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Prognostic Features of Colorectal Cancer in the Young Adult

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Abstract Several prior studies have shown that the prognosis of young adult patients with colorectal cancer is poor. To clarify the definition of "young adults", a comparative clinical study was performed in 10 patients diagnosed in the third decade (group A) and 15 patients diagnosed in the fourth decade (group B). The clinico-pathologic characteristics of group A were as follows: male predominance; high frequency of distant metastases including liver metastases and peritoneal dissemination; and more advanced cases. The cumulative 5-year survival rate of patients in group A was 32%, with a median survival of 83.7 months. Patients in group B had a 5-year survival rate of 64%, with a median survival of 152.1 months. In patients undergoing tumor resection, the 5-year survival rates in group A and B were 42% and 64%, respectively. The survival rates in patients having curative resection were 60% and 80%, in group A and B respectively. Moreover, colorectal polyposis was observed in 4 patients (40%) in group A, but in none of the patients in group B. These data suggest that the clinical characteristics of patients diagnosed with colorectal cancer in the third decade were quite different from the characteristics of patients diagnosed in the fourth decade.

A high index of suspicion and early diagnostic evaluation in patients with colorectal symptoms younger than 30 years old is warranted due to the aggressive nature of large bowel cancer in this age group.

Key Words : Colorectal cancer in the third and fourth decades, Clinico-pathologic findings, Colorectal polyposis

Introduction

Cancer of the colon and rectum is one of the most commonly occurring visceral malignancies in Japan. Moreover, the incidence of this disease has been increasing (1). Although large bowel cancer is primarily a disease of the elderly, 4 to 8 percent of these cancers are found in patients under 40 years of age (2). Young patients with colorectal cancer have been reported to have a particularly poor prognosis, because they tend to have a higher incidence of undifferentiated or mucinous tumors, and present with more advanced

disease (3).

The definition of what age group constitutes "young adult" remains controversial. Many reports have selected patients younger than 40 years of age, and some reports have selected only patients younger than 30. Thus, the aim of this study was to determine if there are clinico-pathologic differences between patients with colorectal cancer in the third decade compared to patients in the fourth decade.

Patients and Methods

Between 1970 and 1990, 511 patients with colorectal cancer underwent surgery in the Department of Surgery II, Yamaguchi University School of Medicine. In this population, 10 patients were less than 30 years old (group A) and 15 patients were between 30 and 39 years old (group B). None of these patients had received any treatment prior to surgery. All the patients received postoperative chemotherapy with 5-fluorouracil or tegafur.

The patients were evaluated uniformly (4) for: gender, symptom duration prior to diagnosis, symptoms, tumor location, distant metastases, gross findings, histologic classification, lymph node metastases, histologic depth of invasion, cancer stage (Japanese Research Society for Cancer of the Colon and Rectum and Dukes classification), curability, and incidence of associated colon polyp(s) or polyposis. The cumulative survival rates also were compared.

Statistics

Fisher's exact probability test was used to compare differences in distribution; $p < 0.05$ was considered statistically significant, with $p < 0.10$ considered to approach statistical significance. The survival of each patient was studied by the Kaplan-Meier method, and statistical analysis was done with the generalized Wilcoxon test.

Results

Patients characteristics

Patients characteristics including gender, symptom duration prior to diagnosis, and tumor location are shown in Table 1. There was a predominance of males in group A compared with an even distribution of males and females in group B. The duration of symptoms prior to diagnosis in the 2 groups was similar, ranging from 1 to 11 months in group A and to 1 to 8 months in group B. Most tumors were located in the rectosigmoid region in both groups.

