Hepatic resection for colorectal liver metastases

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ABSTRACT

Introduction: Nearly 50 percent of patients who have colorectal carcinoma will develop liver metastases, which is frequently the cause of death. Liver resection is the only curative treatment for patients with colorectal metastases confined to the liver. However, liver resection can be performed in only ten percent of patients. A strategy to improve resectability and outcome of patients with colorectal liver metastases is needed.

Methods: The progress and outcome of patients, who had colorectal liver metastases and underwent liver resection in a tertiary surgical centre between January 1998 and December 2002, were retrospectively studied.

Results: During the five-year study period, 42 patients with colorectal liver metastasis underwent hepatic resection. 36 patients received primary liver resection. Six patients with initially unresectable disease received salvage surgery after tumour downstaging with systemic chemotherapy. Five of the 42 patients needed repeat liver resection for recurrent colorectal liver metastases. The hospital mortality rate was 2.1 percent. 11.9 percent of patients had major postoperative complications. The median survival was 49 months. The one-, three- and five-year overall survival rates after resection were 91 percent, 54 percent, and 37 percent, respectively; and the recurrence rate was 76 percent. The five-year survival rate with salvage surgery after tumour downstaging was 34 percent, and the corresponding figure, after repeat liver resection, for recurrent liver metastases was 27 percent.

Conclusion: Hepatic resection for colorectal metastases confined to the liver resulted in reasonably good long-term survival, with acceptably low operative mortality and morbidity. Our results were compatible with the international standard of liver resection for colorectal liver metastases.

Keywords: colonic cancer, colorectal liver metastasis, colorectal neoplasms, hepatectomy, tumour downstaging

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INTRODUCTION

Nearly 50% of patients with colorectal carcinoma will develop liver metastases, which are frequently the cause of death. Liver resection is the only curative treatment for patients with colorectal metastasis confined to the liver. There is a five-year survival rate of 22%–40% for this procedure.[1-4] Unfortunately, liver resection is possible in only 10% of patients. For patients with unresectable disease and who receive systemic chemotherapy, the median survival is 11–19 months only.[5-9] Several strategies, including two-stage hepatectomy, liver resection with preoperative portal vein embolisation, combination of hepatectomy and local ablative treatment, and salvage surgery following tumour downstaging, have been developed to increase the resectability and improve the outcome.[10-15] The aim of the present study was to audit and review our own experience on liver resection for colorectal liver metastases.

METHODS

The medical and pathological records of patients, who were presented with the diagnosis of colorectal liver metastases and treated with partial hepatectomy, in a single tertiary referral centre between January 1998 and December 2002, were studied. We limited our study period in order to assess the survival rates in patients with a long enough follow-up period. The clinical progress, operative records and pathology results were retrospectively reviewed. Ultrasonography (US) and computed tomography (CT) were used for tumour staging and assessing resectability. Imaging for preoperative investigation and tools for staging were not standardised during the study period because of the evolution of the investigation modalities. In the latter part of our study, positron emission tomography (PET) for tumour staging before laparotomy was used. Survival was calculated by

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Table I. Characteristics of primary tumours and colorectal liver metastases in 42 patients.

Cite of primary colorectal cancer	No. of patients (%)
Colon	23 (55)
Rectum	19 (45)
Dukes' staging at time of resection for colorectal cancer	
A	3 (7)
B	12 (29)
C	18 (43)
D	9 (21)
Number of liver resections	47
Liver metastases	
Synchronous	9
Bilobar	5
Mean size (cm)	4.8 (range 0.8–11.5)
Number of tumours	
1	31
2	10
3	3
4	2
5	1

