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Original research

## The impact of primary tumor resection on overall survival in patients with colorectal carcinoma and unresectable distant metastases: A prospective cohort study



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#### A R T I C L E I N F O

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### ABSTRACT

*Background:* To compare the patients with primary colorectal carcinoma (CRC) and non-resectable distant metastases with or without primary colorectal tumor resection as a primary treatment in terms of postoperative mortality and overall survival (OS).

*Patients and methods:* The clinicopathological data of 188 CRC patients with non-resectable distant metastases was analyzed. All patient data were collected prospectively. Colorectal tumor was resected in 121 patients (64.3%). Kaplan—Meier method was used for calculation and plotting of the OS curves of the patient groups, and log-rank test was used for the comparison of the survival curves. The relative importance of the prognostic features was investigated using the Cox proportional hazards model.

*Results:* In the whole series and in the patient group undergoing emergency surgical intervention, mortality rate was lower in patients having colorectal tumor resection compared with non-resected patients, with differences approaching the significance level (p = 0.072 and p = 0.076, respectively). Median OS time was significantly longer in resection group (11.0 months), compared with non-resection group (5.5 months) (p < 0.001); in the multivariate Cox analysis colorectal tumor resection had independent prognostic significance (p < 0.001).

*Conclusion:* Resection of colorectal tumor in primary CRC patients with non-resectable distant metastasis gives significant survival advantage without increasing postoperative mortality compared with non-resection.

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#### 1. Introduction

Of patients with primary colorectal carcinoma (CRC), approximately 20% present with distant metastasis at the time of diagnosis [1–3]. Only 10–30% of patients with distant metastasis (stage IV disease according to American Joint Committee on Cancer (AJCC)/ International Union Against Cancer (UICC) tumor (T)- node (N)- metastasis (M) classification) [4] can have potentially curative resection of the primary carcinoma and the distant metastasis [5–8]. Currently, a palliative resection of the primary colorectal tumor before initiation of systemic therapy is frequently performed [2–9]. There are different approaches regarding the resection of the primary CRC in patients with non-resectable distant metastases and asymptomatic or minimally symptomatic colorectal tumor, without complications requiring urgent surgical intervention (obstruction, perforation, intractable bleeding). Some authors suggest that resection of colorectal tumor has advantages compared to non-resection, such as prolonging the survival [1,5,10–13], prevention of future complications related to the primary tumor [3,14,15], and psychological support to the patient [14]. Other authors suggest that this approach may have been correct in the past, but treatment with current chemotherapeutic (irinotecan, oxaliplatin) and biologic targeted therapy (bevacizumab, cetuximab) agents can provide similar or longer survival compared to colorectal tumor resection [1,7,15–17]; that in some patients distant metastases may turn out to be potentially curable by resection [15,18]; that the patient would be spared the morbidity and mortality associated with primary surgery [1,5,8]. Furthermore, they point that adjuvant therapy may be delayed or may not be applied as a result of surgery [3,8,17].

In this study, patients with primary CRC and non-resectable distant metastases with or without primary colorectal tumor

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resection as a primary treatment were compared in terms of postoperative mortality and overall survival (OS).

#### 2. Patients and methods

#### 2.1. Patients

Between January 1993 and December 2004, 1255 patients were operated for primary CRC, with no past or concurrent malignancy otherwise. Distant metastases were present in 208 (16.5%) of the patients. Sixteen patients who had potentially curative resection of the colorectal tumor and the distant metastases, and four patients who received preoperative chemotherapy were not included in the study. Thus, our series consisted of 188 patients with nonresectable distant metastases. Colorectal tumor was resected in 121 patients (64.3%) in the series depending on the intraoperative findings and the surgeon's preference (resection group: segmental colectomy, 74 patients; subtotal colectomy, 1 patient; low-anterior resection, 30 patients; abdominoperineal resection, 16 patients). No resection was performed in 67 patients (35.7%) (non-resection group: diverting stoma, 47 patients; enteric bypass, 11 patients; exploration only, 9 patients). Elective surgery was performed in 160 patients in the series who were either asymptomatic or had minor symptoms, while emergency surgery was performed in 28 patients who had symptoms requiring urgent surgical intervention (complete obstruction, 27 patients; perforation, 1 patient).

