

Original Research Article

## Higher Body Mass Index Is a Simple Favorable Non-cancer Prognostic Marker for Japanese Elderly Colorectal Cancer Patients after Curative Resection

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### Abstract

**Objectives:** In elderly colorectal cancer (CRC) patients, preoperative surgical indications can be controversial in some cases depending on the patient's physical condition. In comparison with younger patients, both cancer-specific survival (CSS) and non-CCS (NCSS) have an impact on the prognosis and both CSS and NCSS should be considered in the preoperative assessment. We aimed to investigate the impact of body mass index (BMI) on CSS and NCSS in Japanese elderly CRC patients.

**Methods:** We retrospectively collected data from 471 Japanese elderly patients ( $\geq 80$  years) with stage I-III CRC who underwent curative surgery from 1998 to 2017. A Kaplan-Meier survival analysis with propensity score matching (PSM) and a multivariate Cox regression analysis were performed.

**Results:** After PSM, 123 higher BMI ( $\geq 23$ ) and 123 lower BMI ( $< 23$ ) cases were matched. The higher BMI group had significantly better survival than the lower BMI group regarding NCSS and overall survival (OS;  $P < .001$  and  $P < .001$ , respectively). The multivariate survival analysis further confirmed that the higher BMI group had significantly better survival than the lower BMI group regarding CSS, NCSS, and OS ( $P = .027$ ,  $P < .001$ , and  $P < .001$ , respectively).

**Conclusions:** In Japanese elderly patients with stage I-III CRC who underwent curative surgery, preoperative higher BMI was a significant and simple favorable prognostic predictor, especially for NCSS and OS.

### Keywords

body mass index, colorectal cancer, elderly, non-cancer-specific survival, octogenarian

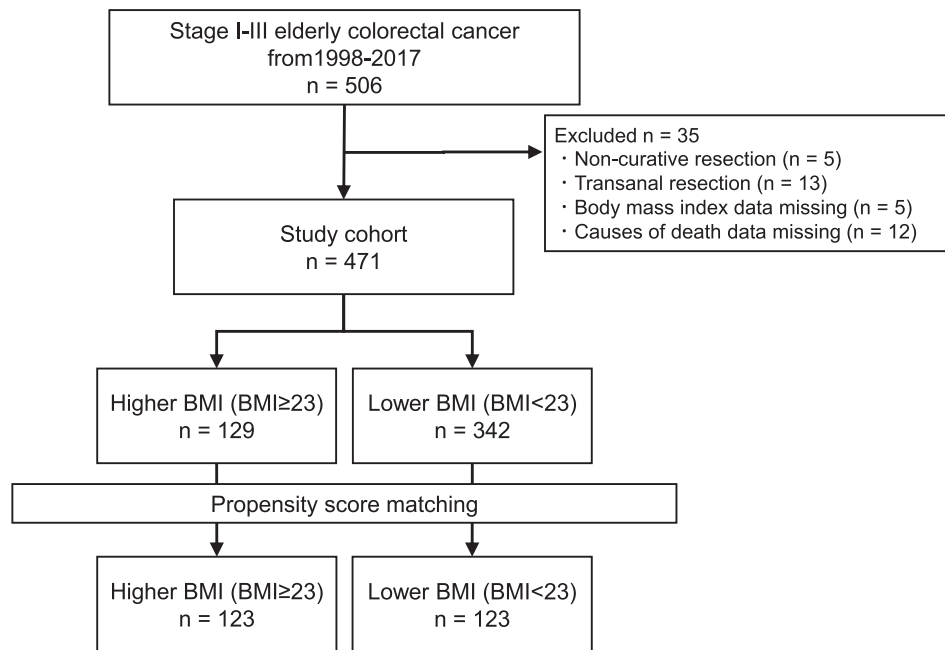
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### Introduction

Colorectal cancer (CRC) is the second leading cause of cancer-related death worldwide[1]. The risk of CRC is highest at around 70 years of age, and 75% of colon tumors are found in patients of  $\geq 65$  years of age[2]. With the increase in age in the general population in developed countries and increasing life expectancy, the incidence of CRC in elderly patients is likely to increase worldwide[3,4].

Recently, accumulated studies have shown that the cancer-specific survival (CSS) of elderly CRC patients was not in-

ferior to that of younger patients and that there is no definitive relationship between malignant aggressiveness and age; however, the overall survival (OS) of elderly CRC patients was worse than that of younger CRC patients[5,6]. Most elderly CRC patients have other comorbidities, such as cardiovascular and pulmonary disease, and decision-making regarding surgical indications for elderly CRC patients can be difficult in some cases as the life expectancy of such patients may be short. Considering the operative risks in elderly patients, not only CSS but also non-cancer-specific survival (NCSS) should be considered[5,7,8]. That is, in elderly



**Figure 1.** Flow diagram of patient disposition. The following variables were used for propensity score matching between the higher body mass indexes (BMI) and lower BMI groups: age, sex, location of lesion, serum carcinoembryonic antigen level, histological type, surgical approach, American Society of Anesthesiologists Performance Status, adjuvant chemotherapy, postoperative complications, and stage.

patients, a careful preoperative assessment of the patient's general physical condition and life expectancy-including NCSS-should be performed.