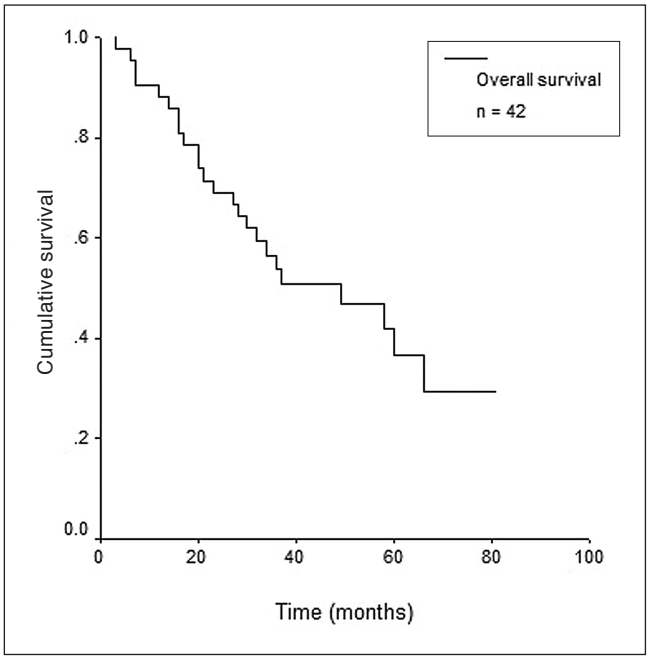

Fig. 1 Survival rates of patients with colorectal liver metastasis and who underwent liver resection.

the Kaplan-Meier method. Statistical comparison of survival distribution was analysed by log-rank test. $p < 0.05$ was regarded as statistically significant.

Table II. Types of 47 liver resections performed in 42 patients.

Type of liver resections	No. of liver resections
Right hepatectomy	17
Right hepatectomy and caudate lobe resection	1
Right hepatectomy and right adrenalectomy	1
Extended right hepatectomy	3
Left hepatectomy	2
Extended left hepatectomy	1
Left lateral sectionectomy	3
Resection of 3 Couinaud segments	5
Resection of 2 Couinaud segments	6
Resection of 1 Couinaud segment	3
Non-anatomical resection	5

RESULTS

During the five-year study period, 42 patients who were diagnosed with colorectal liver metastasis, underwent surgical resection. There were 22 men and 20 women, with a mean age of 60.3 years (range 36–83 years). 36 patients received primary liver resection. Six patients with initially unresectable disease received salvage surgery after tumour downstaging with systemic chemotherapy (5-fluorouracil (5FU)/ leucovorin (LV), n = 2; 5FU/LV combined with oxaliplatin, n = 2; 5FU/LV combined with irinotecan, n = 2). The liver metastases were unresectable because of large solitary tumours with insufficient liver remnants (n = 3) or extensive bilobar disease (n = 3). Response to chemotherapy was evaluated with serial US and CT. A partial response (defined as ≥ 50% decrease in total tumour size) was observed in five patients, while a minor response (< 50% decrease in tumour size) was observed in one patient. Five of the 42 patients (12%) were found to have recurrent colorectal liver metastases on follow-up and needed repeat liver resection (repeat liver resection after primary liver resection, n = 4; repeat liver resection after salvage surgery and tumour downstaging, n = 1).

The details of the primary colorectal tumour and the colorectal liver metastases are shown in Table I. The types of the 47 hepatic resections in the 42 patients are listed in Table II. 70% of the hepatic resections were major resections involving three or more Couinaud liver segments. 98% of the hepatic resections had clear resection margins (R0 resection). The mean hospital stay was 13 days (median, ten days; range, 5–90 days). Seven patients had postoperative adjuvant chemotherapy (5FU/LV, n = 5; 5FU/LV combined with

oxaliplatin, n = 1; 5FU/LV combined with irinotecan, n = 1) after the first liver resection. The mean follow-up was 36 months.

The hospital mortality rate was 2.1% (n = 1). This patient with recurrent liver metastasis died because of postoperative haemorrhage after repeat liver resection. Five patients (11.9%) had major postoperative complications, including postoperative haemorrhage (n = 1), bile leak (n = 1), intra-abdominal collection (n = 2) and pleural effusion (n = 1).