Of clinicopathological features, colorectal wall invasion and metastatic sites [M1a (metastasis confined to one organ or site). M1b (metastases in more than one organ/site or the peritoneum)] were grouped according to the TNM classification [4]. Metastatic sites were determined by preoperative imaging and intraoperative findings. Tumor size, wall invasion and lymph node status were determined by pathological examination in the resection group only. 5-fluorouracyl-based chemotherapy was used in all patients receiving adjuvant chemotherapy. Patients who received at least two cycles of chemotherapy were considered to have received adjuvant chemotherapy. All patient clinicopathological data were collected prospectively, taking advantage of the Oncology Clinic records of our hospital regarding adjuvant therapy. Survival data of the patients discharged from the hospital after surgery were collected by phone interviews with the patient or patient's relatives. All the patients died by reason of cancer.

Postoperative mortality was defined as death occurring in hospital or within 30 days. OS was defined as the period starting from the date of surgery until death. Patients with postoperative mortality were not included in the survival analysis.

#### 2.2. Statistics

The chi-square test was used to evaluate the differences between proportions and Student's *t*-test was used to evaluate the continuous data for comparisons of the clinicopathological features of the patient groups. Kaplan—Meier method was used for calculation and plotting of the OS curves of the patient groups, and logrank test was used for the comparison of the survival curves. The relative importance of the prognostic features was investigated using the Cox proportional hazards model. All comparisons were two-tailed. *p* values less than 0.05 were considered to be statistically significant. All statistical analyses were performed using SPSS version 17.0 (SPSS, Inc., Chicago, IL).

#### 3. Results

Table 1 presents clinicopathological and treatment features of the patients. Resection and non-resection groups were not

Clinicopathological and treatment features of the patients.

Feature	Resect	Resection group		Non-resection group	
	n	%	n	%	
Gender					0.149
Female	43	35.5	31	46.3	
Male	78	64.5	36	53.7	
Age, years					0.410
Mean		57.3		59.0	
Median		60.0		60.0	
Range	2	1-87		26-83	
Age, years					0.329
<70	99	81.8	50	74.6	
>70	22	18.2	17	25.4	
Tumor site					0.008
Colon	75	62.0	28	41.8	
Rectum	46	38.0	39	58.2	
Tumor size, cm					
≤5	53	43.8			
>5	68	56.2			
T stage					
T2-T3	13	10.7			
T4	108	89.3			
Nodal status	100	0010			
Negative	19	15.7			
Positive	102	84.3			
Histological type					0.284
Non-mucinous	109	90.1	56	83.6	0.201
Mucinous	12	9.9	11	16.4	
Distant metastasis	12	5.5		10.1	< 0.001
M1a	98	81.0	27	40.3	0.001
M1b	23	19.0	40	59.7	
Surgery	23	15.0	10	55.7	0.824
Elective	104	86.0	56	83.6	0.024
Urgent	104	14.0	11	16.4	
Adjuvant chemotherap		14.0		10.4	0.040
Yes	y 73	60.3	30	44.8	0.040
No	48	39.7	30	55.2	
Adjuvant radiotherapy	-10	33.7		JJ.2	0.439
Yes	21	17.4	8	11.9	0.435
No	100	82.6	° 59	88.1	
INU	100	02.0	29	00.1	

significantly different in terms of gender, age, histological type, emergent or elective surgery, and adjuvant radiotherapy. The rate of colon tumor (p = 0.008), M1a distant metastasis (p < 0.001), and adjuvant chemotherapy use (p = 0.040) was significantly higher in the resection group, compared with the non-resection group. Table 2 presents the organs/sites of distant metastasis. Distant metastasis was present in a single organ/site in 137 patients, multiple organs/sites in 51 patients.

Mortality developed in 24 (12.7%) patients. Table 3 presents the relationship between clinicopathological factors, surgical method and mortality. Mortality rate was higher in patients aged 70 years and above compared to patients under 70 years of age; the difference was near to the limit of significance (p = 0.058). In the whole series and in the patient group undergoing emergency surgical intervention, mortality rate was lower in patients having colorectal tumor resection compared with non-resected patients, with differences approaching the significance level (p = 0.072 and p = 0.076, respectively).

Median OS times according to clinicopathological and treatment features in the whole series are presented in Table 4. Median survival time was significantly longer in resection group (11.0 months), compared with non-resection group (5.5 months) (p < 0.001) (Fig. 1); in the multivariate Cox analysis colorectal tumor resection had independent prognostic significance (p < 0.001) (Table 5). Among 143 patients having elective surgery, median OS time was significantly longer in the resection group (95 patients, 11.0 months) compared with the non-resection group (48 patients, 6.0 Download English Version:

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