

RAPID COMMUNICATION

## Prognostic factors of young patients with colon cancer after surgery

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### Abstract

**AIM:** To investigate the prognostic factors of 96 young patients with colon cancer within a cancer center by univariate and multivariate analysis.

**METHODS:** A total of 723 patients with colon cancer were treated surgically during a period of 10 years. Ninety six of them were 40 years old or younger. R0, R1 and R2 operations were performed in 69 (71.9%), 4 (4.1%) and 23 patients (24%), respectively. Left hemicolectomy was performed in 43 patients, right hemicolectomy in 37 patients, transverse colon resection in 9 patients and low anterior resection in 7 patients. Cox multivariate regression analysis was performed to identify predictors of survival.

**RESULTS:** The operation mortality was 0%, 54 patients died within 111 mo after operation due to occurrence or metastases of the tumor. Liver, lung and bone metastases occurred in 3, 1 and 5 patients, respectively. The mean survival time for all patients was  $77.9 \pm 5.01$  mo and the overall 3-, 5- and 10- year survival rates were 66.68%, 58.14% and 46.54%, respectively. In the univariate survival analysis, patient age, type of operation, radical resection, blood transfusion, histological type, diameter of tumor, depth of tumor invasion, lymphatic invasion, distant metastases, liver metastases and TNM stage were found to be predictors of survival in young patients with colon cancer. In the Cox-regression analysis, blood transfusion and lymphatic invasion were determined as independent prognostic factors of survival.

**CONCLUSIONS:** Age, type of operation, radical resection, blood transfusion, histological type, diameter of tumor, depth of tumor invasion, lymphatic

invasion, distant metastasis and TNM stage are the predictors of survival in young patients with colon cancer after surgery.

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**Key Words:** Prognosis; Colon cancer; Young patient; Surgery

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### INTRODUCTION

Colorectal cancer is one of the most common malignancies and nearly 600 000 cases are diagnosed annually worldwide [1]. Advances in the management of colon cancer over the past decades have resulted in improvement of the prognosis of this disease. The proportion of early stage (stages I and II) patients has increased from 39.6% to 56.6%, with a corresponding decrease in the proportion of patients with advanced stages, leading to an improvement in five-year relative survival from 33.0% in 1970s to 55.3% in 1990s [2]. The 5-year survival rate is around 60% [3].

Most of the patients with colon cancer are middle-aged or older and the peak of morbidity is around 65 years of age [2]. However, young patients are not rare and the incidence of colon cancer in young patients has increased gradually in recent years. We therefore analyzed retrospectively the clinical and pathological characteristics of a large cohort of colon cancer patients (40 years old or younger) treated in a cancer center over a 10-year period to investigate the prognostic factors.

### MATERIALS AND METHODS

#### Patients

A total of 723 patients with colon cancer were treated between January 1991 and January 2000. All the patients were surgically treated, diagnosed pathologically and included in follow-up procedure. Ninety-six (13.3%) were 40 years old or younger. The cancer was found in the ileocecal junction of 23 patients, in ascending colon of 19 patients, in hepatic flexure of 7 patients, in transverse colon of 11 patients, in splenic flexure of 4 patients, in descending colon

