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Effect of bowel obstruction on stage IV colorectal cancer

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Abstract. Colorectal cancer (CRC) is the third most commonly diagnosed cancer worldwide, with a high mortality rate, particularly among patients with advanced-stage disease complicated by bowel obstruction. The present study aimed to investigate the value of different surgical procedures and potential predictors of survival for patients with stage IV CRC, with or without bowel obstruction. Between August, 1994 and December, 2005, a total of 2,950 CRC patients were diagnosed and treated at our hospital. Among these, 381 patients had stage IV disease and were divided into two groups according to the presence (n=295) or absence (n=86) of bowel obstruction. The clinical data of all the patients with stage IV CRC were retrospectively analyzed and all the patients were followed up. Our results demonstrated statistically significant differences in gender, radical resection, histological type, ascites, tumor location, peritoneal and liver metastases between the obstruction and non-obstruction groups. We also observed that hepatic metastases and radical resection were factors associated with prognosis according to the univariate and multivariate analyses. Furthermore, the mean/median survival time was 49.4/21.6 and 37.2/17.1 months in the non-obstruction and obstruction groups, respectively. In conclusion, obstruction was not found to be an independent indicator of survival for patients with stage IV CRC, with patients in the obstruction group exhibiting a worse overall survival compared to those in the non-obstruction group, whereas active radical surgery significantly improved the prognosis of patients with stage IV CRC.

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Introduction

Colorectal cancer (CRC) is the third most commonly diagnosed cancer worldwide. Despite advances in diagnosis and treatment, CRC mortality has remained unchanged over the last 50 years and prognosis is closely associated with the disease stage at the time of diagnosis (1), with a 5-year survival rate of only 8% in patients with stage IV CRC (2).

Several patients develop bowel obstruction, which is a well-recognized complication of advanced-stage CRC, with an incidence of 7-47% (3,4). Compared to those with non-obstructive CRC, the 5-year survival rate of patients with obstructive CRC was reported to be ~20% (5-7). In addition, certain factors are significantly different between the two groups, including peritoneal metastasis, histological grade and recurrence. As regards the treatment of patients with stage IV CRC, opinions vary widely. For patients with complications, surgical treatment is required. The development of modern technology enables the effective treatment of a number of asymptomatic or minimally symptomatic patients with stage IV CRC. The major aims of therapy are to prolong survival and maintain the quality of life. Asymptomatic patients may be treated without resection in order to avoid complications and the risk of perioperative morbidity (8,9). When compared to asymptomatic patients who underwent surgical resection, asymptomatic patients with distant metastasis who underwent resection exhibited no survival benefits (10). Kaufman *et al* (11) reported that patients receiving surgical resection, chemotherapy, or a combination of the two, had median survival times of 22, 15 and 30 months, respectively. In order to avoid local tumor complications and improve the chances of further treatment, some studies recommend palliative resection of the primary tumor in asymptomatic patients (12-14).

Table I. Analysis of demographic, patient and pathological characteristics in patients with colorectal cancer, with or without bowel obstruction (n=381).

Characteristics	Cases	Obstruction		P-value
		No	Yes	
Gender				0.003
Female	227	164	63	
Male	154	131	23	
Radical resection				0.005
No	180	128	52	
Yes	201	167	34	
Age (years)				0.165
<60	189	152	37	
≥60	192	143	49	
Family history				0.159
No	367	282	85	
Yes	14	13	1	
Blood transfusion				0.087
No	186	151	35	
Yes	195	144	51	
Histological type				<0.001
Villous adenocarcinoma	57	47	10	
Tubular adenocarcinoma	262	210	52	
Mucinous adenocarcinoma	39	30	9	
Signet ring cell tumor	23	8	15	
Ascites				<0.001
No	295	222	73	
Yes	86	41	45	
Tumor size (cm)				0.041
≤5	221	180	41	
>5	160	116	44	
Tumor location				<0.001
Colon	147	115	32	
Rectum	234	180	54	
Peritoneal metastasis				<0.001
No	331	279	52	
Yes	50	16	34	
Hepatic metastasis				<0.001
No	285	240	45	
Yes	96	55	41	
Histological differentiation				0.520
High	40	33	7	
Moderate	241	188	53	
Poor	100	74	26	

Although the effects of obstruction and surgery on survival were previously reported, the number of available studies investigating the factors of obstruction in patients with stage IV CRC in China is currently limited. Therefore, in the present study, we aimed to investigate bowel obstruction in patients with stage IV CRC and retrospectively analyze the clinicopathological characteristics and long-term outcomes for such patients.

Patients and methods

Study population. Between August, 1994 and December, 2005 a total of 2,950 patients were diagnosed with CRC and treated at the Sixth Affiliated Hospital of Sun Yat-sen University (Guangzhou, China). A total of 381 patients were diagnosed with stage IV CRC and were divided into two groups according

Table II. Univariate analysis of patients with stage IV colorectal cancer (n=381).

