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ORIGINAL ARTICLE

Repeat liver resection for recurrent colorectal metastases: a single-centre, 13-year experience

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Abstract

Objectives: Isolated intrahepatic recurrence is noted in up to 40% of patients following curative liver resection for colorectal liver metastases (CLM). The aims of this study were to analyse the outcomes of repeat hepatectomy for recurrent CLM and to identify factors predicting survival.

Methods: Data for all liver resections for CLM carried out at one centre between 1998 and 2011 were analysed.

Results: A total of 1027 liver resections were performed for CLM. Of these, 58 were repeat liver resections performed in 53 patients. Median time intervals were 10.5 months between the primary resection and first hepatectomy, and 15.4 months between the first and repeat hepatectomies. The median tumour size was 3.0 cm and the median number of tumours was one. Six patients had a positive margin (R1) resection following first hepatectomy. There were no perioperative deaths. Significant complications included transient liver dysfunction in one and bile leak in two patients. Rates of 1-, 3- and 5-year overall survival following repeat liver resection were 85%, 61% and 52%, respectively, at a median follow-up of 23 months. R1 resection at first hepatectomy ($P = 0.002$), a shorter time interval between the first and second hepatectomies ($P = 0.02$) and the presence of extrahepatic disease ($P = 0.02$) were associated with significantly worse overall survival.

Conclusions: Repeat resection of CLM is safe and can achieve longterm survival in carefully selected patients. A preoperative knowledge of poor prognostic factors helps to facilitate better patient selection.

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Introduction

Colorectal cancer (CRC) is the third most common malignancy and the second most common cause of cancer-related deaths worldwide.[1] Up to 70% of patients with CRC develop either synchronous (15–25%) or metachronous (20–40%) liver metastases.[2,3] Despite the recent advances in chemotherapeutic agents, liver resection remains the only potentially curative treatment for colorectal liver metastases (CLM).[4–8] Reported 5-year overall survival rates following curative liver resection lie in the range of 35–58%.[9–12] However, about two thirds of patients develop tumour recurrence and the recurrent disease is limited to the liver in up to 40%.[13–16] Advances in surgical techniques and perioperative management have enabled some centres to perform repeat hepatectomy in selected groups of patients.[17–20] Experiences with repeat resections are limited and the published literature is confined to a few retrospective studies.[21–24] The aims of this study were to analyse the outcomes of repeat hepatectomy performed for recurrent CLM and to identify factors predicting survival.

This study was presented at the Third Biennial Congress of the Asian Pacific Hepatopancreatobiliary Association, 27–30 September 2011, Melbourne, Victoria.

Materials and methods

Following approval of the study protocol by the institutional review board, all patients who underwent surgery for CLM between January 1998 and January 2011 were identified. Data were collected retrospectively using the prospectively maintained liver unit data-

base. Only patients who underwent more than one liver resection were included in the study. Patients with recurrent liver disease treated with radiofrequency ablation (RFA) were excluded. Information collected included data on patient demographics, clinicopathological features of the primary and metastatic tumours, operative data and postoperative complications in both the single hepatectomy group and the repeat liver resection group. Rates of 1-, 3- and 5-year overall survival were calculated from the time of first hepatectomy and were compared with those in the single hepatectomy group. A further analysis was performed to identify factors influencing survival in the repeat liver resection group.

Preoperative staging included contrast-enhanced, triple-phase computed tomography and liver-specific magnetic resonance imaging. All imaging was discussed at a multidisciplinary meeting. Neoadjuvant chemotherapy was considered in patients with borderline resectable disease or a clinical risk score of >3.[25]

The criteria for consideration for repeat liver resection were similar to those for initial liver resection: patients were required to show the presence of resectable liver disease, the absence of unresectable extrahepatic disease and the likelihood of an adequate functional liver remnant following resection. Intermittent inflow occlusion was used selectively and parenchymal transection was performed using the Cavitron Ultrasonic Surgical Aspirator (CUSA; Valleylab™, Covidien, Inc., Boulder, CO, USA) and/or a harmonic scalpel according to the surgeon's preference. A thoracic epidural infusion of bupivacaine and fentanyl was used routinely to provide postoperative pain relief.

