Comparisons of Characteristics and Outcome of Colorectal Cancer in Different Age Categories: A Retrospective Analysis of a Single Institution in Taiwan

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Purpose. The purpose of this retrospective study was to investigate differences in clinic features, pathologic findings, and outcomes of patients with colorectal cancer among different age groups.
Methods. Colorectal cancer patients (N = 1116) who had undergone surgical treatment were divided into three groups according their age: young (40 years and under), middle-age (41-70 years) and old (71 years and above). The medical records of all patients were reviewed, and compared by age categories.
Results. Tumor location, N status, M status, and TNM stage were associated with age categories, but grade, histological subtype, and T stage were not. There were 32 patients (3.2%) with diagnosis of colorectal cancer found in screening programs, and they were all in group M ($p < 0.001$). Hematochezia (54.3%) was the most common symptom leading to diagnosis. Abdominal pain was more prevalent in the young group (30.4 vs. 20.9 vs. 15.4%, $p = 0.03$), and obstruction was more frequent in old group (6.5 vs. 8.4 vs. 19.2%, $p < 0.01$). The average 5-year overall survival rates of the young and middle-age groups were similar and significantly better than that of the old group ($p < 0.001$) when compared overall, or by stage.
Conclusion. Young patients were diagnosed at a later stage, but did not have a worse overall outcome. Although the suspicion of malignancy in the young is low, symptoms such as abdominal pain or change in bowel habit should not be regarded lightly. If the disease is detected early, survival of young patients may be improved even better.
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Colorectal cancer (CRC) ranks as the third most commonly diagnosed cancer overall, and the second most common cause of cancer-related death in the United State.[1,2] CRC is usually thought of as a disease of the elderly, with certain study demonstrating more than 90% of patients diagnosed after 55 years of age.[3] However, CRC does afflict the younger population as well; several studies have reported that 2-7% of all CRC present in patients ≤ 40 years of age.[4-7] Despite many studies aimed at evaluating whether the

features of CRC in younger patients differ from those in older patients, the results are still controversial. Some studies have found that CRC in the younger patients appears to be more aggressive, to present at later stage, and to have poorer prognosis and lower survival rates.[7-10] However, other studies have indicated no significant differences.[11-15]

The purpose of this study was to determine whether Taiwanese patients with CRC in different age groups (young, middle-age, and old) exhibit any unique clinical, pathological, or epidemiological features of the disease.

Materials and Methods

Patient population

The records of 1116 consecutive patients who had surgery for primary colorectal adenocarcinoma at the Division of Colorectal Surgery, Department of Surgery, Tri-Service General Hospital, National Defense Medical Center, Taipei, ROC during the years 1999-2008 were retrospectively reviewed and analyzed. Records were retrieved from the computerized database. All patients were divided into three groups according their age: young (40 years and under; group Y), middle-age (41-70 years; group M), old (71 years and above; group O). The cutoffs of 40 and 70 years were used because most studies defined "young" as patients < 40 years old,[3,4,6-8] and patients older than 70 years have fewer remaining years of life irrespective of disease.

Data collected included age at time of surgery, gender, hereditary syndromes (familial adenomatous polyposis), family history of colorectal cancer, reason for diagnosis (screening or symptoms), tumor characteristics such as anatomic location, stage, histological subtype (intestinal or mucinous/signet ring), grade, and acute presentation (obstruction or perforation). The diagnosis of colorectal adenocarcinoma was confirmed at surgery by the surgeon and by histopathological analysis. The pathological report of each lesion was reviewed and restaged according to the AJCC TMN staging system (7th edition, 2010). After surgery, routine follow-up was performed as usual,

and follow-up data was available for all patients.

Statistical analysis

All statistical analyses were performed with SPSS 15.0 statistical software (SPSS Inc., Chicago, IL, USA), and a significance level of 0.05 was used. Continuous variables were expressed as median with inter-quartile range (IQR, the range between 25th and 75th percentiles) because of non-normal distribution, and the Kruskal-Wallis test was performed for comparisons between age groups. Discrete variables were expressed as counts with percentages, and were tested with Fisher's exact test. Five-year survival rates in each age group at different stages were estimated by Kaplan-Meier survival curves. Log-rank test was performed for the comparisons of Kaplan-Meier survival curves.

