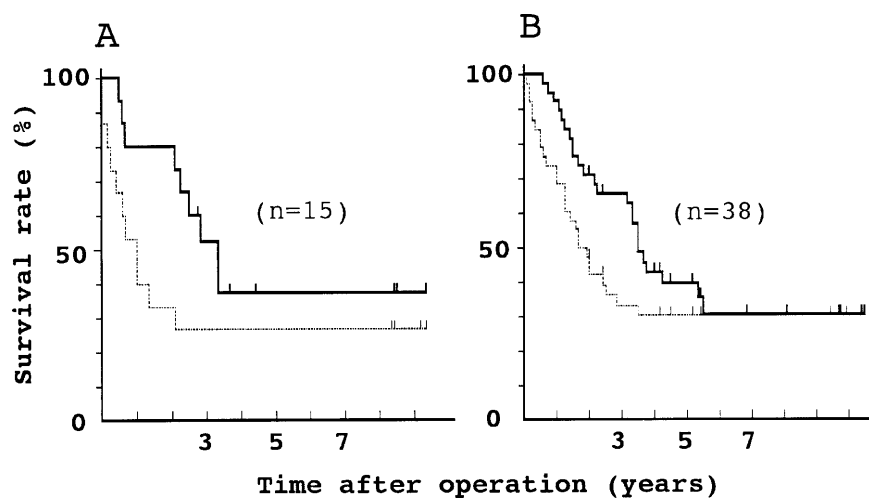


Fig. 2. **A** Survival (solid line) and disease-free survival (dotted line) after second hepatic resection for 15 patients with recurrent disease of the liver. **B** Survival (solid line) and disease-free survival (dotted line) for the 38 patients in the study after first hepatic resection

respectively). In fact, in the 19 patients with a solitary liver lesion, 7 (37%) patients had a tumor greater than 6 cm in size, but only 2 (18%) of the 11 patients with bilobar lesions had a tumor greater than 6 cm in size.

After the first hepatic resection, most patients are at high risk for recurrence in the liver. Most patients with isolated liver recurrence are identified within 2 years postoperatively.^{8,17} In our experience of the 38 patients noted here, recurrent liver disease occurred within 26 months after the first hepatic resection. Furthermore, it is reported that isolated liver recurrence occurs in approximately 30% of patients.^{8,16,17} Repeated hepatic resections are now considered for such patients, but 10% to 20% of patients are good candidates for a second liver resection.^{17,18} Fernandez-Trigo et al.¹⁹ and Sugarbaker²⁵ reported a series from 20 different institutions around the world, which comprised 170 patients who had undergone repeated hepatic resections. They showed the 3- and 5-year survival rates after a second hepatic resection to be 45% and 32%, respectively. These results did not differ from those after a first hepatic resection. Other investigators^{2,20,26} also reported repeat hepatic operations to be successful. In our series, 15 patients underwent a second hepatic resection, and the 5-year survival rate after the second hepatic resection was 38%. No significant differences were observed, even when comparisons were made regarding the survival of the 38 patients after a first hepatic resection. Five of the 15 patients had bilobar liver metastases at the first hepatic resection, and they survived for 42–117 months after the first hepatic surgery and for 27–101 months after the second hepatic surgery. In patients who underwent repeated hepatic surgery, there seemed to be no difference in survival between those with bilobar and those with unilobar metastatic lesions.

Based on these findings, we consider that bilobar hepatic metastases are not a limiting factor in the progn-

osis of these patients. A hepatic resection may therefore increase longevity and improve the quality of life in selected patients with bilobar liver metastases.

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