**Table 1** Prognostic factors of young patients with colon cancer after surgery

Items		Number of cases	AST(m)	3-YSR (%)	5-YSR (%)	10-YSR (%)	<i>t</i>	Degree of freedom	<i>P</i> value
Gender	Male	58	81 ± 6.42	69.92	61.35	45.30	0.46	1	0.499
	Female	38	73.62 ± 7.92	62.48	53.69	48.32			
Age	≤30	30	49 ± 5.47	52.50	47.73	47.73	2.4	1	0.0387
	30-40	66	82.74 ± 5.76	73.32	63.12	49.55			
Duration of symptoms (m)	≤1	15	34 ± 5.28	45	36	-	5.33	4	0.2553
	1-3	37	108 ± 30.25	77.04	67.56	40.04			
	3-6	25	69	60	60	50			
	6-12	5	71.80 ± 20.15	53.33	53.33	-			
	≥12	14	80.55 ± 12.34	78.57	56.25	56.25			
Operation	LHC	43	67 ± 1.95	97.14	60.43	10.34	9.43	3	0.0241
	RHC	37	78 ± 9.00	83.20	62.04	15.75			
	TCR	9	52 ± 20.99	85.71	42.86	0			
	LAR	7	37	66.67	0	0			
Radical resection	R0	69	98.2 ± 4.92	87.92	77.67	63.40	80.72	2	<0.01
	R1	4	32 ± 3.50	50	75	75			
	R2	23	24 ± 2.04	6.52	0	0			
Blood transfusion (mL)	0	60	85 ± 6.3	72.59	64.10	59.17	7.69	2	0.0214
	400	29	69 ± 8.7	61.29	54.08	38.93			
	≥800	7	31 ± 9.89	35.71	17.86	-			
Pathological type	WDAC	5	92.75 ± 15.80	100	75	-	21.69	6	0.0014
	MDAC	27	101.89 ± 7.20	88.09	83.68	75.32			
	PDAC	18	31 ± 3.09	37.50	31.25	-			
	PAC	4	58.75 ± 11.47	75	75	-			
	MAC	27	60 ± 24.73	67.73	46.95	31.30			
	SRCC	3	23.33 ± 5.39	0	0	0			
	Others	12	76 ± 15.11	58.33	58.33	58.33			
Diameter of tumor (cm)	≤4	16	101.19 ± 9.68	78.97	78.97	78.97	14.16	2	<0.001
	4-8	53	84.02 ± 6.25	76.79	61.93	48.38			
	≥8	27	31 ± 8.83	39.16	39.16	-			
T	T1	4	-	100	100	100	57.91	3	<0.001
	T2	10	111.5 ± 8.06	90	90	90			
	T3	58	108 ± 29.54	82.34	68.15	38.94			
	T4	24	24 ± 3.13	10.33	-	-			
N	N0	45	111.71 ± 3.93	95	91.72	78.62	51.40	2	<0.001
	N1	30	37 ± 2.42	51.85	34.90	29.08			
	N2	21	23 ± 2.86	28.57	19.05	-			
M	M0	75	94.59 ± 4.95	84.66	73.58	61.45	80.03	1	<0.001
	M1	21	24 ± 2.29	4.76	0	0			

AST: average survival time; 3-YSR: 3-year survival rate; 5-YSR: 5-year survival rate; 10-YSR: 10-year survival rate; LHC: left hemicolectomy; RHC: right hemicolectomy; TCR: transverse colon resection; WDAC: well-differentiated adenocarcinoma; MDAC: moderately-differentiated adenocarcinoma; PDAC: poorly-differentiated adenocarcinoma; PAC: papillary adenocarcinoma; MAC: mucinous adenocarcinoma; SRCC: signet-ring cell carcinoma

of 6 patients and in sigmoid colon of 26 patients. Stage III or IV disease was found in 54.2% of the patients, lymph node metastasis occurred in 53% of the patients, poorly-differentiated mucinous adenocarcinoma and/or signet-ring cell carcinoma were found in 48 patients (Table 1).

### Treatment methods

All patients received surgical treatment. Right hemicolectomy was performed in 37 patients, left hemicolectomy in 43 patients, transverse colon resection in 9 patients and low anterior resection in 7 patients. R0 (pathological radical resection of tumor) operation was performed in 69 patients (71.8%), R1 (positive microscopic margins) in 4 (4.2%) patients and R2 (gross tumor was seen at the resection margins) in 23 (24%) patients.

### Follow-up

All the patients were followed up through telephone, letter

or re-examination in outpatient department annually. The dead line of follow-up was up to January 2002. The longest follow-up time was 120 mo with an average period of 67.6 mo.

### Statistical analysis

All data were analyzed by SPSS 10.0 statistical software. Analysis of variance was used to determine significant differences in prognosis of patients. Cox multivariate regression analysis was performed to identify predictors of survival. Quantitative data were expressed as mean ± SD. Survival was analyzed using the Kaplan-Meier survival method. *P* < 0.05 was considered statistically significant.