Results

Patient population

A total of 1,116 patients were enrolled into the study, including 621 males and 495 females, with a mean age of 65.0 ± 14.4 years (range, 21.0 to 94.0 years). The patients were divided into three groups, 65 (5.8%) patients who were ≤ 40 years of age were group Y (mean age, 33.43 ± 5.86 years), 586 (52.5%) patients who were 41-70 years of age were group M (mean age, 57.91 ± 8.32 years), and the remaining 465 (41.7%) patients who were ≥ 71 years of age were group O (mean age, 78.32 ± 4.83 years). The comparison between patient characteristics of the three age groups is presented in Table 1. With respect to risk factors for CRC, there was a higher incidence of familiar adenomatous polyposis (FAP) in group Y ($p < 0.001$), with a trend toward a higher rate of family history of CRC ($p = 0.06$). Although there were only 32 patients (3.2%) with diagnosis of CRC as a result of screening, they were all in group M ($p < 0.001$).

Tumor characteristics

A comparison of tumor characteristics between

Table 1. Comparison of patient characteristics in three age groups

	All groups[a] (N = 1,116)	Group Y (n = 65)	Group M (n = 586)	Group O (n = 465)	*p*-value
Gender					0.109
Male	621/1,116 (55.6%)	42/65 (64.6%)	311/586 (53.1%)	268/465 (57.6%)	
Female	495/1,116 (44.4%)	23/65 (35.4%)	275/586 (46.9%)	197/465 (42.4%)	
FAP					< 0.001*
Yes	5/995 (0.5%)	4/60 (6.7%)	1/527 (0.2%)	0/408 (0.0%)	
No	990/995 (99.5%)	56/60 (93.3%)	526/527 (99.8%)	408/408 (100.0%)	
Family history of CRC					0.06
Yes	84/995 (8.4%)	7/60 (11.7%)	40/527 (7.6%)	37/408 (9.1%)	
No	911/995 (91.6%)	53/60 (88.3%)	487/527 (92.4%)	371/408 (90.9%)	
Reason for diagnosis					< 0.001*
Screening	32/995 (3.2%)	0/60 (0.0%)	32/527 (6.1%)	0/408 (0.0%)	
Symptoms	963/995 (96.8%)	60/60 (100.0%)	495/527 (93.9%)	408/408 (100.0%)	

FAP = familial adenomatous polyposis; CRC = colorectal adenomatous polyposis.

All data was expressed as count with percentage.

* Indicates there's significant association between the corresponding variable and age.

[a] Data of 121 patients were missing regarding FAP, family history of CRC, and reason for diagnosis.

the three age categories is presented in Table 2. Four variables, tumor location, N status, M status, and TNM stage were associated with age. The rectum and sigmoid colon were the most common sites of CRC in all patients, and the locations were: right colon (cecum, ascending colon, hepatic flexure), 19.5%; transverse colon, 5.0%; left colon (splenic flexure, descending colon), 9.9%; sigmoid colon, 24.5%; and rectum, 40.1%. The only significant difference among tumor location by age was that a location in the right colon was more common in group O (18.5 vs. 15.7 vs. 24.5%, *p* = 0.042). With respect to N status, 61.6% of patients in group Y had nodal involvement (N1 + N2), while 50.9% and 43.9%, respectively, in group M and O had nodal involvement (*p* = 0.025). Group Y had a higher rate of distant metastasis (M1a + M1b) than the other two groups (30.7 vs. 20.9 vs. 16.8%, *p* = 0.024). In addition, TNM stage II tumors were more frequent in group O, and stage IV tumors were more frequent in group Y (stage II: 16.9 vs. 25.8 vs. 33.8%; stage IV: 30.8 vs. 20.8 vs. 16.8%, *p* = 0.017). There were no significant differences between the groups with respect to other features such as grade, histological subtype, or T stage.

Symptoms for diagnosis

Data regarding FAP, family history of CRC, and

reason for diagnosis was missing for 121 patients. Data of the remaining 995 patients were analyzed regarding presenting symptoms leading to diagnosis. Hematochezia (54.3%) was the most common symptom, followed by change in bowel habit (41.7%), and abdominal pain (19.3%). Abdominal pain and tumor obstruction were associated with age. Abdominal pain was more frequent in group Y (30.4 vs. 20.9 vs. 15.4%, *p* = 0.03), and tumor obstruction was more frequent in group O (6.5 vs. 8.4 vs. 19.2%, *p* < 0.01).