Table 1. Patients Characteristics

Third decade (<30 years old)					Third decade (<30 years old)				
No	Gender	Age	Duration	Location	No	Gender	Age	Duration	Location
1	M	24	3 M	T	1	M	35	3 M	c
2	F	23	4 M	Rb	2	M	30	1 M	Rs
3	M	29	11M	RbP	3	F	33	11M	Rs
4	M	29	2 M	Rb	4	F	38	7 M	Rb
5	M	27	4 M	D,S	5	F	36	2 M	S
6	F	27	3 M	S	6	F	36	2 M	S
7	M	23	3 M	T	7	M	33	5 M	S
8	M	28	1 M	Rb	8	F	30	3 M	Rb
9	F	19	6 M	T,S,Ra	9	F	38	3 M	S
10	M	28	8 M	T	10	M	38	8 M	T
					11	M	35	1 M	S
					12	F	30	3 M	RbP
					13	M	34	7 M	Rs
					14	M	37	2 M	Rb
					15	F	37	3 M	Rb

Duration : symptom duration prior to diagnosis. M : male, F : female, C : Cecum, T : Transverse colon, D : Descending colon, S : Sigmoid colon, Rs : Rectosigmoid colon, Ra : upper rectum, Rb : lower rectum, P : anal

Symptoms

All the patients in this study were symptomatic (Table 2). The most common symptoms in both groups were bloody stool, anal bleeding, abdominal pain, or change of bowel habit. A palpable mass was rare.

Distant metastases (Table 3)

At diagnosis, 4 of 10 patients in group A had distant metastases in the liver (3 patients) or in the peritoneum (1 patient). In contrast, only 1 patient in group B had distant disease characterized by peritoneal dissemination. This approached significance ($p=0.064$).

Gross findings of colorectal cancer (Table 4)

The most common types of colorectal cancer in both groups were type 2 (localized-ulcerating type) and type 1 (protuberant type). Only one patient in group B had type 4 (diffuse infiltrating type).

Histologic classification (Table 5)

Eight patients in group A and all 15 patients in group B could be evaluated for histologic type. In the both groups the most common histologic type was well or moderately differentiated adenocarcinoma. In group B, there was 1 patient with poorly differentiated adenocarcinoma and 1 patient with mucinous adenocarcinoma.

Lymph node metastases (Table 6)

Six of 10 patients (60%) in group A had lymph node metastases, and 7 of 15 patients (46.7%) in group B had lymph node metastases. No significant difference existed between the two groups.

Histologic depth of invasion (Table 7)

Seven patients in group A had invasion of the muscularis propria or deeper, and in 11 patients in group B the tumor penetrated through the muscularis.

Table 2. Clinical Symptoms in Young Patients with Colorectal Cancer

Chief complaints	<30 years	30-39 years
	10 patients	15 patients
Bloody stool or anal bleeding	7	11
Change of bowel habit	5	11
Abdominal pain	8	10
Palpable mass	1	2
No symptom	0	0

Table 3. Distant Metastasis

	<30 years 10 patients	30-39 years 15 patients
H ₀	7	15
H ₃	3	0
P ₀	9	14
P ₃	1	1
M(-)	10	15
M(+)	0	0

H₀ : no liver metastases, H₃ : numerous metastases in both lobes, P₀ : no dissemination, P₃ : marked dissemination in the remote peritoneum, M(-) : no metastases to the remote extraperitoneal organs, M(+): positive metastases to the remote extra-peritoneal organ(s) and positive cervical lymph node.

Table 4. Gross Findings of Colorectal Cancer

Gross type	<30 years 10 patients	30-39 years 15 patients
	0	0
1	2	4
2	7	10
3	0	0
4	0	0
5	0	0
Unknown	1	0

0 : superficial type, 1 : protuberant type, 2 : localized-ulcerating type, 3 : infiltrating-ulcerating type, 4 : diffuse infiltrating type, 5 : special type. Gross type in one patient was judged only by endoscopy.

Table 5. Histologic Classification of Colorectal Cancer

Histologic type	<30 years	30-39 years
	10 patients	15 patients
Well-differentiated ad.	3	5
Moderately differentiated ad.	5	8
Poorly differentiated ad.	0	1
Mucinous carcinoma	0	1
Unknown	2	0

ad. : adenocarcinoma

Table 6. Microscopic Lymph Node Metastases

Lymph node	<30 years	30-39 years
	10 patients	15 patients
n(-)	4	8
n ₁ (+)	1	3
n ₂ (+)	2	1
n ₃ (+)	1	1
n ₄ (+)	0	1
Unknown	2	1

n(-) : no metastases, n₁(+) : metastases in group 1 lymph nodes, n₂(+) : metastases in group 2 lymph nodes, n₃(+) : metastases in group 3 lymph nodes, n₄(+) : metastasis in group 4 lymph nodes