## RESULTS

### Operative mortality

Operative procedure was carried out in all patients. No pa-

**Table 2** Multivariate analysis of prognosis of patients with colon cancer

	<b>B</b>	<b>SD</b>	<b>Wald</b>	<b>Exp (B)</b>	<b>P</b>
Gender	0.094	0.455	0.043	1.099	0.836
Age	0.280	0.396	0.502	0.756	0.479
Duration of symptoms	0.017	0.183	0.008	0.983	0.927
Operation	0.285	0.228	1.563	1.329	0.211
Radical resection	0.341	0.602	0.321	1.407	0.571
Blood transfusion	0.683	0.325	4.421	1.980	0.035
Pathological type	0.135	0.109	1.513	1.144	0.219
Diameter of tumor	0.233	0.445	0.274	0.792	0.601
Depth of tumor invasion	0.976	0.537	3.303	2.655	0.069
Lymph node metastasis	0.949	0.390	5.910	2.583	0.015
Distant metastasis	0.211	0.928	0.052	0.810	0.820
TNM	0.666	0.622	1.145	1.946	0.285
Liver metastasis	0.566	0.321	3.106	1.761	0.078

tient died within 30 d after operation, and 2 patients died within 3 mo after operation.

### Metastasis

A total of 54 patients died of recurrence and/or metastasis within 111 months after operation. Liver, lung and bone metastases were found during follow-up in 3, 1 and 5 patients, respectively.

### Survival

The average survival time of the 96 patients was  $77.90 \pm 5.01$  months. The 3-, 5- and 10-year survival rates were 66.68%, 58.14% and 46.54%, respectively. The average survival time for male and female patients was  $81.00 \pm 6.41$  months and  $73.62 \pm 7.92$  months, respectively. The 3-, 5- and 10-year survival rates were 69.92%, 61.35%, 45.5% for male patients respectively and 62.48%, 53.69%, 48.32% for female patients respectively ( $P = 0.499$ , Table 1).

### Results of univariate analysis

The prognostic factors of young patients with colon cancer are demonstrated in Table 1. Among them, age, operative procedures, perioperative blood transfusion, pathological staging, diameter of tumor, depth of tumor invasion, lymph node metastases, distant metastases and liver metastases had a significant impact on the prognosis of young patients with colon cancer.

### Results of multivariate analysis

Perioperative blood transfusion and lymph node metastases were the only independent factors of postoperative survival in young patients with colon cancer (Table 2).

## DISCUSSION

Colorectal cancer is a predominant disease of elderly. The risk of developing this disease increases with age, but is not unusual in young patients at the age of 40 years or under<sup>[1]</sup>. It was reported that the incidence of colon cancer

remains stable while rectal cancer incidence is decreased 11% in old patients, while the incidence of colon cancer is increased 17% and rectal cancer incidence is increased 75% in young patients<sup>[4]</sup>. A total of 723 patients with colon cancer were treated in our hospital in a 10-year period. Among them, 96 patients were under 40 years of age (13.3%). The incidence of colon cancer in young patients is higher than that of gastric cancer (4.9%)<sup>[3]</sup>. Only 3-4% and 1.6% of colorectal cancer patients in Europe and United States are 40 years old or younger<sup>[5-7]</sup>, but the proportion of young patients is 30% in a domestic report<sup>[5]</sup>. Hereditary colorectal tumors [hereditary nonpolyposis colorectal cancer (HNPCC), adenomatosis coli, and suspected HNPCC] occur in 38.4% of patients younger than 40 years old and in only 3.5% of individuals older than 55<sup>[8]</sup>. Thus, hereditary colorectal tumors are detected more often in young individuals demonstrating hereditary factors rather than dietary and life-style<sup>[9]</sup>.