Survival

Average 5-year overall survival rates adjusted for cancer stage at presentation are presented in Table 4. The number of patients in group Y with stage I and stage II disease was low, thus 5-year survival rates could not be estimated. The overall 5-year survival for patients in groups Y and M were similar (61.9% and 62.7%), and significantly better than group O (*p* < 0.001 by log-rank test, Fig. 1). When compared by stage, 5-year survival rate was significantly lower in group O than groups M or Y (Table 4).

Discussion

CRC is the most common cancer of the gastroin-

Table 2. Comparison of tumor characteristics in three age groups

	All groups (N = 1,116)	Group Y (n = 65)	Group M (n = 586)	Group O (n = 465)	*p*-value
Tumor location[a]					0.042*
R	218 (19.5%)	12 (18.5%)	92 (15.7%)	114 (24.5%)	
T	56 (5.0%)	3 (4.6%)	29 (4.9%)	24 (5.2%)	
L	111 (9.9%)	7 (10.8%)	55 (9.4%)	49 (10.5%)	
S	273 (24.5%)	15 (23.1%)	159 (27.1%)	99 (21.3%)	
R	458 (41.0%)	28 (43.1%)	251 (42.8%)	179 (38.5%)	
Histology					0.153
Mucinous/signet ring	49 (4.4%)	6 (9.2%)	23 (3.9%)	20 (4.3%)	
NOS	1067 (95.6%)	59 (90.8%)	563 (96.1%)	445 (95.7%)	
Grade[b]					0.976
I	81 (7.3%)	4 (6.2%)	44 (7.5%)	33 (7.1%)	
II	883 (79.1%)	52 (80.0%)	459 (78.3%)	372 (80.0%)	
III	152 (13.6%)	9 (13.8%)	83 (14.2%)	60 (12.9%)	
T stage					
Tis	43 (3.9%)	2 (3.1%)	20 (3.4%)	21 (4.5%)	0.056
T1	58 (5.2%)	7 (10.8%)	31 (5.3%)	20 (4.3%)	
T2	172 (15.4%)	7 (10.8%)	95 (16.2%)	70 (15.1%)	
T3	727 (65.1%)	37 (56.9%)	392 (66.9%)	298 (64.1%)	
T4	116 (10.4%)	12 (18.5%)	48 (8.2%)	56 (12.0%)	
N status					0.025*
N0	574 (51.4%)	25 (38.5%)	288 (49.1%)	261 (56.1%)	
N1	249 (22.3%)	15 (23.1%)	140 (23.9%)	94 (20.2%)	
N2	293 (26.3%)	25 (38.5%)	158 (27.0%)	110 (23.7%)	
M status					0.024*
0	896 (80.3%)	45 (69.2%)	464 (79.2%)	387 (83.2%)	
1a	121 (10.8%)	11 (16.9%)	73 (12.5%)	37 (8.0%)	
1b	99 (8.9%)	9 (13.8%)	49 (8.4%)	41 (8.8%)	
TNM stage					0.017*
0	44 (3.9%)	2 (3.1%)	20 (3.4%)	22 (4.7%)	
I	182 (16.3%)	11 (16.9%)	103 (17.6%)	68 (14.6%)	
II	319 (28.6%)	11 (16.9%)	151 (25.8%)	157 (33.8%)	
III	351 (31.5%)	21 (32.3%)	190 (32.4%)	140 (30.1%)	
IV	220 (19.7%)	20 (30.8%)	122 (20.8%)	78 (16.8%)	

[a] R = right colon (cecum, ascending colon, hepatic flexure); T = transverse colon; L = left colon (splenic flexure, descending colon);
  S = sigmoid colon; R = rectum.
[b] I = well differentiated; II = moderately differentiated; III = poor differentiated.
All data was expressed as count with percentage. NOS = not otherwise specified.
* Indicates there's significant association between the corresponding variable and age.

