

Original Article

Colorectal Cancer in Patients under the Age of 40: Tri-Service General Hospital Experience

Yi-Chiao Cheng
Shu-Wen Jao
Chia-Cheng Lee
Tsai-Yu Lee
Cheng-Wen Hsiao
Chang-Chieh Wu

Division of Colon and Rectal Surgery,
Department of Surgery, Tri-Service General
Hospital, National Defense Medical Center,
Taipei, Taiwan

Key Words

Colon cancer;
Rectal cancer;
Young age

Abbreviations

CRC, Colorectal cancer;
SEER program, Surveillance
epidemiology and end results program

Background. In Taiwan, colorectal cancer is the first common cancer and is the third most common cause of cancer related death. In recent years, patients with colorectal cancer became younger. The purpose of this study was to analyse the patients under the age of 40 years suffering colorectal cancer.

Material and Methods. We conducted a retrospective study in Tri-Service General Hospital. From January 2007 to December 2011, patients under the age of 40 years with colorectal cancer were included. Patient demographics, tumor type, tumor stage, tumor differentiation, tumor location, treatment and mean survival time were analysed.

Results. Totally 52 patients, including 34 males and 18 females had colorectal cancer under the age of 40 years. The most common symptom was anal bleeding. Except 4 patients with carcinoid, all of the other patients had adenocarcinoma. Thirty-six patients had stage III/IV at diagnosis. Twenty-eight patients with adenocarcinoma had moderate differentiation. Twenty-three patients suffered from rectal cancer. Mean survival time of adenocarcinoma of colo-rectum was 4.1 ± 0.6 years in stage III patients, and 1.8 ± 0.5 years in stage IV patients.

Conclusion. All patients with suspicious symptoms of colorectal cancer merit undergoing large bowel evaluation.

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The incidence of colorectal cancer (CRC) is the third and cancer related death is the second in the United States.¹ According to the American Cancer Society's estimates, the number of new CRC cases in the United States for 2013 are 102,480 of colon and 40,340 of rectal cancer. In Taiwan, CRC is the first common cancer and is the third most common cause of cancer related death.

More than 9 out of 10 people diagnosed with CRC

are at least 50 years old in the National Cancer Database Report on CRC.² The American Cancer Society suggests people at "average risk" for developing CRC beginning screening tests at age 50. People with "increased risk" such as family history of CRC or adenomatous polyps, family history of hereditary CRC syndrome, and personal history of inflammatory bowel disease, are advised to begin screening tests before age 50.³

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Corresponding author: Dr. Chang-Chieh Wu, Division of Colon and Rectal Surgery, Department of Surgery, Tri-Service General Hospital, National Defense Medical Center, No. 325, Section 2, Cheng-Kong Rd., Neihu District, Taipei 114, Taiwan. Tel: +886-2-8792-3311 ext. 88052; Fax: +886-2-8792-7411; E-mail: eric@mail.ndmctsgsh.edu.tw

According to the Surveillance Epidemiology and End Results (SEER) Program data from 2006-2010, the incidence of patients under 40 years old was only 6.6 per 100,000 patients. Although the incidence of CRC in young patient is low, the data suggests the incidence is increasing.⁴

There were a number of reports regarding young patients with CRC. Some of them have reported that young patients have worse prognosis. However, there reports were published more than decades.⁵⁻¹⁰ Recent reports discussed more in the clinicopathological features of young patients.¹¹⁻¹³ They found although CRC in young patients present with more aggressive histopathological subtypes and more late stages, these patients have the same or a better cancer-related survival.¹² However, they were all focused in western people.

The aims of the study were to analyze the patient demographics, tumor type, tumor stage, tumor differentiation, tumor location, treatment and mean survival time to realize the different of younger patients in colorectal cancer in Taiwan.

Materials and Methods

We conducted a retrospective study in Tri-Service General Hospital. We searched the cancer boarding database from January 2007 to December 2011. Patients under the age of 40 years with CRC were included. For three patients were not treated after diagnosis in our hospital, totally 52 patients were included. We reviewed their admission notes, discharge summaries, and pathology reports for further analysis.

The follow-up of these patients have been achieved in our outpatient department. The patients have been regularly followed up every 3 months for the first 5 years, and then every 6 months until their death. During each follow-up, physical examinations, complete blood cell counts, CEA/CA-199 level were obtained. Colonoscopy was performed 3 months after surgery. Chest film, abdominal sonography and colonoscopy were performed every year in initial 5 years and then every 2 years. Abdominal computed tomog-

raphy, magnetic resonance imaging or positron emission tomography was preserved for the situation of elevated CEA/CA-199 level or any other obscure findings. The study was reviewed and approved by the institutional review board for human subjects in Tri-Service General Hospital (TSGHIRB: 2-03-05-009).

Statistical analysis

Continuous variables are expressed as mean and standard deviation. Categorical variables are expressed as percentages. The survival years are defined as the interval between initial diagnosis to death. Each stage of patients was analyzed using the Kaplan-Meier method. All analyses of the data were performed using the Statistical Program for Social Sciences version 20.0 for Windows (SPSS, Inc. Chicago, Illinois, USA).

