• COLORECTAL CANCER •

Prognostic factors in 165 elderly colorectal cancer patients

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Abstract

AIM: To analyse the prognostic factors in 165 colorectal cancer patients aged ≥ 70 .

METHODS: One hundred and sixty-five elderly patients with colorectal cancer diagnosed by histology were entered into the retrospective study between 1994 and 2001. Patients were given optimal operation alone, chemotherapy after operation, or chemotherapy alone according to tumor stage, histology, physical strength, and co-morbid problems. Survival rate was calculated by Kaplan-Meier method, and compared with meaningful variances by Log-rank method. Prognostic factors were analyzed by Cox regression.

RESULTS: The 1, 2, 3, 4, 5 year survival rate (all-cause mortality) was 87.76 %, 65.96 %, 52.05 %, 42.77 %, 40.51 %, respectively. The mean survival time was 41.89 ± 2.33 months (95 % CI: 37.33-46.45 months), and the median survival time was 37 months. Univariate analysis showed that factors such as age, nodal metastasis, treatment method, Duke's stage, gross findings, kind of histology, and degree of differentiation had influences on the survival rate. Multivariate analysis showed that factors such as treatment method, Duke's stage, kind of histology and degree of differentiation were independent prognostic factors.

CONCLUSION: This study suggests that the prognosis of elderly colorectal cancer patients is influenced by several factors. Most of elderly patients can endure surgery and/or chemotherapy, and have a long-time survival and good quality of life.

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INTRODUCTION

Colorectal cancer (CRC) is one of the most common malignant tumors in the world^[1-5]. In China it is the fifth of malignant tumor, and the third of alimentary tract malignant tumor^[6, 7]. Its incidence rises with increasing age^[8, 9]. Currently, the majority of colon and rectum tumors arise in patients aged 70 and over. Improvements in public health, nutrition and the prevention and treatment measures have prolonged the life of elderly individuals. The average life expectancy of a 70-year-old man can be prolonged ten years and of a 70-year-old woman 15 years. As a result, there will be a rise in the prevalence of

CRC in elderly patients in the coming decades. But the elderly always have some co-morbid problems, and their clinical, pathological characteristics are different from young patients, so how to rationally treat CRC cancer of the old becomes very important.

MATERIALS AND METHODS

Clinical data

There were 205 elderly colorectal patients (aged ≥ 70) in the First Hospital of Xi'an Jiaotong University from 1994 to 2001, accounting for 12.1 % of the total colorectal cancer patients. One hundred and sixty-five cases were enrolled into the study that had full histology, clinical and follow-up records. There were 105 males, and 60 females (sex ratio was 1.75:1). All patients were aged from 70 to 91 (the median 74 years), and the mean age was 74.67 ± 0.54 years. The latent period ranged from 1 day to 4.5 years, and the mean latent time was 6.21 ± 0.69 months. One hundred and three tumors were located in colon, and 68 in rectum, respectively, including 3 simultaneous double-tumors and 3 different time double-tumors. In the 129 resection specimens, the dimension was smaller than 5 cm in 74 and ≥ 5 cm in 55. Forty-six patients had adenomatous polyps simultaneously. One hundred and forty-five had co-morbidity, among them 73 had cardiovascular diseases, 24 respiratory tract disorders, and 17 cerebral vessel disorders, 16 diabetes mellitus, and 15 other diseases.

Treatment methods

Operation 118 Duke's A, B, C, D stage patients received curative resection, 27 received palliate resection, and 4 received only emergency surgery. 16 cases received no surgery because of their reluctance or bad status.

Chemotherapy Patients who conformed with the requirements were given chemotherapy: PS 0-2 with Duke's C or D or high risk Duke's B tumors (having any characteristic such as perforated or obstructed tumors, T4 tumors, poor differentiation in histology, extra-mural vascular invasion, or mucinous differentiation). They were given 5-Fu/CF+L-OHP every 21 days, L-OHP 80-100 mg·m⁻² >2 h iv d₁, LV 200 mg·m⁻²·d⁻¹ 2 h iv d₁₋₅, 5-Fu 400 mg·m⁻²·d⁻¹ iv d₁₋₅. Forty-seven patients with Duke's B and C tumors had 197 cycles of chemotherapy. Patients with Duke's D tumor accepted 154 cycles of chemotherapy. Among them, 15 cases received post-operation chemotherapy, and 28 cases pure chemotherapy.