Table 8. Cancer stage

stage	<30 years	30-39 years
	10 patients	15 patients
I	3	3
II	0	4
III	0	4
IV	1	2
V	6	2

* Japanese classification

Cancer stage (Table 8)

In group A, 7 of 10 patients had stage IV or V (Japanese Research Society staging), whereas 4 of 15 patients in group B stage IV or V. This difference approaches statistical significance, $p < 0.10$. There was no significant difference in Dukes stage between two groups.

Table 7. Histologic Depth of Invasion

Depth	<30 years	30-39 years
	10 patients	15 patients
m	0	2
sm	1	2
pm	2	0
ss, a ₁	0	4
s, a ₂	3	3
si, ai	2	4
Unknown	2	0

m : carcinoma is limited to within the mucosa, sm : within the submucosa, pm : within the profer muscle, ss or a₁ : carcinoma reaches the submucosal layer or adventitia, s or ai : carcinoma infiltrates the other organs.

Dukes	<30 years	30-39 years
	10 patients	15 patients
A	3	6
B	1	2
C	6	7

* Dukes classification

Table 9. Curability of the Operation for Patients with Colorectal Cancer

Curability	<30 years	30-39 years
	10 patients	15 patients
Absolute curative resection	4	11
Relative curative resection	1	1
Relative noncurative resection	1	1
Absolute noncurative resection	2	2

Absolute curative resection : The n(+) number is smaller than R number. Relative curative resection : When the complete removal of a cancer seems feasible, this is called a relative curative resection. Absolute noncurative resection : When carcinoma definitely remains in situ, it is called an absolute noncurative resection.

Table 10. The Incidence of Associated Colon Polyp(s) or Polyposis

	<30 years 10 patients	30-39 years 15 patients
Polyp(-)	4	12
Polyp(+)	1	3
Polyposis	4	0
Unknown	1	0

Curability of the operation (Table 9)

Two patients in group A had a laparotomy without tumor resection. Four patients (40%) in this group had an absolute curative resection, while 11 of 15 patients (73.3%) in group B an absolute curative resection. Although the curability of patients in group A was low, this difference between two groups was not statistically significant.

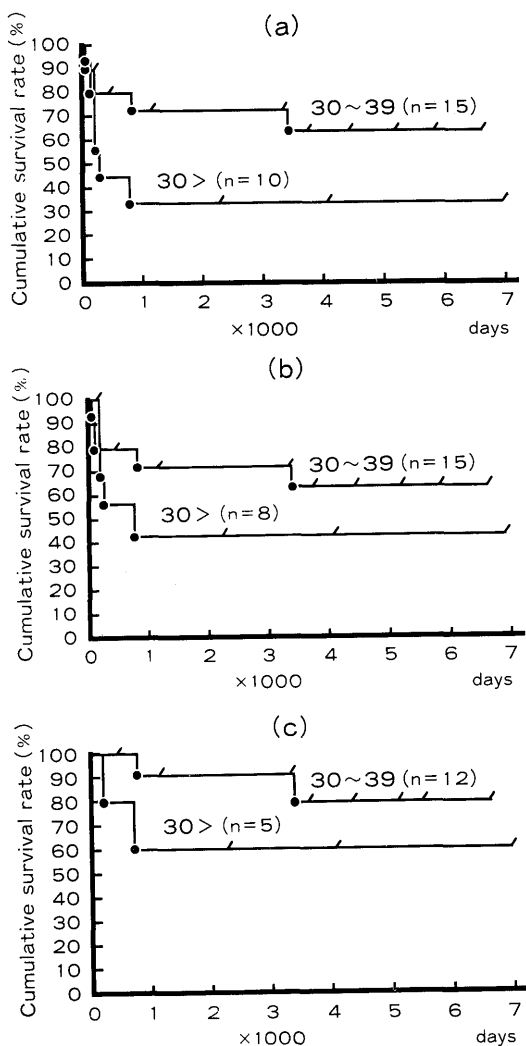


Fig 1. a: The overall cumulative survival rate in young adults with colorectal cancer.
 b: The cumulative survival rate in patients undergoing resection.
 c: The cumulative survival rate in patients having curative resections.