Results

Of the 52 patients, mean age was 32.8 ± 5.8 years old. Male patients account for 65.4% patients. The only patient less than 20 years old had carcinoid of rectum. There were 4 patients with carcinoid. Three of them had stage I carcinoid of rectum, which were cured by transanal wide excision. The rest was stage IV carcinoid of ascending colon. Due to carcinoma-tosis, palliative treatment was done. The other 48 patients had adenocarcinoma. Thirty-five patients of them were stage III or IV at diagnosis. Thirty-eight patients with adenocarcinoma had pathologic report. Of them, only 1 showed well differentiation. Thirty-four patients underwent curative operation but 10 underwent palliative treatment at diagnosis. Within all patients, only three patients had family history of CRC. All of them were second-degree relatives. We listed the characteristics including age, gender, tumor stage, tumor differentiation, type of treatment, and family history in Table 1.

Initial symptoms were varied and unspecific. The most common symptom was anal bleeding (38.5%). The second one was change in bowel habits (36.5%). Only 5 patients had diagnosed via screening. Table 2

Table 1. Demographics of patients

	Patients (n = 52)
Age (y)	32.8 ± 5.8
< 20	1
20-24	6
25-29	6
30-34	13
35-39	26
Male/Female (%)	34 (65.4)/18 (34.6)
Tumor stage (%)	
0	2 (4.2)
I	8 (16.7)
II	3 (6.3)
III	18 (37.5)
IV	17 (35.4)
Carcinoid	4 (I/I/I/IV)
Tumor differentiation of adenocarcinoma	
Well	1
Moderate	28
Poor	9
Treatment	
Curative	34
Palliative	8
None	10
Family Hx	3 (second-degree)

Table 2. Initial symptoms of patients

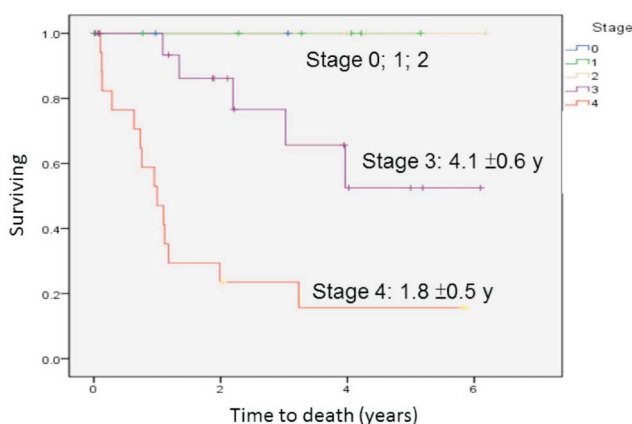
Clinical presentation	n = 52 (%)
Anal bleeding	20 (38.5)
Poor appetite	7 (13.5)
Abdominal pain	11 (21.2)
Change in bowel habits	19 (36.5)
Body weight loss	6 (11.5)
Bloating	6 (11.5)
Palpable mass	1 (1.9)
Anal pain	2 (3.8)
Screening	5 (9.6)

showed initial symptoms in detail.

Most of the patients had CRC distal to the splenic flexure (76.9%). The majority of tumors were located at rectum (42.3%) (Table 3). Mean survival years of adenocarcinoma of colo-rectum were analyzed by stage. Thirteen patients had stage 0, I, and II disease. All these patients survived after surgical treatment without recurrence. In stage 3 disease, mean survival time was 4.1 ± 0.6 years. In stage IV patients, it was 1.8 ± 0.5 years (Fig. 1). By stage median follow-up

Table 3. Location of tumors

Location of cancers	n = 52 (%)
Cecum	3 (5.8)
Ascending colon	6 (11.5)
Hepatic flexure	1 (1.9)
Transverse colon	1 (1.9)
Splenic flexure	2 (3.8)
Descending colon	6 (11.5)
Sigmoid colon	7 (13.5)
Rectosigmoid colon	3 (5.8)
Rectum	22 (42.3)
Other (Interposed colon for esophageal reconstruction)	1 (1.9)

**Fig. 1.** Mean survival years in individual stage of adenocarcinoma.

period were 24.2 months (range 11.7-36.8 months) in stage 0, 33.4 months (range 0.1-61.8 months) in stage I, and 51.5 months (range 47.8-74.1 months) in stage II patients. In stage III and IV patients, the median follow-up period were 25.8 months (range 0.3-73.2 months) and 12.0 months (range 1.26-70.5 months). The 5-year-survival rate was 53% in stage III and 16% in stage IV patients.