Variables	Overall survival rate (%)			P-value
	1-year	3-year	5-year	
Gender				0.194
Female	95.6	87.8	78.9	
Male	93.5	81.3	68.6	
Age (years)				0.235
<60	96.7	88.8	75.4	
≥60	98.3	83.8	71.5	
Family history				0.850
No	97.5	92.4	87.3	
Yes	48.6	20.8	20.8	
Histological type				0.796
Villous adenocarcinoma	81.3	43.8	13.5	
Tubular adenocarcinoma	96.5	90.8	82.9	
Mucinous adenocarcinoma	71.5	22.0	22.0	
Signet ring cell tumor	52.9	21.2	21.2	
Blood transfusion				0.373
No	96.2	86.8	75.1	
Yes	94.8	84.7	72.2	
Tumor size (cm)				0.362
≤5	95.4	87.8	76.8	
>5	94.4	82.2	69.5	
Tumor location				0.308
Colon	94.6	85.7	73.1	
Rectum	95.3	85.2	73.2	
Ascites				<0.001
No	96.6	91.1	82.2	
Yes	92.2	73.5	83.3	
Peritoneal metastasis				0.290
No	96.8	91.1	84.4	
Yes	90.5	65.5	41.7	
Hepatic metastasis				0.010
No	95.2	84.5	73.0	
Yes	95.2	82.9	64.5	
Radical resection				<0.001
No	93.9	84.2	72.3	
Yes	96.5	87.1	78.5	
Histological differentiation				0.630
High	67.6	16.5	16.5	
Moderate	94.6	84.6	73.4	
Poor	94.9	83.3	67.8	
Obstruction				0.044
No	96.9	90.7	84.3	
Yes	89.2	64.1	34.4	

to the presence (n=295) or absence (n=86) of obstruction. We retrospectively analyzed the clinicopathological characteristics of the CRC patients from a computerized database and the patients were divided into subgroups according to the recorded variables as follows: i) gender, age (<60 and ≥60 years) and family history; ii) tumor location (colon and rectum), tumor differentiation (well-, moderately and poorly differentiated adenocarcinoma) and tumor size (≤5 and >5 cm); iii) blood

Table III. Multivariate analysis of factors associated with survival in patients with stage IV colorectal cancer.

							95% CI for Exp(B)	
Factors	B	SE	Wald	df	Sig.	Exp(B)	Lower	Upper
Obstruction	0.262	0.152	2.953	1	0.086	1.299	0.964	1.752
Ascites	0.152	0.144	1.105	1	0.293	1.164	0.877	1.545
Hepatic metastasis	0.195	0.055	12.522	1	<0.001	1.215	1.091	1.354
Radical resection	0.693	0.110	39.976	1	<0.001	2.000	1.613	2.480

CI, confidence interval; SE, standard error; df, degrees of freedom; sig., significance.

transfusion, resection of the primary tumor, ascites, peritoneal metastasis and hepatic metastasis.

Statistical analysis. Patient survival was analyzed with the Kaplan-Meier method and the variables were compared using the log-rank test. A multivariate analysis of the patients was performed using the Cox proportional hazards model, which is mainly used in the analysis of survival data for investigating the association between patient survival and covariates (independent variables or predictors).

Results

Patients and tumor characteristics. The demographic, patient and pathological characteristics of CRC are summarized in Table I. The mean age of the patients was 58.18 years (range, 25-87 years) in the non-obstructive and 56.58 years (range, 19-87 years) in the obstructive CRC groups. The number of blood transfusions was similar between the two groups and there was no significant difference in survival rate between patients who received a blood transfusion and those who did not (P=0.373) (Table II). The overall survival rate was also compared by gender, family history of CRC, age, tumor size, tumor location, peritoneal metastasis, histological grade and histological type, but the differences were not found to be statistically significant (Table II).

Univariate and multivariate analysis of patients with stage IV CRC. The univariate prognostic factors in patients with stage IV CRC are summarized in Table II. Ascites (P<0.001), hepatic metastasis (P=0.010) and radical resection (P<0.001) were found to be associated with outcome in stage IV CRC. However, certain factors, including gender, age, family history, blood transfusion, histological grade and tumor location, were not found to affect survival. In the analysis of obstruction, the multivariate analysis demonstrated that obstruction, ascites, hepatic metastasis and radical resection were independent factors for the survival of patients with stage IV CRC (Table III).

