

ORIGINAL ARTICLE

Case-controlled study comparing peri-operative and cancer-related outcomes after major hepatectomy and parenchymal sparing hepatectomy for metastatic colorectal cancer

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Abstract

Introduction: Liver resection is potentially curative in selected patients with colorectal liver metastases (CLM). There has been a trend towards parenchyma sparing hepatectomy (PSH) rather than major hepatectomy (MH) due to lower perioperative morbidity. Although data from retrospective series suggest that long-term survival after PSM are similar to MH, these reports may be subject to selection bias. The aim of this study was to compare outcomes of PSH and MH in a case-controlled study.

Patients and methods: 917 consecutive patients who underwent liver resection for CLM during 2000–2010 were identified from a prospective database. 238 patients who underwent PSH were case-matched with 238 patients who had MH, for age, gender, tumour number, maximum tumour diameter, primary Dukes' stage, synchronicity and chemotherapy status using a propensity scoring system. Peri-operative outcomes, recurrence and long-term survival were compared.

Results: Fewer PSH patients received peri-operative blood transfusions ($p < 0.0001$). MH patients had greater incidence of complications ($p = 0.04$), grade III/IV complications ($p = 0.01$) and 90-day mortality ($p = 0.03$). Hospital stay was greater in the MH group ($p = 0.04$). There was no difference in overall/disease-free survival.

Conclusion: Patients with resectable CLM should be offered PSH if technically feasible. PSH is safer than MH without compromising long-term survival.

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Introduction

Colorectal cancer is the second commonest cause of cancer-related death in the western world, and more than half of patients will develop metastatic disease, frequently limited to the liver.^{1,2} Without treatment, the prognosis of patients with colorectal cancer liver metastases (CLM) is dismal. For selected patients with CLM, long-term survival and even cure has become feasible due to advances in liver surgical techniques and availability of effective chemotherapeutic agents.^{1–3} In recent years, there has been a trend in favour of parenchymal-sparing hepatectomy (PSH) over major hepatectomy (MH) for patients with resectable liver-only disease.^{4,5} Early reports indicated that PSH was associated with higher positive margin rates and worse long-

term survival compared to MH.^{6–8} These differences were not observed in several recent series,^{1,9} including a meta-analysis of 1662 patients.⁵ Due to the retrospective, uncontrolled nature of these studies, it is feasible that any differences in oncological results between PSH and MH may have been concealed by selection bias.¹⁰ Risk factors for disease recurrence after resection of CLM, such as tumour size and number, use of perioperative chemotherapy, perioperative blood transfusion and post-operative complications,^{1,2,5,11} must be taken into account when evaluating the relative merits of PSH and MH. Our aim was to perform a case-controlled analysis of the outcomes of patients undergoing parenchymal-sparing or major hepatectomy for colorectal liver metastases in a single high volume institution.

Patients and methods

This was a case controlled comparison analysis of prospectively collected data over an eleven year period (January 2000 to December 2010). All consecutive patients who underwent liver resection for CLM during the study period were identified ($n = 917$, Table 1). Data were anonymous according to the ethical standards of the *Medical Research Council Good Clinical Practice in Clinical Trials*.¹²

Patients were grouped according to type of liver resection; those who had major hepatectomies (MH, $n = 634$) and those who had parenchymal sparing hepatectomy (PSH, $n = 283$). At the time of surgery, patients were selected for MH or PSH according to the surgeon's preference. MH were defined as liver resections removing ≥ 3 segments, and PSH had fewer than 3 segments removed. Patients receiving PSH were 1:1 matched to MH on a case by case basis using a propensity scoring system,¹³ which was guided by a statistician (JH).

Patients were included if they potentially could have undergone either MH or PSH on review of the preoperative imaging. Exclusion criteria included patients with small isolated peripheral lesions, left lateral segmentectomies, portal vein embolisations, and patients who underwent radiofrequency ablation.

Table 1 All available cases prior to matching

	Major hepatectomy ($n = 634$)	Parenchymal sparing hepatectomy ($n = 283$)
Gender ratio M:F	1.7:1	1.8:1
Mean age/years (range, SD)	67 (21–86, 2.02)	67 (31–87, 1.90)
Chemotherapy		
Yes (%)	401 (63.3)	170 (60.1)
No (%)	233 (36.8)	113 (39.9)
Number of CLM/n (%)		
Single metastasis	382 (60.3)	190 (67.1)
2 metastases	124 (19.6)	57 (20.1)
3 metastases	78 (12.3)	16 (5.7)
4 metastases	34 (5.4)	12 (4.2)
>4 metastases	16 (2.5)	8 (2.8)
Mean maximum tumour diameter/mm (range, SD)	4.7 (0.1–20, 3.46)	3.2 (0.5–14, 1.90)
Primary tumour Dukes' Stage (%)		
A	14 (2.2)	13 (4.6)
B	147 (23.2)	65 (23.0)
C	398 (62.8)	193 (68.2)
D	2 (0.3)	1 (0.4)
Synchronous metastases/n (%)	41 (6.5)	18 (6.4)

SD = Standard deviation.

Furthermore, patients with large lesions that could not have undergone PSH safely were also excluded. Therefore, 238 PSH patients were included in the study.

The factors used in the matching were age, gender, tumour number, maximum tumour diameter, primary Dukes' stage, cancer involved resection margins, synchronous metastases and chemotherapy status (238 patients in each group). Age matches were within ± 2 years, whilst the dichotomous variables (e.g. gender) were matched exactly. Where a PSH patient could potentially be paired with multiple MH patients, the match whose date of surgery was closest chronologically was used.

The pre-operative imaging of patients who underwent MH were reviewed and those who were potentially eligible for parenchymal-sparing resection were included in the matching process. Standardised differences were calculated for each matched variable, to determine the quality of matching.¹⁴ A standardised difference of <0.1 was deemed to be indicative of a closely matched variable.¹⁴

Parenchymal sparing resections were undertaken in a non-anatomical fashion, with the objective of achieving negative margins. Nine of the PSH patients had a laparoscopic resection.

Data included patients' demographics, peri-operative blood transfusions, peri-operative complications, 30-day, 90-day and hospital mortality, lengths of critical care (intensive care or high dependency) and hospital stays, resection margin status, hepatic insufficiency (defined by the International Study Group of Liver Surgery),¹⁵ neo-adjuvant chemotherapy, disease free survival (DFS) and overall survival (OS). Cancer involved resection margins (R1) were defined as <1 mm. Peri-operative complications were graded according to the Clavien classification.¹⁶ Post-operative mortality was defined as death in hospital or within 90 days of surgery. DFS and OS were defined from the date of index liver resection to the date of first recurrence, death or latest follow up appointment. Patients were followed up six monthly for the first 3 years, and once a year thereafter. Patients underwent redo liver resections if the disease was technically resectable and the patient was deemed fit and willing for further surgery.

Statistical analyses were performed using SPSS (version 21). Continuous data was reported as means and SD with p values from Paired T tests, and categorical data reported as percentages and p values from McNemar or Fishers exact tests. Survival curves were constructed using the Kaplan–Meier technique with log-rank tests used to compare between groups. Recurrence and death were considered time-to-event end points in the Kaplan–Meier analysis. Odds ratios (OR) and 95% confidence intervals (CI) were estimated and $p < 0.05$ was considered to be statistically significant throughout.

All clinically relevant variables were included in a multivariable cox regression model, alongside the type of surgery, in order to account for potentially confounding factors for the entire cohort prior to matching. All statistical analyses were guided by our specialist statistician (Mr James Hodson).

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