Discussion

Patients below age 40 with CRC accounts to 2-3.1% of patients with CRC worldwide.^{12,14,15} However, incidence rates for colon and rectal cancers in young patients are rising.¹⁶ Some people believed patients with CRC in young age have significant family

history. A literature review showed the family history of CRC in patients below age 40 varied from 3.2% to 61%.¹⁷ Our study showed only three patients (5.8%) had family history of CRC, and all of them were second-degree relatives. In all ages of CRS patients, the percentage of the patients with positive family history is 15-20%.¹⁸ Thus, it seems no difference in family history between young patients and other patients.

SEER stage distribution data from 2003-2009 revealed 36% patients had regional disease, and 20% had distant disease at the time of diagnosis. Thus, there were 56% had stage III and IV disease. O'Connell JB *et al* reviewed 43 articles discussing young population. 66% of patients below age 40 had stage III or IV disease.¹⁷ Our study showed 36 (69.2%) patients had stage III or IV disease at diagnosis. Thus, our study supports that advanced stage (stage III or IV) is more common in young patients compared to all population with CRC.

In regard of tumor differentiation, two previous studies showed 15% of colorectal adenocarcinomas are poorly differentiated.^{19,20} O'Connell JB *et al* reviewed 25 articles noted the presence of poorly differentiated tumors. Poorly differentiated tumors were in the average of 27% (range 8% to 54%).¹⁷ In our study, 9 in 38 (23.7%) patients had poorly differentiated tumors. It provides an explanation of the higher incidence of advanced stage tumors in our patients.

It has been suggested that delays in diagnosis may be contributed to more advanced stage tumors in younger CRC patients.¹³ The symptoms of our patients were mostly unspecific. Twenty (38.5%) patients experienced anal bleeding, 19 (36.5%) of them had change in bowel habit. Physicians may attribute these symptoms to benign anorectal diseases or simple gastrointestinal upset. In the other hand, younger patients may delay in visiting physicians due to fear, busy to work, or ignorance.

The majority of our patients had CRC distal to the splenic flexure (76.9%), with 42.3% in rectum. Myers EA *et al*¹³ showed their patients under age 50 had similar distribution of tumor location. However, they reported that in patients older than 50 years old, only 57% had CRC distal to the splenic flexure. The different distribution of CRC in young patients enhances

the importance of sigmoidoscopy.

Some studies suggested young patients with stage I/II CRC have better survival.²¹⁻²³ Our patients in stage I/II are all alive during follow-up period. Better tolerance of surgery and adjuvant surgery may contribute to better prognosis in these patients. Mean survival year was 4.1 ± 0.6 years in stage III patients and 1.8 ± 0.5 years in stage IV patients. The 5-year-survival rate was 53% in stage III and 16% in stage IV patients. In Taiwan, national health insurance has paid Bevacizumab for first line treatment in stage IV CRC since Jun. 1, 2011, and Cetuximab for third line treatment in stage IV CRC since Mar. 1, 2007 and first line treatment in stage IV CRC since Dec. 1, 2012. Our patients were treated from Jan., 2007 to Dec., 2011. Thus, not all of them received target therapy and it may influence the prognosis of stage IV patients. In comparison with other series discussing young CRC patients,¹⁷ our patients had better 5-year survival. It may be related to national health insurance in Taiwan supports most of the cost in adjuvant chemotherapy.

Limitations

The present study had some limitations. Our study was conducted at a single center and was a retrospective review. These patients do not compare with the patients above 40 years old in our hospital. Moreover, we do not analyze the differences in treatment for stage III/IV patients. It needs to conduct prospective randomized controlled studies with larger sample sizes.

Conclusion

For patients below age 40 with CRC, worse differentiation in histology, advanced stage, most of the tumors were located in distal colon and rectums were observed. To obtain better prognosis, it's worth to perform colonoscopy, at least sigmoidoscopy for any symptomatic patients regardless of their age or family history.

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原 著

四十歲以下大腸直腸癌病患：三軍總醫院經驗

鄭屹喬 饒樹文 李家政 李才宇 蕭正文 吳昌杰

國防醫學院 三軍總醫院 外科部 大腸直腸外科

背景 大腸癌是國人第一好發及第三死亡率的癌症，近年來，大腸癌的病患年輕化的趨勢，本篇文章的目的是以回溯性研究的方式對單一醫學中心中 40 歲以下大腸直腸癌病患進行分析。

方法 回溯性病例回顧於 2007 年 1 月至 2011 年 12 月，搜索本院癌症登記資料庫 40 歲以下，且診斷為大腸癌的病患，分析病患平均年齡、性別、腫瘤性質、分期、發生位置以及治療方式預後等進行討論。

結果 共 52 位病患，男性 34 人、女性 18 人，症狀最常見為肛門出血，除 4 位類癌病患，其他 48 人均為腺癌，以 3、4 期最多共 36 位，分化以中度 28 位最多，部位以直腸最多佔 23 位，其中 3 期病患平均存活 4.1 ± 0.6 年，4 期病患平均存活 1.8 ± 0.5 年。

結論 所有有大腸癌相關症狀的 40 歲以下之病患，建議接受大腸癌相關檢查，以早期發現、早期治療。

關鍵詞 大腸癌、直腸癌、年輕人。