Incidence of associated colon polyp(s) or polyposis (Table 10)

One patient in group A had colon polyp(s), and 3 patients in group B. colon polyp(s). In contrast, 4 patients in group A had colon polyposis, but none of the patients in group B had colon polyposis. The incidence of polyposis in group A was significantly higher than that in group B ($p < 0.02$).

Prognosis

The cumulative survival rate of all patients in group A was 32% at 5 years, with a median survival of 83.7 months. In group B, the overall 5-year survival rate was 64%, with a median survival of 152.1 months. Patients in group B had a higher survival rate than patients in group A, but this difference was not significant ($p = 0.17702$). In patients having tumor resection, the 5-year survival rates in group A and B were 42% and 64%, respectively, and following a curative resection, the 5-year survival rates were 60% and 80%, respectively (see Figure 1).

Discussion

The definition of age in young patients with colorectal cancer remains controversial. Many reports have selected patients younger than 40 years of age, but some reports have limited selection younger than 30. Katho et al. found that the survival rate among patients less than 40 years old were similar(5), and that compared to older patients, patients younger than 40 years of age tended to have a poorer prognosis, more advanced stage, and a high incidence of peritoneal dissemination or lymph node metastases (6). However, Okumoto et al. found that patients younger than 30 years of age had a high

incidence of poorly differentiated adenocarcinoma (7) and colon polyposis, which may suggest that hereditary factors play a stronger etiologic role in this age group (8).

Many authors have reported no difference in the gender ratio in early-onset colon cancer (3,7,8,9,10,11), but there have been reports of female (6) or male predominance (12). We observed a difference in sex ratios between group A (male dominance) and group B patients. The duration of symptoms prior diagnosis may reflect a delay in diagnosis and has been reported to correlate adversely with survival rates (10,13). In our study, the duration of symptoms was identical in patients in group A and B. In both groups, the most common symptoms were bloody stool or anal bleeding, abdominal pain, and change of bowel habit. Most tumors were located in the rectosigmoid, which is compatible with previous reports (7,11,14,15). The characteristic gross findings and histologic types found in young adults with colorectal cancer have been reported to be infiltrating ulcerating type or diffuse infiltrating type (6) and poorly differentiated or mucinous tumors (3,6,7,8,10,14,16,17,18). These characteristics may be a reason for the prognosis of young adult patients with colorectal cancer is poor. Our patients did not have such characteristics. However, another poor prognostic factor is far advanced stage such as Dukes C or B, including distant metastases (peritoneal dissemination and liver metastases) (6,14,19). Our data showed a high incidence of distant metastases and advanced stage in patients in group A, but not group B. Therefore, the tumors of patients less than 30 years old have more biologically aggressive characteristics.

It has been reported that the 5-year survival rates in young adult patients with colorectal cancer are 23% (18), 30% (3), 33% (9), 41% (14), or 44.4% (7). These survival rates are similar to our data for patients in group A. However, the 5 year survival rate of patients in group B was 64%. This difference could be due to the more advanced tumors in group A. However, in patients undergoing curative resection, the 5-year survival rate has been reported to be 51% (20), 53% (9), 70% (18), 71.6% (14), or 75% (7). These survival rates are similar to the survival rates in

patients older than 40. In our study, the 5-year survival rate in group B (80%) was slightly better than the survival rate in group A (60%).

Mayo et al. (11) reported that 42 of 126 patients diagnosed with colorectal cancer at an age less than 30 had colon polyposis. This strongly suggests that hereditary factors play an etiologic role in patients diagnosed in the third decade. We observed 4 patients with colon polyposis in group A, but none in group B.

Finally, although our numbers were small, there were differences in the sex ratio, cancer stage, prognosis, and incidence of colon polyposis between patients diagnosed with colorectal cancer in the third and fourth decades. Thus, "less than 30 years of age" may be the appropriate definition of "young adult" in patients with colorectal cancer.

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