

Colorectal Cancer in Patients Older than 75 Years of Age

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Abstract: Five hundred and nine patients who underwent surgery for colorectal cancer during 1970-1988 at the First Department of Surgery, Nagasaki University School of Medicine, were studied retrospectively to compare the clinicopathological features in 65 cases older than 75 years of age and 409 ranged from 40 to 75 years of age. Older patients revealed a high frequency of right-sided tumors including the transverse colon (32.3%). The older patient group presented with a fewer Dukes stage D in 3.1% of cases compared with 16.4% of the middle age group with low incidences of hepatic metastasis ($p < 0.05$), but there were no significant differences in lymph node involvement and peritoneal dissemination. A few vascular invasion was found on histologic examination in the older group, but no significant differences in the frequency of gross appearance, cell differentiation, lymphatic invasion were observed among two groups. DNA ploidy pattern in the older group was also similar to that in the middle age group. The overall perioperative mortality rate was 1.4% (older: 1.5%; control: 1.5%; not significantly). Curative resection rates were 84.6% in older and 76.0% in middle age patients. Overall 5-year survival rate were 65.4% in older and 54.1% in control group. However, 14.5% of the older patients died from non-cancer related causes. The 5-year survival rate by exclusion of these cases was 72.4% with similar rate of the control group. This study suggests that age should no longer be considered a major risk factor for surgical outcome in colorectal cancer, and that the preoperative indication and careful preoperative assessment including operative risks may improve the patient's survival.

Key Words: Crohn's disease, aptoid ulcer, longitudinal ulcer, cobblestone appearance.

Introduction

The number of elderly people is increasing in Japan. In 1990, the National Institute of Statistics and Economic Studies census found 1,480,000 Japanese people older than 65 years of age. There will be 3,200,000 in the year 2020 and the rate of older people seems to increase from 12% in 1990 to 23% in 2020. Colorectal cancer in our country also

increases in frequency with increasing age. Hirayama postulates that colorectal cancer will be the first leading cause of death as well as gastric cancer in men and the second behind breast cancer in women¹⁾. On the other hands, many authors have reported increased cardiorespiratory problems in older patients and have estimated mortality to be two to five times greater in the elderly, a cause of poor prognosis²⁻⁵⁾. However, the recent studies suggest that the prognosis for patients in this age group may be similar to that reported on the general population^{6,7)}. We have attempted to analyse the patients with colorectal carcinomas in order to determine if there are any different clinicopathologic characteristics of colorectal cancer in patients over age 75 years compared to those from 40 to 75 years of age, and to review our experience with prognosis in this population.

Patients and Methods

Five hundred and nine consecutive patients from the First Department of Surgery, Nagasaki University School of Medicine with a histologic diagnosis of carcinoma of the colon and rectum who had resection of their primary tumor were reviewed retrospectively for clinical characteristics and surgical outcome.

In accordance with the World Health Organisation Classification of Elderly People and geriatric classifications, the minimum age was set at 75 years old⁸⁾. Of these 509, 66 (13%) were older than 75 years of age (old group) and 409 (80.4%) ranged from 40 to 75 years of age (control group) at the time of diagnosis and/or operation. The two groups were compared with respect to age, sex, distribution of tumors, hepatic metastasis, peritoneal dissemination, histologic classification, lymphnode metastasis, Dukes' classification, rate of curative resection, and prognosis. The study reports the results of patients for the period 1970 to 1988, inclusive, with follow-up to the end of December

1989.

Cellular DNA content was also measured in paraffin-embedded materials from 235 cases of colorectal cancer available by flow cytometry (FCM) according to the Schutte's method⁹.

Pathological findings were evaluated on the basis of the General Rules for Clinical and Pathological Studies on Cancer of Colon, Rectum and Anus¹⁰. However, pathologic staging was done according to the Astler-Coller system, with stage D added for distant metastasis¹¹.

Survival was estimated from the date of resection of the tumor until death from any cause. Censored patients were alive at the last follow-up. Differences between survival curves were assessed for statistical significance using the Kaplan-Meier method. Differences in pathologic factors of the groups were analyzed by Students' t test. Results were reported as statistically nonsignificant when the P value was greater than 0.05.