Statistical analysis

Kaplan-Meier method was used to calculate survival rate, and Log rank test was used in the univariate analysis. Cox regression Model was used in the multivariate analysis. The SPSS 10.0 for windows was used for all the statistical analyses.

RESULTS

General information

In this study, the 1, 2, 3, 4, 5 year survival rate (all-cause mortality) was 87.76 %, 65.96 %, 52.05 %, 42.77 %, 40.51 %, respectively. The mean survival time was 41.89 ± 2.33 months (95 % CI: 37.33-46.45 months), and the median survival time

was 37 months. The mortality of surgery was 2.8 % (4/145), and death occurred due to perforation, pulmonary infection, and cachexia, respectively. The rate of chemotherapy side effect was 87.3 %, but besides 1 IV⁰ diarrhea and 1 IV⁰ myelosuppression, all others were 0-III⁰.

Univariate analysis

There were several risk factors by univariate analysis as shown in Table 1. But other factors had nothing to do with prognosis, such as gender, latent period, tumor size, co-morbid problems, precancerous lesion, and bloody stool.

Table 1 Results of univariate analysis

Variance	n	1 year survival rate (%)	3 year survival rate (%)	5 year survival rate (%)	P value
Age					0.0332
70-75	96	91.49	59.40	48.62	
75-91	69	82.58	41.79	28.84	
Treatment					
Curative resection+ chemotherapy	47	95.67	78.24	60.72	
Curative resection	71	95.65	62.62	55.01	
Palliate resection + chemotherapy	21	71.43	11.11	0	<0.005
Palliate resection	6	50.00	0	0	
Chemotherapy	16	75	0	0	
Emergency surgery	4	0	0	0	
Duke's stage					
A	8	100	75	37.5	
B	35	100	79.16	64.57	<0.005
C	72	97.16	70.55	56.05	
D	50	63.88	6.74	0	
Gross finding					
Ulcer form	66	92.40	64.88	53.52	
Projection form	57	92.88	58.86	49.15	<0.005
Infiltration form	6	100	50	33.33	
Type of histology					
Tubular adenoma	130	91.41	55.33	44.77	
Mucinous adenocarcinoma	23	73.91	29.12	23.29	0.0018
Other types	12	75.0	56.25	0	
Differentiation of tumor					
High	10	100	74.07	44.44	
Middle	123	95.87	57.84	47.55	<0.005
Low	32	52.78	22.62	14.14	
Nodular metastasis					
No	43	100	79.62	67.24	0.0008
Yes	122	83.52	42.69	31.21	

Table 2 Results of multivariate analysis for elderly colorectal cancer

Factors	Regression coefficient	Standard error	OR	OR 95 % CI		P value
				Lower	Upper	
Treatment method	2.028	0.356	7.603	3.782	15.284	0.000
Duke's stage	0.648	0.295	0.523	0.293	0.933	0.028
Type of histology	-0.824	0.248	0.439	0.270	0.713	0.003
Differentiation of tumor	-0.850	0.246	0.427	0.264	0.692	0.016

Value: resection + chemotherapy=0, resection only=1. Duke's A+B stage=0, Duke's C+D stage=1. Other type=0, tubular adenoma=1. Low differentiation=0, middle and high differentiation=1.

Multi-variate analysis

The factors associated with the risk of colorectal cancer at $P<0.05$ were further tested using backward stepwise conditional Cox regression. The final model consisted of the variables having a significant association with the risk of elderly colorectal cancer at $P<0.05$. The results are shown in Table 2.

DISCUSSION

Though the number of elderly CRC patients is increasing, study about their treatment is rare, especially in China. A number of factors may account for the reluctance to receive operation and chemotherapy in elderly CRC patients. For example, family members do not want them to accept operation and chemotherapy in their old age, co-morbid problems may complicate or even preclude operation and chemotherapy, elderly patients may be more susceptible to side-effects of operation and chemotherapy which may decrease their quality of life^[10], studies on the efficacy and toxicity of chemotherapy in elderly group are limited^[11,12].

