

ORIGINAL ARTICLE

Outcomes of extended versus limited indications for patients undergoing a liver resection for colorectal cancer liver metastases

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Abstract

Background: Currently, resection criteria for colorectal cancer liver metastases (CRCLM) are only limited by remnant liver function. Morbidity and survival after a partial hepatectomy with limited or extended indication criteria were compared.

Methods/Design: Between 1991 and 2010, patients undergoing a liver resection for CRCLM with limited ($n = 169$) or extended indication criteria ($n = 129$) were retrospectively identified in a prospectively collected single-centre database. Limited indication criteria were defined as less than three unilateral, not centrally located liver metastases in the absence of extra hepatic metastases. The extended criteria were only limited by predicted remnant liver volume and patients fitness. Data on co-morbidity, resection margin, short- and long-term morbidity, disease-free (DFS) and overall survival were compared.

Results: Patients with limited indications had less major complications (19.5% vs. 33.1%, $P < 0.01$), longer overall survival of 68.8 months [confidence interval (CI) 46.5–91.1] vs. 41.4 months (CI 33.4–49.0, $P \leq 0.001$) and longer median DFS of 22.0 months [confidence interval (CI) 15.8–28.2] vs 10.2 months (CI 8.4–11.9, $P < 0.001$) compared with the extended indication group. Cure rates, defined as 10-year DFS, were 35.5% and 15.8%, respectively. Fewer patients in the extended indication group underwent an R0 resection (92.9% vs. 77.5%, $P < 0.001$). Only 17% of all R1 resected patients had recurrences at the transection plane.

Conclusion: A partial hepatectomy for CRCLM with extended indications seems justified but is associated with higher complication rates, earlier recurrence and lower overall survival compared with limited indications. However, the median 5-year survival was substantial and a cure was achieved in 15.8% of patients.

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Introduction

During the last decade, the limited criteria for a partial liver resection have been replaced by more extended indication criteria.

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Improvements in surgical technique, optimization of peri-operative care, improvements in diagnostic imaging, pre-operative liver remnant volume modulation and effectiveness of modern chemotherapy regimens have boosted the widening of resectability criteria. Traditionally, only patients with a maximum of three colorectal cancer liver metastases, located peripherally at one side of the liver with an anticipated resection margin greater than 10 mm and without signs of extrahepatic disease were considered eligible for a partial liver resection.^{1–4} Based on these limited

criteria, only 10–20% of patients with colorectal cancer liver metastases were eligible for a resection. Recent studies have shown that a liver resection in patients with multiple and/or bilateral colorectal liver metastases results in overall 5-years survival rates between 23% and 51%.^{3,5} Moreover, centrally located liver metastases are no longer a contraindication for liver surgery. In patients with a normal functioning liver, extended hemihepatectomies can be performed safely and mesohepatectomy or a central liver resection is an alternative for an extended hemihepatectomy when parenchymal loss needs to be minimized.⁶ If resectable extrahepatic metastases are present, a resection can be offered with 5-year overall survival rates up to 28%.^{6,7} Thus, liver resection criteria for colorectal cancer liver metastases (CRCLM) are at present only limited by an anticipated R0 status and an adequate functional liver remnant. Patients in good general health, with technically resectable metastatic disease limited to the liver, regional lymph nodes or/and lungs, are considered for resection regardless of associated clinical predictive factors.^{8–10}

Parallel to the expanding indications for a liver resection new strategies to improve resectability have also been popularized.^{11–13} A liver resection combined with ablation of metastases^{14–16} and/or induction chemotherapy to reduce the hepatic tumour size or tumour load may render unresectable metastases resectable or may help reduce the extent of liver resections.¹⁷ Staged resections, with or without portal vein embolization/ligation, can be used for a two-step clearance of liver metastases, to increase future remnant liver volume and to achieve a definitive R0 status.

Expanding the indications and application of the aforementioned strategies has increased the number of patients becoming resectable.¹⁸ The objective of the present study was to evaluate the post-operative clinical outcome and long-term survival in patients undergoing a liver resection for colorectal cancer liver metastases based on limited compared with extended indications.

Material and methods

Patients

A prospective database became operational in the Maastricht University Medical Centre HPB unit in 2001. All patients that underwent liver surgery before this date were included retrospectively. Patients undergoing liver surgery for CRCLM between 1991 and 2010 were included in the present study and assigned to a group with limited indication criteria or a group with extended indication criteria for resection. Patients were staged using a four-phase contrast enhanced abdominal CT scan. All patients with either primary or secondary liver tumours were discussed at a multidisciplinary liver meeting. Patient-specific co-morbidities and diagnostic procedures were assessed and the definitive treatment strategy was decided in consensus. Induction chemotherapy in irresectable patients, a liver resection combined with tumour ablation, pre-operative portal vein embolization, liver first policy in rectal cancer and a repeat hepatectomy were all among potential surgical strategies. Obviously some of these strategies became available only in more recent years. Vascular reconstructions were

Table 1 Indication criteria for resection of colorectal liver metastases

Limited indication criteria	Extended indication criteria
1. Three or less liver metastases	1. Four or more liver metastases
2. Located at one side of liver only	2. Bilateral metastases
3. No signs of extra hepatic metastases	3. Presence of resectable extra hepatic metastases
4. Anticipated resection margin more than 10 mm.	4. Centrally located metastases

occasionally used. In recent years, patients not undergoing liver surgery were assigned to stereotactic radiotherapy, percutaneous tumour ablation, Y⁹⁰- selective internal radiotherapy or palliative chemotherapy.

Study groups

Pre-operative CT-, MRI- or PET-CT-scans were used to determine the number and location of liver metastases. Operation notes gave insight in the specific type of resection, relation of metastases to the transection line, duration of surgery, the amount of blood loss and complications during surgery. Patients were, using predefined criteria, retrospectively assigned to either the extended indications group or to the limited indications group. Criteria for limited and extended indications are depicted in Table 1. Only patients with colorectal cancer liver metastases and a follow-up of at least 6 months were included in the present study.

Liver resections

All liver resections were classified in accordance with the IHPBA Brisbane nomenclature (Table 2).¹⁹ A liver resection was performed as described previously.²⁰ To determine the definitive extent of hepatic metastases and transection line, intra-operative ultrasound was used routinely.

Peri-operative care

In February 2005, the Enhanced Recovery After Surgery (ERAS®) fast track peri-operative care programme was introduced in liver surgery at our centre. This programme enhances post-operative recovery and as a consequence reduces hospital length of stay (LOS).²¹ Before the introduction of the ERAS programme there was no standard peri-operative care protocol.

Oncological follow-up

Follow-up consisted of outpatient visits with plasma carcinoembryonic antigen levels, every 3 months, and liver imaging twice in the first 2 years and annually up to 5 years after surgery. The median follow-up was 33 months (range, 0–235). In case of recurrence, patients were assessed with PET-CT and the indication for repeat liver or lung surgery was discussed in the multidisciplinary oncology meeting.

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