The median survival rate for the 42 patients was 49 months (range 3–81 months). The one-, three- and five-year overall survival rates after hepatic resection were 91%, 54%, and 37%, respectively (Fig. 1). At the end of the study period, 18 of the 42 patients were alive with a mean follow-up of 51 months, and seven patients were disease-free. Tumour recurrence during follow-up occurred in 76% of the 42 patients (distant metastasis, n = 29; local recurrence, n = 1; distant metastasis and local recurrence, n = 2). The mean interval from liver resection to recurrence was 18.7 months (range 5–55 months). 69% of the recurrence occurred within the first two years of liver resection. In the six patients who underwent salvage surgery after tumour downstaging, the five-year overall survival rate after resection was 34% (Fig. 2). 66.7% of patients developed recurrence after a mean follow-up of 45.2 months. At the end of the study period, two patients were alive and disease-free at 37 months and 42 months, respectively, after liver resection. In the five patients who underwent repeat liver resection for recurrent liver metastasis, the five-year overall survival rate after resection was 27% (Fig. 3). At the end of the study period, one patient was alive and disease-free at 12 months after the second liver resection, and the other patient was alive at 42 months after the second liver resection but with disease recurrence.

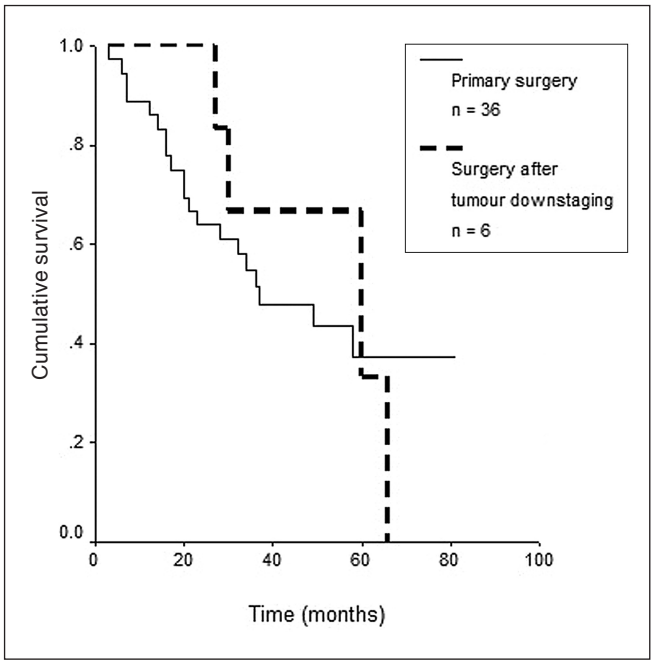

Fig. 2 Comparison of survival of patients with colorectal liver metastases who underwent primary liver resection, with patients with initial unresectable colorectal liver metastases who underwent salvage surgery after tumour downstaging (p = 0.86).

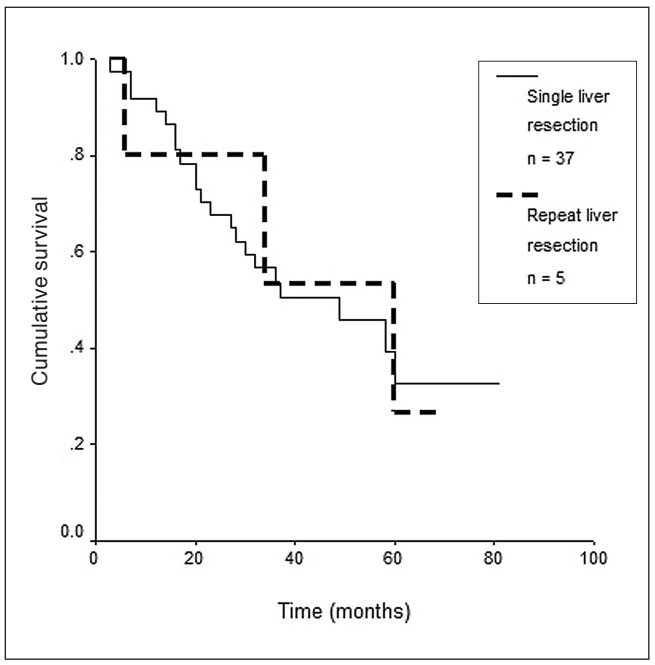

Fig. 3 Comparison of survival of patients with colorectal liver metastases who underwent single liver resection, with patients with recurrent colorectal liver metastases who underwent repeat liver resection (p = 0.85).

