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Ten years experience of managing the primary tumours in patients with stage IV colorectal cancers

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ABSTRACT

Introduction: Approximately 20% of patients with colorectal cancer have metastases at the time of presentation. Such patients are often offered systemic chemotherapy but debate continues as to whether these patients benefit from resection of the primary tumour. We describe our ten years experience of managing the primary tumours in patients with stage IV colorectal cancer. The aim of this study was to describe the overall survival of patients undergoing surgery in these circumstances and to determine whether any prognostic indicators could be identified.

Patients & methods: 920 consecutive patients presenting with stage IV colorectal cancer disease were identified from the Leicester Colorectal Cancer database. Patients undergoing resection of the primary tumour (Resection Group) with the residual metastatic disease were compared to those patients who had not their primary tumour excised (Non-Resection Group). Various different variables in two groups were compared by using Mann-Whitney U test. Kaplan–Meier survival analysis and log-rank test were used to compare the overall survivals. Univariate analysis was performed for each group to elicit the significant prognostic factors whereas Cox regression model was used to identify the independent predictors of overall survival.

Results: The Kaplan–Meier survival analysis of two groups showed prolonged survival for Resection Group compared to the Non-Resection Group (median; 14.5 Vs 5.83 months, $p = <0.005$). The multivariate analysis of different survival predicting variables, revealed the resection of the primary tumour as an independent predictor of overall survival ($p < 0.001$). The univariate analysis of resection group identified age at presentation, tumour site, tumour stage (pT), lymph nodal stage (pN), complete histological resection, tumour fixity, ASA grade, mode of surgery, post-operative chemotherapy and sites of metastasis as significant factors ($p < 0.05$) for survival prediction. When these factors were used in Cox-Regression model, only the age at presentation ($p = 0.001$), tumour fixity ($p = 0.012$) and lymph nodal involvement ($p = 0.042$) were independent predictors for overall survival. Treatment with post-operative chemotherapy and a smaller volume of liver metastases were associated with prolonged survival ($p < 0.05$).

Conclusions: Surgical resection of primary tumour for stage IV colorectal cancers is associated with prolonged survival for selected patients. Age at presentation, extent of liver involvement, tumour fixity and ASA grade can help to decide the patients who will benefit from surgery.

1. Introduction

Colorectal cancer (CRC) is the third most common malignant neoplasm worldwide[1] and the fourth leading cause of cancer-related deaths worldwide (World Health Organization, 2008). It is a significant health problem in the UK, accounting for 28.3 deaths per 100,000 in men and 24.2 deaths per 100,000 in women in 2007.[2] Around 100 new cases of colorectal cancer are diagnosed each day in the UK; around two-thirds in the colon and one-third in the rectum. The survival and prognosis of CRC depends on the stage of the tumour at the time of detection and unfortunately more than 20% of patients with cancer have distant spread of their disease (stage IV) at the time of diagnosis.[3,4] Despite significant investment and advances in the management of cancer, the overall survival for

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Table 1
Comparison of demographics, clinical and tumour characteristics of patients in the colorectal cancer Resection and Non-Resection Groups.

Demographics	Characteristics	Resection *n* (%)	Non-resection *n* (%)	*p*-values
Patient (*n*)	Number of patients	366	281	NS
Age	Median (range) years	70 (27–92)	72 (31–96)	NS
Gender	Male	198 (54.1)	219 (78.0)	<0.05
	Female	168 (45.9)	62 (22.0)	
Site of tumour	Right colonic	144 (39.3)	65 (23.2)	<0.05
	Left colonic	114 (31.1)	97 (34.5)	
	Rectal	108 (29.5)	119 (42.3)	
Tumour fixity	Fixed	34 (9.2)	25 (8.9)	<0.05
	Mobile	135 (36.9)	02 (0.7)	
	Tethered	73 (19.9)	09 (3.2)	
	Unknown	124 (33.9)	245 (87.1)	
Detection of metastasis	Radiology imaging	232 (63.4)	242 (86.1)	<0.05
	Radiology imaging & histology	10 (2.7)	11 (3.9)	
	Radiology imaging & surgery	16 (4.4)	05 (1.8)	
	Surgery ± histology	108 (29.5)	23 (8.2)	
Distant metastasis site	Liver – solitary	55 (15.0)	12 (4.8)	<0.05
	Liver – multiple unilobar	56 (15.3)	13 (4.6)	
	Liver – multiple unilobar and lungs	05 (1.4)	02 (0.7)	
	Liver – multiple bi-lobar	130 (35.5)	111 (39.5)	
	Liver – multiple bilobar and lungs	16 (4.4)	42 (14.9)	
	Multi-organ excluding lungs	19 (5.2)	15 (5.3)	
	Lungs only	12 (3.8)	20 (7.1)	
	Peritoneal spread	49 (13.4)	44 (15.6)	
	Extra-mesenteric lymph nodes	37 (10.1)	13 (4.6)	
Oncology treatment	Radiotherapy	20 (5.5)[a]	25 (8.9)	NS
	Chemotherapy	21 (5.7)[b]	101 (35.9)	<0.05
		231 (63.1)[c]		
ASA score	ASA – II	213 (58.2)	47 (16.7)	<0.05
	ASA – III	101 (27.6)	37 (13.2)	
	ASA – IV	19 (5.2)	12 (4.3)	
	Unknown	33 (9.0)	185 (65.8)	
Mode of surgery	Urgent	112 (30.6)	N/A	N/A
	Not recorded	14 (3.8)		
	Routine	240 (66.5)		

[a] Pre-operative radiotherapy.
[b] Pre-operative chemotherapy.
[c] Post-operative chemotherapy.

advanced and metastatic disease has changed little over the past 20 years with 5-year survival at almost 90% for stage I cancers to 5%–15% for stage IV disease.[2,5,6] Approximately 10–25% of patients with stage IV cancer present with metastatic disease that can be resected surgically.[7] Such low rates of resectability are attributed to the heterogeneous nature of metastasis, severity of presenting symptoms, general health of persons and well-defined indications for resection of metastasis in liver and lungs.[8,9] The management of patients with stage IV colorectal cancer is a matter of ongoing controversy, which is further complicated by the introduction of effective chemotherapy and targeted therapy regimens that have been proven to result in resectable metastatic disease in many patients. This paper aims to describe the outcomes of such surgery in a population of patients presenting with metastatic (stage IV) colorectal cancers. To help in the decision making process for individual patients, this study aims to identify different variables predicting overall survival for patients undergoing resection of their primary tumours without the resection of their metastases.

2. Patients & methods

The University Hospitals of Leicester (UHL) Colorectal Cancer Database, a prospective audit of patient outcomes, was examined for all patients diagnosed with stage IV colorectal cancer at presentation between January 1998 and December 2007.

Table 2
Comparison of mean and median survivals of Resection and Non-Resection Groups.

Operation	Mean survival time (months)				Median survival time (months)			
	Survival (months)	Std. error	95% Confidence interval		Survival (months)	Std. error	95% Confidence interval	
			Lower bound	Upper bound			Lower bound	Upper bound
Resection	24.6	1.780	21.05	28.11	14.53	0.77	13.01	16.06
Non-Resection	9.3	0.56	8.52	10.37	5.83	0.55	4.74	6.92
Overall	21.5	1.50	18.55	24.41	12.400	0.801	10.82	13.98