Results

Age and sex: The general age distribution is given in Table 1. The average age of men was 59.9 years and of women, 60.3 years. There was a large number of patients in their 50s and 60s. The mean age of the older was 78.5 years. The men to women ratio was 1.2:1 in the old group and 1.3:1 in the control group.

Tumor location: The primary site tumor was shown in Table 2. There was a higher incidence of rectal tumors in

Table 1. Age and Sex Distribution of 509 Cases with Colorectal Carcinoma

Age	No.	Men	Women
20-29	4	2	2
30-39	31	14	17
40-49	68	43	25
50-59	117	64	53
60-69	169	87	82
70-79	97	55	42
80-89	22	14	8
90-	1		1
Total	509	279	230

Table 2. Site Distribution of Colorectal Carcinoma

Site	> 75 yrs		40-75 yrs	
	No.	%	No.	%
Caecum	7	10.8	28	6.8
Ascending colon	6	9.2	30	7.3
Transverse colon	8	12.3	19	4.6
Descending colon	2	3.1	18	4.4
Sigmoid colon	15	23.1	120	29.3
Rectum	25	38.5	175	42.8
Anus	2	3.1	19	4.6
Total	65	100	409	100

the two age groups (38.5% in the older and 42.8% in control group). However, the distribution differed slightly between the two age groups; a higher frequency of the right-sided tumors including the transverse colon was found in the older group, but the frequency of the left-sided tumors was not significantly different among the two groups.

Pathologic features

Gross appearance: The type of Borrmann 2 was the most common type in the two groups with the incidence about 70% (Table 3). However, there was no significant difference in the frequency of the other types between the two groups.

Table 3. Macroscopic Findings of Colorectal Carcinoma

Macroscopic Findings	> 75 yrs		40-75 yrs	
	No.	%	No.	%
Early cancer	2	3.1	11	2.7
Advanced cancer				
Borrmann 1	9	13.8	41	10.0
Borrmann 2	46	70.8	289	70.7
Borrmann 3	7	10.8	63	15.5
Unclassified	1	1.5	5	1.2
Total	65	100	409	100

Cell differentiation: In the older group, the tumors were well-differentiated adenocarcinoma in 26.2% of cases, moderately differentiated in 55.4%, poorly differentiated in 7.7%, mucinous in 6.2% and undifferentiated in 3.1% of cases (Table 4). There were no significant difference in each types between the two age groups.

Table 4. Histological Findings of Colorectal Carcinoma

Histology	> 75 yrs		40-75 yrs	
	No.	%	No.	%
Adenocarcinoma				
Well	22	33.8	166	40.5
Moderately	31	47.7	200	48.9
Poorly	5	7.7	19	4.6
Mucinous carcinoma	4	6.2	17	4.2
Undifferentiated	2	3.1	4	1.0
Others	1	1.5	2	0.5
Total	65	100	409	100

Microscopic vascular and lymphatic invasion (v-, ly-factor): The older group microscopically presented 44.6% of positive venous invasion and 72.3% of positive lymphatic invasion of cancer cells, of which vascular invasion was significantly fewer than that in the control groups ($p < 0.05$) (Table 5).

DNA analysis: Of 65 older patients, 31 (47.7%) had aneu-

Table 5. Microscopic Invasion of Venous and Lymphatic Vessels in Colorectal Carcinoma

Microscopic Invasion	> 75 yrs		40-75 yrs	
	No.	%	No.	%
Venous				
v (-)	36	55.4	184	45.0
v (+)	29	44.6	225	55.0*
Lymphatic				
ly (-)	18	27.7	91	22.2
ly (+)	47	72.3	318	77.8
Total	65	100	409	100

* p < 0.05

ploid tumors and 34 (52.3%) had diploid tumors, whereas 134 out of 235 patients (59.8%) in the control group had aneuploid tumors and 90 (40.2%) had diploid tumors. There was no significant difference in the frequency of aneuploid tumors between the two groups.