It is generally believed that young patients with colorectal cancer have a worse survival rate. Reports from Europe demonstrate that the 5-year survival rate for patients (30 years old or younger) is only 25-30%<sup>[10, 11]</sup>. Young patients are more likely to present with late-stage disease. The young patients also have higher grade tumors<sup>[12]</sup>. About 60-67% of young patients with colorectal cancer have a later stage (III/IV) disease<sup>[11, 13]</sup>, most of which are poorly-differentiated or mucinous tumors<sup>[11-15]</sup> indicating a very poor prognosis. Domestic reports demonstrate that the 5-year survival rate of patients 30 years old or younger is 40.1%<sup>[16]</sup>. The 5-year survival rate of patients at the age of 30-40 years in the present study was 63.12%. Poorly-differentiated and mucinous tumors were present in about 50% of them. On the other hand, patients at the age of 30 years or younger are more likely to present with late-stage disease, lymph node metastasis and distant metastasis compared to patients at the age of 30-40 years, but the difference is not significant. It was reported that patients younger than 40 years old with colorectal cancer display three biological indicators of aggressive and potentially

metastatic tumor biology, signet-ring cell carcinoma, infiltrating tumor edge, and aggressive histologic grade in primary adenocarcinoma<sup>[16]</sup>.

The gender was not a prognostic factor for young patients in the present study. The 3- and 5-year survival rates were better for male patients than for females (69.92% *vs* 61.35% and 62.48% *vs* 53.69%). The prognosis of female colorectal cancer patients is better than that of male colorectal cancer patients, especially those with rectal cancer<sup>[17]</sup>.

Location of tumors is one of the prognostic factors. Patients with colon cancer are considered having a better prognosis than those with rectal cancer<sup>[18]</sup>. Distal location and advanced stage of tumor are determined as independent prognostic factors for survival of young patients with colorectal cancer<sup>[19]</sup>. The present study indicated that there was no relationship between tumor location and prognosis. The prognosis of the patients undergone left hemicolectomy (splenic flexure of colon, descending colon and most part of sigma colon) was not different from that of the patients undergone right hemicolectomy (caecum, ascending colon and hepatic flexure of colon).

The diameter of tumors is also a prognostic factor. The prognosis of the patients in different groups with different tumor diameters (<4 cm, 4-8 cm, >8 cm) was significantly different ( $P<0.001$ ).

The current data indicate a significant difference in the 5-year survival rate among patients who did not received blood transfusion but 400 mL and  $\geq 800$  mL blood transfusion. Perioperative blood transfusion produces host immunosuppression and contagious diseases, increasing postoperative infectious complications<sup>[20]</sup>. Blood transfusion may be associated with the tumor staging. In our study, more advanced diseases (stages III and IV) were found in patients who received 400 mL or  $\geq 800$  mL blood transfusion than in patients who did not receive blood transfusion (50%, 58.6% and 71.4%). The 10-year survival rate of patients who received blood transfusion was significantly lower than patients who did not received blood transfusion (38.93%, 59.17%). Therefore, blood transfusion is a prognosis factor for young patients with colon cancer.

Pathological classification is one of the prognostic factors for patients with colorectal cancer. Patients with different papillary adenocarcinoma have the best outcome, patients with moderately-differentiated and mucinous adenocarcinoma have a moderate outcome, patients with signet-ring cell poorly-differentiated adenocarcinoma have a poor prognosis. Carcinoma and data from a national registry including 164 628 colorectal cancer patients<sup>[21]</sup> indicate that the signet-ring cell subtype has worse outcomes, whereas survival rate for mucinous tumor patients is similar to that of adenocarcinoma patients.

Radical resection is one of the important prognostic factors. In our study, the average survival time for patients who received R2 procedure was 24 months, the 3-year survival rate was 6.5%. Therefore, it is important to emphasize the radical resection.

Another important factor of prognosis is pathological stage. In our study, the 3-year survival rate for IV stage patients was 8.7%. When distant metastasis (including liver metastasis) occurred, the 3-year survival rate was only

4.76%. The 5-year survival rate decreased from 92% to 35% when lymph node metastasis occurred and was 19% when N2 was positive. Multivariate analysis showed that lymph node metastasis was an independent prognostic factor for young patients with colon cancer.

The prognosis of young patients with colon cancer depends mainly on the clinicopathological characteristics. A high proportion of advanced stage tumors is the main reason for the worse prognosis of patients under 30 years old. The prognostic factors for young patients with colon cancer are age, surgical procedure, radical resection, blood transfusion, pathological type, diameter of tumor, depth of tumor invasion, lymph node metastasis and distant metastasis. The independent prognostic factors are only blood transfusion and lymph node metastasis.

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