DISCUSSION

Our study demonstrated that reasonably good long-term survival with a low operative mortality and morbidity, can be achieved in patients with advanced colorectal liver metastasis through an aggressive surgical approach. In our series, 19% of liver resections involved tumours with size > 5 cm, 6% of liver resections involved tumour numbers > 3, 11% of liver resections involved bilobar disease, 70% of liver resections were major resections, 12% of patients underwent repeat liver resection for recurrent colorectal liver metastasis, and 14% of patients with initially unresectable colorectal liver metastases underwent salvage surgery after tumour downstaging. The five-year overall survival was 37%. Our postoperative mortality and morbidity rates were 2.1% and 11.9%, respectively.

With the introduction of the effective chemotherapeutic agents, like oxaliplatin and irinotecan, the survival and tumour response rates have improved significantly for advanced colorectal disease.[5] In

multicentre, randomised, controlled studies, shrinkage of tumour volume of 50% or more were shown in 41%–59% of patients with advanced colorectal liver metastases.[6-9] This response rate was twice that of the regimen of 5-FU and LV. With the breakthrough in chemotherapy, salvage surgery after tumour downstaging becomes increasingly feasible in patients with initially unresectable disease. The term, downstaging, should be differentiated from the term, neoadjuvant therapy. For tumour downstaging, the tumour is initially unresectable either because of the local extent of the disease or because of distant metastases. For neoadjuvant therapy, the tumour is resectable, and the treatment is given preoperatively to improve on the results of surgery. The concept of tumour downstaging followed by salvage liver resection is still new, and the evidence of efficacy in the medical literature is limited.[10-12]

In a large series of 1,104 patients with unresectable colorectal liver metastasis reported by Adam et al, systemic chemotherapy consisting of 5-FU and LV alone (12%) or combined with oxaliplatin (70%), irinotecan (7%) or both (4%), tumour downstaging followed by salvage liver resection, was possible in 138 patients (12.5%).[11] After a mean follow-up of 48.7 months, 80% of these 138 patients developed tumour recurrence. The overall five-year survival rate was 33%. Our study showed comparable results. The five-year survival rate of patients, who underwent salvage surgery after tumour downstaging, in our series was 34%. 66.7% developed tumour recurrence after a mean follow-up of 46.2 months. It is interesting to note that tumour downstaging and salvage liver resection have also been reported to be effective for unresectable hepatocellular carcinoma and hepatoblastoma.[16-21] There are several prerequisites for a successful tumour downstaging and salvage surgery treatment regimen: (1) an effective treatment which can shrink the tumour in a significant proportion of patients; (2) a close radiological monitor on the tumour response to the treatment; (3) repeated assessment by a liver surgeon with a view to carry out liver resection at the right time; and (4) an aggressive surgical approach to liver resection. In our centre, we carried out liver resection within one month, after completion of the systemic chemotherapy, in patients who showed a good response to chemotherapy. This timing was chosen by balancing between the patients' recovery rate from chemotherapy and opportunity for tumour regrowth from a viable part of the tumour.

It has been reported that 50%–80% of patients developed recurrent metastases after primary resections of liver metastases,[22-26] and only one-third had isolated liver metastases. There is increasing evidence in the medical literature to show that repeat liver resection for recurrent colorectal liver metastasis gives similar results to primary liver resection. The reported five-year survival rate after repeat liver resection varied from 21% to 41%.[22-25] In our series, the five-year survival was 27%. Our study shows that an aggressive surgical approach, which has a low surgical mortality and morbidity, provides survival benefits in patients with colorectal liver metastases. Our results are compatible with the international standard of liver resection for colorectal liver metastasis.

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