



Curative-intent treatment of recurrent colorectal liver metastases: A comparison between ablation and resection

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Abstract

Background: Liver-limited recurrence after resection of colorectal liver metastases is a frequent occurrence, and can in some cases be treated with curative intent. Although surgical re-resection remains standard of care, there is growing interest in the role of ablation in this setting. The aim of this study was to compare the outcomes after curative-intent ablation and resection in patients with recurrent colorectal liver metastases.

Methods: We retrospectively analysed data from 366 consecutive patients who underwent liver resection for colorectal liver metastases between June 2010 and August 2015. Sixty-four developed liver-limited recurrence which was treated with curative intent, thirty-three (51.6%) by ablation and 31 (48.4%) by repeat resection.

Results: Patient groups were well matched, with surgically resected patients showing higher pre-operative carcinoembryonic antigen levels and larger metastases. There were fewer post-operative complications and shorter length of stay in the ablation group ($p < 0.02$). After a median follow-up of 36.2 months, median overall survival was the same for both the resected and ablated groups at 33.3 months. Median progression-free survival was longer for patients treated with surgery (10.2 months) compared to ablation (4.3 months) ($p = 0.002$).

Conclusions: Ablation or resection for liver-limited recurrence after surgery for colorectal liver metastases is associated with improved overall survival compared with systemic chemotherapy alone, and should always be considered for patients with resectable liver recurrence. Although ablation seemed to be associated with a shorter progression-free survival, post-procedure morbidity was significantly lower. The choice between ablation and resection should therefore be made on a personalised basis.

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Keywords: Colorectal liver metastases; Ablation; Liver surgery; Hepatectomy; Recurrence

Introduction

Liver surgery remains the only potentially curative treatment for colorectal liver metastases (CLM). Thanks to contemporary multimodal treatment, 5-year overall survival (OS) rates of up to 51% have been reported after resection [1]. However, around 75% of patients will develop disease recurrence within 2 years [2], and nearly 40% will require repeat surgery [1]. In case of liver-limited recurrence, repeat resection appears to offer a comparable survival

benefit to primary liver resection, with median OS rates ranging from 31.9 to 87 months and 5-year OS after re-resection of up to 67% [3–8].

Locoregional ablative strategies delivered either intraoperatively or percutaneously have also been used for the treatment of CLM and can be combined with liver resection to enable curative-intent treatment [9]. Five-year overall survival rates of up to 50% have been reported in selected groups after ablation for resectable disease [10], but the quality of evidence is low and so surgical resection remains the standard of care [11]. However, in the context of intrahepatic recurrence after resection, ablation may offer theoretical advantages in difficult local conditions [12], such as extended adhesions

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related to previous laparotomies or major post-operative complications following the primary liver or colonic resection [13]. In addition, there remains concern that post-surgery liver regeneration may also accelerate the progression of occult disease, something that could be avoided by ablation.

The aim of this study was therefore to compare the outcomes of patients with intrahepatic recurrence after an earlier liver resection, treated with either ablation or further resection.

Patients and methods

Patient selection

We retrospectively analysed data from a prospectively maintained database of all patients undergoing liver resection for CLM at a large tertiary hepatobiliary unit between June 2010 and August 2015. All patients identified during routine follow up as having recurrence were re-discussed at a specialist hepato-biliary multidisciplinary team (MDT) meeting attended by surgeons, oncologists and interventional radiologists. All patients with recurrence had a triple phase computed tomography (CT) chest, abdomen and pelvis, a diffusion-weighted liver magnetic resonance imaging (MRI) and a positron emission tomography-CT scan, unless absolute contra-indications existed. Patients with liver-limited recurrence treated with further resection and/or ablation were included for subsequent analysis. If ablation or resection were both considered technically feasible but no consensus was reached at MDT, the final decision was made at surgical hepatobiliary clinic by the patient in consultation with a hepatobiliary surgeon. Patients were excluded from analysis if they had unresectable extra hepatic disease (EHD), or if the treatment of the recurrence was planned but not yet performed when the analysis was completed.

Procedures

All repeat resections and intraoperative ablations were performed through a reverse L-shaped laparotomy. Intraoperative ultrasound was routinely performed for staging and to guide surgical resection or ablation. A parenchymal preserving approach was performed whenever possible and use of intermittent Pringle manoeuvre was at the discretion of the operating surgeon. Liver parenchyma was transected with the Cavitron ultrasonic surgical aspirator (Valleylab, Boulder, CO). Intraoperative ablation technique was always microwave ablation (MWA) with standard energy delivery of 100 W for 90 s per lesion. For percutaneous approach, RFA and MWA were used at the discretion of the interventional radiologist. Irreversible electroporation was only used in case of CLM in contact with major vessels that would preclude other ablation techniques. Percutaneous ablations were ultrasound or CT-scan guided, depending on the echogenicity of the target lesions. Patients treated with an open approach were managed post-operatively within an enhanced recovery program [14].

Follow-up

Postoperative 90-day morbidity and mortality were recorded, and postoperative complications were graded using the Dindo classification [15]. Follow-up included regular outpatient visits with the first scheduled at one month (with a contrast CT-scan for patients treated with ablation), followed by every three months for the first year, and every six months thereafter. All follow up visits included physical examination, carcinoembryonic antigen (CEA) measurements and contrast CT-scans of chest abdomen and pelvis. Margin recurrence was defined as radiological evidence of recurrence at the resection margin and/or the ablation site, whilst intrahepatic recurrence was defined as evidence of disease recurrence elsewhere within the liver substance.

Statistical analysis

The patients were divided into two groups: those who had an ablation only (Group A) and those who had a liver resection (Group S).

Demographic, preoperative and surgical data from the two groups were compared using Fisher's exact test for categorical variables and a non-parametric Mann-Whitney *U* test for continuous variables. Overall survival was calculated from the date of liver-directed treatment of the recurrence to the date of death from any cause or date of the last follow-up (censored observation). Progression-free survival (PFS) and hepatic PFS were measured from the date of liver-directed treatment to the time of disease progression (or hepatic disease progression for hepatic PFS) or death, or was censored at the last follow-up. Survival estimates were calculated using the Kaplan–Meier method. Differences in survival between groups were assessed by log-rank test. Median follow-up was calculated using a reverse Kaplan–Meier estimate. All variables associated with PFS or OS on univariate analysis with p value < 0.10 were included in a multivariate cox proportional hazard model. A p value ≤ 0.05 was considered statistically significant. All analyses were performed with EZR software [16].

Results

Patient characteristics and perioperative data

Between June 2010 and August 2015, 366 patients underwent liver resection for CLM. Of those, 267 (72.9%) developed recurrence. The majority (176, 65.9%) were treated with palliative intent due to unresectable disease and received chemotherapy, except 18 patients (10.2%) who received best supportive care. Six patients also had radiotherapy and 8 patients had intra-hepatic chemotherapy. The number of patients with unresectable liver-limited, lung-limited, liver plus lung, and widespread recurrence was 27 (15.3%), 29 (16.5%), 20 (11.4%) and 78 (44.3%), respectively. Sixty-four patients developed liver-limited

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