Lymph node involvement: The frequency of lymph node involvement was 44.6% in the older group and 49.1% in the control group. The metastasis in the intermediate or more distant lymph nodes were 26.2% in the older group and 24.9% in the control group (Table 6). These positive involvements between two groups were not significant.

Table 6. Lymphnode Involvement of Colorectal Carcinoma

Grade of lymph node Involvement	> 75 yrs		40-75 yrs	
	No.	%	No.	%
n ₁	36	55.4	208	50.9
n ₁	12	18.5	89	21.8
n ₂	15	23.1	77	18.8
n ₃	2	3.1	24	5.9
n ₄	0	0	11	0.2
Total	65	100	409	100

Hepatic metastasis and peritoneal dissemination: Hepatic metastasis reviewed on the basis of macroscopic findings at operation was found in 3.1% of the older group and 10.8% of the control group with significant difference (p < 0.05), but there was no significant difference in the frequency of peritoneal dissemination between the two groups (Table 7).

Duke's staging: Analysis of the classification of the patients according to Duke's staging failed to show any significant difference with respect to the two age groups. However, there was a tendency of fewer stage D tumors in the older group than in the control group (3.1% vs 16.4%) (Table 7).

Operation and Survival

The overall perioperative mortality was 1.4 percent (7 of 509 cases). The older patients had 1.5 percent (1 of 65 cases) and the control group 1.5 percent (6 of 409 cases) perioperative mortality. The difference was not significant.

Table 7. Tumor Stage According to Duke's Classification and Metastasis

Duke's stage	> 75 yrs		40-75 yrs	
	No.	%	No.	%
A	22	33.8	118	28.9
B	13	20.0	79	19.3
C	28	43.1	145	35.5
D	2	3.1*	67	16.4
Total	65	100	409	100
Metastasis				
Hepatic	2	3.1	49	10.8
Peritoneal	2	3.1	21	5.2

* p < 0.05

A majority of the mortality in either group was directly attributed to surgery. The rate of curative resection in the older group (84.6%) was higher than that in the control group (76.0%).

The overall 5-year survival rate was 65.4% in the older group and 54.1% in the control group. The survival rate after curative resection in the older group was 83.8% at 3 years, 72.4% at 5 years and 63.7% at 7 years (Fig. 1). Of these, 14.5% of the patients died from non-cancer related causes. All of the non-curative cases died during the first 3 years.

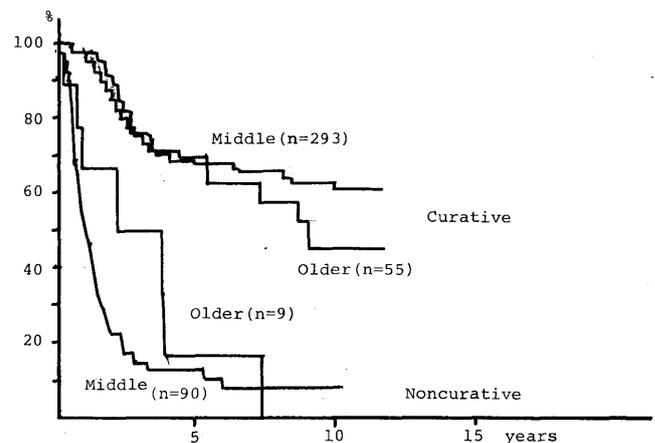


Fig. 1. Survival curves after curative resection in patients with colorectal carcinoma
Older: patients over 75 years of age
Middle: patients ranging from 40 to 75 years of age

Discussion

The present series showed that the incidence peaks in patients in their 50s and 60s at the time of operation. However, patients older than 75 years of age accounts for 13% of the cases (65 out of 509 cases), which was similar to the incidence of Japanese series (13.1%)¹²⁾. Although some investigators have proposed defining the age range

for older patients with colorectal cancer as being more than 70 years of age^{3,9}, the majority of recent series have referred to the age more than 75 years as the appropriate age range for older patients. These papers were reported in accordance with the World Health Organisation Classification of Elderly people and geriatric classifications⁹.