Table 3. Comparison of presenting symptoms for diagnosis in three age groups

Symptoms[a]	All groups (N = 995)	Group Y (n = 60)	Group M (n = 527)	Group O (n = 408)	*p*-value
Hematochezia	540 (54.3%)	38 (63.0%)	299 (56.8%)	203 (49.7%)	0.088
Change in bowel habit	415 (41.7%)	25 (41.3%)	223 (42.4%)	166 (40.8%)	0.912
Abdominal pain	192 (19.3%)	18 (30.4%)	110 (20.9%)	63 (15.4%)	0.030*
Tumor obstruction	125 (12.6%)	4 (6.5%)	44 (8.4%)	78 (19.2%)	< 0.001*
Anemia	61 (6.1%)	0 (0.0%)	32 (6.0%)	29 (7.2%)	0.173
Weight loss	49 (4.9%)	3 (4.3%)	19 (3.7%)	27 (6.5%)	0.218
Tumor perforation	28 (2.8%)	1 (2.2%)	9 (1.8%)	17 (4.1%)	0.181

[a] Data was expressed as count with percentage.
* Indicates there's significant association between the corresponding variable and age.

Table 4. Five-year survival rates in each age group by stage

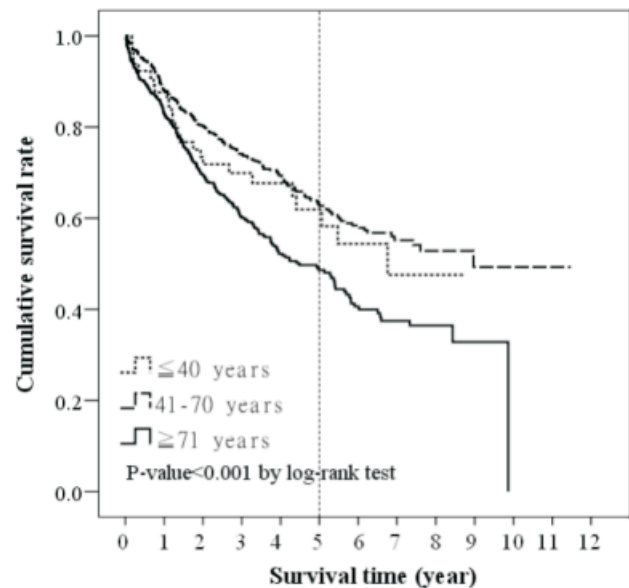| Age group	Stage				
	All	1	2	3	4
Group Y	61.9%	-	-	71.1%	10.0%
Group M	62.7%	91.0%	78.9%	65.0%	11.4%
Group O	48.7%	69.7%	63.8%	46.1%	5.1%
p-value*	< 0.001	< 0.001	0.001	< 0.001	0.006

- No estimated 5-year survival rate for group Y in stage 1 and 2 were all censored, and only one event in stage 2 occurred after 5.5 years.
* By log-rank test.

Fig. 1. Overall survival by age groups.

testinal tract. It is the third most commonly diagnosed cancer overall, and the third leading cause of cancer-related deaths in Taiwan for 2007.[16] On base of the retrospective analysis at our institution, the average age at diagnosis is 65 years, which is similar to that seen in Western countries. Most patients with colorectal cancer were > 40 years of age, and only 5.8% of the patients in our study with CRC were ≤ 40 years of age. This is similar to previously reported data from Western countries which indicate that 2-7% of CRCs occur in those ≤ 40 years of age.[4-7] We observed a trend toward a male preponderance in the overall cohort, and in each age group ($p = 0.109$), in contrast to other studies showing an equal proportion of males and females.[7,11,17]

It is still unclear whether a family history of CRC is a significant predisposing factor of CRC in a young population because similar to other studies,[7,12,14] our data indicated a higher incidence of family history of CRC in the younger population, but the value did not reach statistical significance. Similar to the previous studies,[12,14] we found a higher incidence of FAP in group Y than the other groups (6.7 vs. 0.2 vs. 0%, $p < 0.001$), although the absolute numbers were small. This result could be attributed to early diagnosis and closed follow-up of FAP, and early surgical intervention at our institution. Our analysis showed that the vast majority of patients (96.8%) were diagnosed via symptoms, and not via screening. The few patients (3.2%) with a screening-prompted diagnosis were all in group M; this is likely because this group includes the target population of CRC screening programs in Taiwan.

In the present study, hematochezia and change in bowel habits were the predominant presenting symp-

toms in the entire cohort, and abdominal pain was more frequently a presenting complaint in group Y. These results are consistent with other series.[12,18,19] Obstruction due to the tumor occurred in a significantly higher percentage of patients in group O than the other groups. Perhaps this age group has a higher threshold for abdominal pain and a high proportion of patients with constipation, which hides the change in bowel habit.

