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ORIGINAL ARTICLE

Combined hepatectomy and hepatic pedicle lymphadenectomy in colorectal liver metastases is justified

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Abstract

Background: The aim of this study was to describe the outcome of patients with colorectal liver metastases (CRLM) and radiological or clinical evidence of metastatic hepatic lymph node involvement who underwent combined hepatectomy and hepatic pedicle lymphadenectomy.

Methods: Retrospective analysis of a prospectively maintained audit of 2082 patients undergoing liver resection for CRLM between 1994 and 2014. Age, type of resection, CT/MRI/PET detection, location, disease recurrence and survival were analysed.

Results: Combined hepatectomy and hepatic pedicle lymphadenopathy was performed on 76 patients who met the inclusion criteria. 46% of enlarged lymph nodes were located in the hepatic ligament, with 38% retroportal, 38% common hepatic and 33% coeliac nodes. 50% of lymph node resections were positive for metastatic tumour. Pre-operative CT, MRI and CT/PET failed to detect histologically proven lymph node disease in 25/38 patients. Patients with negative nodal histology had a significant overall (44 vs 20 months, $p = 0.008$) and disease free (20 vs 11 months, $p < 0.001$) survival advantage.

Conclusion: Combined hepatectomy and lymph node resection for CRLM in the setting of enlarged or suspicious lymphadenopathy is justified as imaging and operative findings are poor guides in determining positive lymph node disease.

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Introduction

Liver resection for isolated colorectal metastases is well recognised as the gold standard of care with excellent long term outcomes with five year survival rates >50% now commonplace.[1,2] The frontier for the treatment of colorectal metastases is now expanding to treating patients with additional extrahepatic metastases, the most prevalent of these being lung metastases which are also amenable to resection.[2] The role of liver resection with extrahepatic lymph node (LN) disease in the hepatic pedicle continues to be debated.[3–5] It appears the therapeutic value of routine lymphadenectomy is low if not non-existent, but there could be a good argument for lymphadenectomy for staging purposes as many micrometastases are missed by imaging and intra-operative assessment.[5,6] The pattern of LN involvement in the hepatic pedicle is not consistent, however, and skipped LN appear to be common, necessitating thorough LN clearance which has not yet become common practice.[7,8]

The other clinical question raised is what to do with enlarged or suspicious LN detected on radiological imaging or intra-operative assessment. Results over the last 20 years have consistently shown poor survival and have led to some suggesting that LN involvement should be a contraindication to liver resection. However not all enlarged or suspicious LN are positive on histology.[9] Median survival for metastatic colorectal cancer without hepatectomy is now up to 24 months,[10] and it remains to be answered if chemotherapy can add further

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gains to patients undergoing hepatectomy and hepatic pedicle lymphadenectomy.

The aim of this study was to assess the outcome of patients undergoing combined hepatectomy and LN resection in the setting of clinically enlarged or suspicious LN within the liver's main lymphatic drainage.

Methods

All patients undergoing liver resection for colorectal metastases at St James's University Hospital, Leeds, UK between the 1st of January 1994 and the 31st of December 2014 were entered into a prospectively maintained database. Data recorded included gender, date of operation, age at operation, type of resection, lymph node group (hepatoduodenal ligament, retroportal, common hepatic, coeliac or para-aortic adjacent to coeliac), R status of resection (R1 < 1 mm clearance of hepatic disease), and number of tumours.

Medical records were sourced for pre-operative reports of CT, MRI and PET scans. PET scans were used only in the last 10 years of the study and only when there was increased suspicion of extrahepatic disease. Lymph nodes were defined as enlarged if described as enlarged or suspicious by the reporting radiologists, typically if >1 cm in size, or increased uptake of FDG (PET). Suspicious lymph nodes were defined by individual surgeons at their discretion, typically if either enlarged, firm or tethered to surrounding structures. Lymph nodes with extranodal extension into main structures (such as hepatic arteries or bile ducts) precluded resection. Lymph node resection was not standardised and was performed according to individual surgeon's preferences, either with en bloc resection of lymph node zones or resection of individual nodes. All specimens were reviewed by pathologists with experience in HPB pathology.

Post-operatively, all patients were entered into an intense surveillance programme with LFT, CEA, CA19-9 and chest, abdominal and pelvis CT at 3, 6, 12, 18, 24 months then years 3, 4, 5, 7 and 10 and clinical exam and bloods at years 6, 8 and 9. Due to this intensive surveillance, all episodes of disease recurrence together with the outcome were recorded.

Survival data up to 30/6/2016 including causes of death were obtained from hospital records and by cross referencing this data with that held by the Northern and Yorkshire Cancer Registry Information Service.

Statistical analysis was performed using SPSS (IBM, New York, USA). Statistical significance was calculated using the log rank (Mantel–Cox) method and Fisher's exact test where appropriate. A p-value of <0.05 was considered statistically significant.

Results

Patient demographics

From the 1st of January 1994 until the 31st of December 2014 there were 2082 liver resections performed for colorectal liver metastases. From this cohort, 76 patients (4%) who had concomitant hepatic pedicle LN resection for enlarged or suspicious nodes were identified. There were no significant differences between those who underwent combined liver and nodal resection vs liver resection alone with regard to age, gender, number of tumours and R status (data not shown). In the LN excision group 38 (50%) patients were found to have positive histology. Demographics, tumour, operative characteristics, and detection on radiological imaging by nodal histology are shown in Table 1.

Disease-free and overall survival

The median (range) followup was 28 (0–214) months. At the end of the study period, 15 (20%) patients were alive with no disease, 7 (9%) were alive with disease and 54 (71%) had died. The LN excision group had a significantly worse disease free survival compared to the total population of patients undergoing hepatic resection for CRLM as shown in Fig. 1 with 1-year, 3-year

Table 1 Demographics of patients who underwent concomitant LN resection with either positive or negative histology

Variable	Histology negative	Histology positive	Significance
Number of patients	38	38	p = ns
Age, median (range)	60 (25–80)	63 (36–83)	p = ns
Gender			
Male	23	19	p = ns
Number of tumours, median (range)	2 (1–7)	3 (1–10)	p = ns
R status			p = ns
R0	25	21	
R1	12	15	
R2	1	2	
Type of resection			p = ns
Minor liver resection (<3 segments)	15	15	
Major liver resection (≥3 segments)	23	23	
Radiologically enlarged/suspicious LN			
CT	2/37	7/38	p = 0.153
MRI	5/35	13/36	p = 0.055
PET	0/7	4/4	p < 0.003
LN region			p = ns
Hepatoduodenal ligament	16	17	
Retroportal	7	12	
Common hepatic artery	10	18	
Coeliac	16	8	
Para-aortic (at level of coeliac)	2	2	

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