Long-term outcomes. A comparison of the survival curves between the non-obstruction and obstruction groups is shown in Fig. 1. The mean/median survival time was 49.4/21.6 and 37.2/17.1 months in the non-obstruction and obstruction groups, respectively. In the colon, the mean/median survival time was 54.4/21.4 and 48.0/17.8 months in the non-obstruction and obstruction groups, respectively. The overall 3- and 5-year survival rates were 90.7 and 84.3% in the non-obstruction group, respectively, and 64.1 and 34.4% in the obstruction CRC group, respectively.

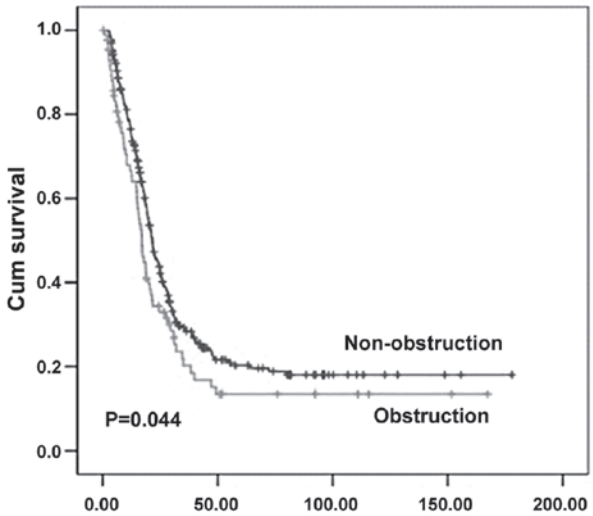

Figure 1. Survival curve for patients with stage IV obstructive and non-obstructive colorectal cancer. Cum, cumulative.

Discussion

It was recently reported that tumor size is associated with the prognosis of CRC (15), which was inconsistent with our results. The fact that the appropriate cut-off values and the dynamic point of the optimal cut-off values were not taken into consideration in this study, may explain the fact that we were unable to verify the prognostic significance of tumor size.

In agreement with previous findings (16), in our study, the survival of patients with radical resection was better compared to that of the patients who had undergone non-radical resection, indicating that complete tumor resection is associated with prognosis in patients with stage IV CRC. The total number of patients with non-obstructive CRC was 295 (~77.4%) and the survival of patients with obstructive CRC was poor. A previous study reported that patients aged <40 or >80 years were at an increased risk of developing bowel obstruction (17). However, our study demonstrated that the percentage of patients with obstructive CRC and advanced cancer did not statistically differ

between age groups. Similarly, the differences in survival did not approach statistical significance in the analysis by obstruction (Table III). However, obstructive CRC was associated with a poor prognosis and shorter overall survival according to the multivariate Cox regression model (Table III). This may due to the number of patients enrolled in this study. Similar conclusions were also reached by previous studies (18,19).

According to our results, the survival of CRC patients with bowel obstruction is significantly associated with radical resection, ascites and hepatic metastasis. The overall 1-, 3- and 5-year survival rates were lower in the obstructive compared to those in the non-obstructive CRC group. However, bowel obstruction was not found to be associated with a poorer prognosis or shorter overall survival in the multivariate Cox regression model, which was a finding inconsistent with previously reported results (20). In addition, intestinal obstruction may occur at any site along the colon and rectum, while the risk of obstruction varies across the intestine. In our study, 27 (31.3%) patients presented with bowel obstruction at the level of the rectum and 59 (68.6%) patients had obstruction of the colon. This result was similar to those of previous studies (21,22). In our study, the histological grade/type of CRC was not found to be an independent prognostic factor (Table II), which was different from previously reported findings (19). The difference observed in our study may be a result of the inconsistent grading criteria and grouping systems among different grades.

The presence of ascites was associated with prognosis in the analysis of obstruction and surgical treatment. Patients with ascites exhibited a significantly worse survival compared to those without ascites, which is consistent with previous findings (23). It is recommended that patients with ascites receive non-surgical treatment, such as hydration, corticosteroids and percutaneous gastrostomy (24). Moreover, the number of patients with hepatic metastases in our study was similar or higher compared to that reported by previous studies. This difference may be a result of the differences in tumor stage and histological type; for example, ulcerated tumors were reported to be associated with a higher metastatic risk (25).

There were some limitations to this study. The number of patients in our study was relatively small and, therefore, some factors associated with prognosis may have been overlooked. In addition, several factors were not investigated in this study, such as the levels of carcinoembryonic antigen and CA19-9, chemotherapy and perineural invasion. Furthermore, data regarding recurrence following surgery in patients with CRC were not available.

In conclusion, we demonstrated that certain prognostic factors may affect the outcome of patients with stage IV CRC, although obstruction was not found to be an independent indicator of survival. The patients with bowel obstruction had a poorer prognosis compared to those with non-obstructive CRC, whereas active radical surgery significantly improved the prognosis of patients with stage IV CRC.

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