Treatment method is the most important prognostic index of elderly CRC in this study. Univariate and multivariate analyses showed that operation combined with post-operation chemotherapy was superior to resection only and chemotherapy only. The curative resection rate of the 165 patients was 71.52 % (118/165), and the total resection rate was 87.88 % (145/165). Operation mortality rate was 2.8 %. So it is evident that age is not the contraindication for surgery^[13,14]. Resection should still be the first choice of treatment for elderly colorectal patients^[15]. Patients who can endure operation after pre-operation management should receive operation in order to decrease the tumor burden. But acute abdomen is frequent in elderly CRC patients, and emergency operation is frequent accordingly, so active peri-operation preparations are necessary^[16,17], such as the selection of optimal anesthesia and operation method to make them more endurable to operation, carefully nursing and supporting to reduce the opportunity of complication. Suitable chemotherapy can prolong the life of advanced patients, and improve their quality of life^[18]. In this study, the patients who received chemotherapy lived longer than those who only received operation, and there were no severe side effects. It is obvious that elderly patients can survive chemotherapy and have a long-time survival and good quality of life, if an optimal chemotherapy scheme is given^[19-23]. Also, because most of CRC relapse or transfer in the following 3 years of operation, it is necessary to give patients adjuvant chemotherapy^[24, 25]. As to the elderly patients, several factors must be taken into consideration when chemotherapy is given, such as suitable chemotherapy regimen with good efficiency and low side effects^[26,27], the importance of the first cycle^[28], liver and kidney function testing and blood cell calculation before every cycle with heart and lung function evaluated if necessary, active support simultaneously, less or no anti-HT3 used to decrease the rate of constipation, long-cycle and convenient scheme to decrease the in-patient time, and changing scheme when it is inefficient^[29].

In this study, univariate and multivariate analyses showed that the patients aged 70-75 years had a longer survival than those aged 75-91 years, which conformed with the study that aging was a risk factor for prognosis^[30]. The elder the patient the lower of sensitivity, so older patients are always diagnosed in their late stage, which significantly influences the treatment and prognosis. But another study showed that aging had nothing to do with prognosis^[31].

Lymph nodular metastasis is a negative indicator of prognosis for elderly CRC patients^[30,32-34]. When cancer cells stay in the celiac lymph node, it is probable that malignant cells have transferred to liver, lung, bone, etc, through lymph

circulation and blood circulation. At last patients may become fatigue, even die of target organ's dysfunction. However, some researchers hold that lymph nodular metastasis is not correlated with prognosis^[25].

Both univariate and multi-variate analyses showed that Duke's stage was an important prognostic factor in this study^[34]. The early the stage, the easy the treatment, and the better the long-survival. Duke's A and some B stage patients did not need to receive chemotherapy at all, but their survival time was the best at all stages. While Duke's C and D patients needed both operation and chemotherapy, but their prognosis was always poor. Precise pre-operation staging is beneficial to the optimal treatment, which has something to do with the prognosis^[35,36]. So doctors must carefully and precisely evaluate the Duke's stage before and during operation so as to give elderly CRC patients the optimal treatment.

Univariate analysis showed that gross finding was another prognostic factor^[34]. In this study, ulcer patients had a longer survival than those with infiltration, which was similar to the result of L.Roncucci's study^[37]. Infiltration type and prominence type always result in intestinal obstruction, which makes the patients have to accept emergency operation. Also, both of them can make patients emaciation, which decreases the endurance to necessary treatment, because of dysfunction of digestion and absorbance. Furthermore, infiltration type always has a poor differentiation in histology.

Univariate and multi-variate analyses showed that histology type and differentiation influenced prognosis in this study^[34,38]. Tubular adenocarcinoma had a better prognosis than mucinous adenocarcinoma. The latter had a poorer differentiation, and this kind of cancer cells had a tendency to transfer to distant sites, which leads to a poor survival. However the high and middle differentiations had a better prognosis and quality of life^[30,39].

In conclusion there are several factors influencing the prognosis of elderly CRC patients. When selecting treatment method, doctors have to take PS, Duke's stage, age, gross finding, histology type, differentiation, lymph node metastasis into consideration. Besides the clinical characteristics that influence the prognosis of elderly CRC patients, other molecular markers such as oncogene mutation, change of chromosome and vascular endothelial growth factor are also significant prognostic factors^[40-46]. Searching for new biology markers and better treatment methods will be one part of the future study.

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