The incidence of patients older than 75 years of age which were reported from Japan, United States and Europe were listed in Table 8. Although the frequency in Japanese series varied from 12.4 to 17.3%, a high frequency was observed in the United States and Europe. Concerning sex distribution in our series, there were many males as females as in colorectal cancer series from all ages. Nevertheless, some authors have reported a greater proportion of males to females in elderly patients^{5,13}.

Table 8. Incidence of Colorectal Carcinoma in Patients Aged 75 Years and Older. Comparison Between Series (Japan, United States, Europe)

Authors	Year	No. of patients	%	Male/Female
Machiki et al ⁶	1991	114	12.4	1:1.59
Sakurai et al ⁷	1990	61	18.7	30:31
Kanda et al ²⁰	1986	144	17.3	77:67
Urakawa et al ¹⁷	1990	47	17.3	—
Umeda et al ²¹	1990	30	14.9	11:19
Japanese series ¹⁰	1987	6,326	13.1	—
Bader et al ⁸	1986	96	46.4	—
Payne et al ¹³	1986	310	30.4	75:25
Ozoux et al ¹⁹	1990	154	—	75:79
Present series	1992	65	13.0	1.2:1

A progressive increase in the frequency of sigmoid lesions has been observed for the general population in Japan¹⁴. However, some series reported a higher proportion of lesions to be right-sided in older patients^{3,5,8,13,15}. In our series, localisation to the left colon remains predominant, but there was a tendency of higher frequency of right-sided colon compared to the control group.

Cancers in the elderly patient are often advanced as seen in most series including patients of all ages. Some authors reported that a higher frequency of liver metastasis, involvement of adjacent organs and lymphatic metastasis were found in the older patients compared with the younger patients^{6,7}. However, Yasutomi et al reported that there were no significant difference of pathologic findings between older and young patients, and stated this results as these three factors being characteristically found in cancers in colon and rectum of all ages¹⁶. In agreement with Yasutomi's report, we found that no significant differences for clinicopathologic factors among older and control patients were recognized, but a fewer incidence of Dukes D including hepatic metastasis and microscopic vascular invasion was observed. Many authors postulate that well-differentiated, localized tumors with slow growth occur in older patients, based on the findings of a higher percentage

of Borrmann 1 and 2 type's cancers^{6,7,16}. However, in our series, there was no significant difference for macroscopic findings or cell differentiation between older and middle age patients.

Recently, many reports have suggested that the DNA content of the tumor was important for the prognosis, but a few have been studied on colorectal tumors of the older patients. In our data, 52 percent were diploid and 48 percent were aneuploid tumors, in which this frequency was similar to that in the middle age population. However, the effect of DNA content of tumors on prognosis of the patients should be confirmed by additional data based on a large group of patients.

Attitudes to operation on the elderly have changed in recent years, and results have improved with better facilities for intensive care and introduction of new technology. In our series, the rate of curative resection for older patients with colorectal cancer was comparable to those obtained in middle age patients (84.6% vs 76.0%) as well as the other series^{6,7,17}.

The perioperative mortality of older patients in large series varied from none to 14.9% (Table 9). In our series, there was only one patient (1.5%) who was a 94-year-old woman undergoing emergency surgery because of abdominal wall abscess due to the direct invasion of cecal cancer.

Table 9. Review of Studies Concerning Surgical Results of Colorectal Carcinoma in Patients Aged 75 Years and Older

Authors	Perioperative mortality (%)	5-year survival (%)
Machiki et al	5.3	47.4
Sakurai et al	1.6	87.5
Kanda et al	9.0	52.9
Urakawa et al	14.9	—
Umeda et al	0	30
Bader et al	7.1	—
Payne et al	9.0	30.0
Ozoux et al	11.9	26.0
Present series	1.5	72.4

Survival comparison with control patients is difficult because a large number of deaths in elderly people are due to intercurrent causes, being 14.5% in our series. However, the five-year survival rate by exclusion patients with non-cancer related deaths after curative resection appears to be even better in the older than that in middle age patients (72.4% vs 68.7%, not significantly). Many authors consider age to be a negative factor, but when one compares survival with that of a aged similarly population, the prognosis seems to be equal to or even better than in younger patients^{2,5,13,18}. Our data suggests that curative resection Dukes staging may be a significant prognostic factor as they are in general population.

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