Liver metastases that were diagnosed within 3 months of the primary tumour were defined as synchronous, whereas those diagnosed >3 months later were classed as metachronous lesions.[26] The extent of liver resection was classified according to the Brisbane 2000 Guidelines. Resections involving more than three Couinaud segments were regarded as major.

Perioperative mortality was defined as death during the same hospital admission or within 90 days of surgery. Postoperative complications were graded using the modified Dindo–Clavien system of classification.[27]

Patients were followed up by clinical evaluation and measurement of serum carcinoembryonic antigen (CEA) every 3 months during the first year, every 4 months during the second, every 6 months during the third and annually thereafter until the fifth anniversary. Computed tomography was performed at 6 and 18 months following surgery and if clinically indicated.

Statistical analysis

Data were analysed using SPSS Version 17 (SPSS, Inc., Chicago, IL, USA). Descriptive statistics were presented as percentages or median values. Non-parametric Mann–Whitney *U*-tests and chi-squared tests were used to analyse differences between the single and repeat hepatectomy groups. Survival was calculated from the time of both the first and second hepatectomies in the repeat hepatectomy group and survival analysis was performed according to the Kaplan–Meier method. Factors associated with survival were assessed using the Cox regression test. A *P*-value of <0.05 was considered to indicate statistical significance in all tests.

Results

A total of 1027 liver resections were performed for CLM during the study period. Of these, 58 (6%) represented repeat hepatectomies performed in 53 patients. Five patients underwent a third liver resection. Single hepatectomy was performed in 916 patients. The median age at presentation in the repeat hepatectomy group was 63 years (range: 38–81 years). A total of 29 (55%) of the 53 patients in the repeat hepatectomy group were male.

Primary tumours were staged according to the Dukes classification system as stage A in three patients, stage B in 15, stage C in 18 and stage D in 17 patients. Hepatic metastases at index presentation were synchronous in 17 and metachronous in 36 patients. Thirty-one patients received chemotherapy prior to first liver resection and three received chemotherapy before the repeat liver resection. The majority of chemotherapy regimens were 5-fluorouracil (5-FU) and oxaliplatin-based The median time interval between the colectomy and the first hepatectomy was 10.5 months (range: 1.9–65.0 months); median intervals were 15.4 months (range: 4.3–60.1 months) between the first and second hepatectomies, and 12.2 months (range: 7.7–33.8 months) between the second and third liver resections.

Operative data

In the 53 patients submitted to repeat liver resection, the first hepatectomy was major in 25 and minor in 28 cases. The repeat liver resection was major in 10 and minor in 43 patients. All of the five third hepatectomies were non-anatomical wedge resections. Types of liver resection in the repeat hepatectomy group are summarized in Table 1.

Blood products were used in 13 patients during the first hepatectomy and in 10 patients during the repeat procedure. None of the patients undergoing third hepatectomies required transfusions.

Metastatic tumour characteristics at first hepatectomy (*n* = 53)

The median size of the tumour was 3.0 cm (range: 1.0–11.0 cm) and the median number of lesions was one (range: 1–9). A bilobar

Table 1 Type of liver resection in the repeat hepatectomy group (*n* = 53)

Type	At first hepatectomy, *n* (%)	At second hepatectomy, *n* (%)
Right hepatectomy	13 (25%)	7 (13%)
Extended right hepatectomy	4 (8%)	2 (4%)
Left hepatectomy	5 (9%)	1 (2%)
Extended left hepatectomy	3 (5%)	0
Left lateral segmentectomy	8 (15%)	2 (4%)
Non-anatomical resections	20 (38%)	41 (77%)