Regarding the tumor characteristics, the location of tumors was in accordance with pervious studies, showing a majority of sigmoid and rectal tumors.[11,12] In the comparison of tumor location of three age categories, we found that group O had a higher rate of right colon lesions than the other groups, despite several studies reporting a predominance of right colon cancer in young patients,[20-22] or no an age-dependent difference in tumor location.[11,23] It is commonly believed that mucinous/signet ring, and poorly differentiated cancers tend to have a poorer prognosis compared to well- and moderately differentiated cancers.[7] Our results were the same as some previous studies,[11,14] and demonstrated no age-associated differences in histologic subtypes and differentiation grade. However, most studies report that in patients < 40 years of age a higher proportion of mucinous/signet ring histology and poor differentiation is found.[7,15,18,23] In this series, we found that CRC in

young patients presented with a higher stage at diagnosis and more extensive nodal involvement and distant metastasis, which is consistent with other series.[7,15,18,23] The more advanced stage at diagnosis may at least in part be explained by delayed diagnosis or the lack of screening in younger age groups. Several series contend that late diagnosis, attributed to low concern, contributes to this finding in younger ages patients,[21,24] and we confirmed a significant difference in the screening-prompted diagnosis among the age categories.

Recent studies have shown that young age is not a poor prognostic factor for survival in patients with CRC.[11-15,18] In contrast, O'Connell et al.[7] reviewed more than 60 publications and concluded that young patients have poorer outcomes in later stages. Others studies have suggested that young age may improve the prognosis in certain stages.[23,25] It is likely that treatment protocols may change over time, and that patients in these series have not all been managed in the same manner. In our study, the average overall 5-year survival of groups Y and M were similar, and were significantly higher than group O, and the same results were found when compared by stage. Young patients were diagnosed at a later stage, but did not have a worse outcome. Perhaps young patients are in better physical condition to receive aggressive surgery and adjuvant treatment; in contrast, old patients have worse physical condition to tolerate the same treatment and fewer remaining years of life. Consequently, young and middle-age patients had similar outcomes, and the outcomes were better than those of old patients in our study.

In those published studies, data was compared between young group and non-young group, and the older patients with fewer remaining years of life may be a bias in the average 5-year overall survival rates of non-young group. In contrast, we divided our patients into three age groups (young, middle-age and old groups) to compare the overall survival could prevent this bias.

Conclusion

In conclusion, we found that younger patients (≤ 40 years of age) had more advanced stages of CRC, but did not have worse 5-year overall survival compared to the older patients (> 40 years of age). Based on our data, young age is not considered as a poor prognostic factor for patients with CRC. Although suspicion of malignancy in the young is low, symptoms such as abdominal pain or change in bowel habits should not be taken lightly. If the disease is detected early, young patients will have even better survival.

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原　　著

在不同年齡組比較大腸直腸癌的臨床特點和預後結果：在台灣單一機構的回顧性分析

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目的　本回溯性研究的目的是調查大腸直腸癌患者在不同年齡群中，是否有臨床特徵或組織病理上的任何差異。

方法　已接受手術治療的大腸癌患者 (n = 1116)，根據他們的年齡分為三組：青年組 (40 歲及以下)，中年組 (41-70 歲) 和老年組 (71 歲及以上)。依據所有患者的醫療記錄進行回顧性分析，並在年齡類別中做比較。

結果　在腫瘤的特點方面，腫瘤的位置，淋巴結狀態，遠處轉移情形，和 TNM 分期，均與年齡分類有關，但是細胞分化，組織學亞型，或腫瘤 T 分類則沒有。有 32 例 (3.2%) 的大腸直腸癌是藉由篩檢診斷出來，且他們都集中在中年組 ($p < 0.001$)。血便 (54.3%) 是最常見的症狀並促進診斷。腹痛較普遍在青年組 (30.4 vs. 20.9 vs. 15.4%, $p = 0.03$)。腫瘤阻塞更頻繁出現在老年組 (6.5 vs. 8.4 vs. 19.2%, $p < 0.01$)。無論在整體或各期別中比較，平均五年生存率在青年和中年組相近，並明顯優於老年組 ($p < 0.001$ by log-rank test)。

結論　年輕的患者有較惡性的腫瘤分期，但沒有較差的預後結果。雖然在年輕人較少會被懷疑惡性腫瘤，但腹痛或大便習慣改變等症狀，不應被輕視。如果及早發現疾病，年輕患者將有更好的存活率。

關鍵詞　年輕、大腸癌、腺癌、年齡。