The body mass index (BMI) is a simple indicator of general physical condition and is associated with all-cause mortality in the general population[9,10]. In general, all-cause mortality depends on the degree of overweight and obesity, as defined by the WHO; obesity (BMI  $\geq 30$ ) is unfavorable and is associated with increased mortality[9,11]. However, BMIs within the overweight range (BMI: 25.0 to  $<30$ ) were favorable among healthy people, regardless of age and were not associated with a significant increase in mortality risk among elderly people[9,12]. In Japanese healthy people of 65-79 years of age, people with BMI  $\geq 23$  had a better prognosis than those with BMI  $< 23$ [13]. Thus, it is hypothesized that a relatively higher BMI (e.g.,  $\geq 23$ ) is preferable for Japanese elderly CRC patients; however, few reports have analyzed the association between the prognosis and BMI among elderly CRC patients[14]. The present study was designed to elucidate the relationship between BMI and the prognosis-including both CSS and NCSS-in elderly CRC patients who received curative resection.

## Methods

### Study design and participants

In this single-center retrospective study, we retrospectively reviewed 506 consecutive elderly CRC patients who underwent colorectal surgery at Toyonaka Municipal Hospital between January 1998 and December 2017. The inclusion criteria were histologically diagnosed adenocarcinoma of the colon or rectum, performance of curative resection, age of  $\geq 80$  years, and Union for International Cancer Control (UICC) Stage I-III (UICC 8<sup>th</sup> edition). Among the 506 consecutive patients, 35 were excluded because of non-curative resection (n = 5), transanal resection (n = 13), and missing data (n = 17; [causes of death data missing, n = 12; BMI data missing, n = 5]). Finally, we analyzed 471 elderly patients with stage I-III CRC who underwent curative surgery. The patient selection flowchart is shown in Figure 1.

Patient data were extracted from medical records. We extracted recorded data, including age, sex, BMI, American Society of Anesthesiologists (ASA) Performance Status, preoperative tumor markers, surgical procedures, postoperative complications including any grade by Clavien-Dindo classification of surgical complication, histological type and its associated TNM category, whether postoperative adjuvant chemotherapy was performed, cause of death, and survival period[15]. We defined CSS as the survival period until

death from primary CRC and defined NCSS as the survival period until death from diseases other than primary CRC. The median follow-up period was 4.03 (interquartile range [IQR]: 1.80-5.49) years. The patients were divided into the following two groups: those with a BMI of  $\geq 23$  kg/m<sup>2</sup> (higher BMI group; n = 129) and those with a BMI of  $< 23$  kg/m<sup>2</sup> (lower BMI group; n = 342). The patient background data are shown in Table 1.

This study was conducted in accordance with the Declaration of Helsinki and was approved by the Institutional Review Board of the Toyonaka Municipal Hospital (approval number: 2020-08-07). All data were subject to strict privacy policies, and the opt-out recruitment method was applied to provide all patients an opportunity to decline to participate. The need for informed consent was waived due to the retrospective nature of the study.

### Propensity score matching

A propensity score-matched (PSM) analysis was performed using a logistic regression model. The following 10 variables were matched: age, sex, surgical approach, serum carcinoembryonic antigen level, ASA Performance Status, tumor location, histological type, TNM stage, adjuvant chemotherapy, and postoperative complication. One-to-one matching was performed by using a caliper width of 0.20 of the standard deviation of the log of the propensity score.

### Statistical analysis

Continuous parameters are presented as the median, interquartile range. The Wilcoxon rank sum test and Fisher's exact test were used for comparisons, as appropriate. The Kaplan-Meier method was used to estimate survival and a log-rank test was used to assess the estimated survival. Hazard ratios (HRs) were estimated using Cox proportional-hazards model and the 95% confidence interval (CI) was calculated. All statistical analyses were carried out using JMP Pro version 11.2.0 (SAS Institute Inc., Cary, NC, USA). Statistical significance was assessed using the 95% CI. In all analyses, two-tailed *P*-values of  $< .05$  were considered statistically significant.

## Results

### Baseline data before and after matching between the higher BMI and lower BMI groups

Table 1 shows the baseline data of all patients (n = 471) and of the PSM patients. A total of 129 (27.4%) patients were classified into the higher BMI group and 342 (72.6%) into the lower BMI group. Before matching, differences were observed between these groups in the age ( $P = .017$ ), surgical approach ( $P < .001$ ), and ASA ( $P < .001$ ). After matching, 123 patients were matched to each of the two

groups; the patient characteristics of the matched groups were similar ( $P > .05$ ; Table 1).

### Patient survival after matching between the higher BMI and lower BMI groups

After PSM, the 5-year CSS rates in the higher and lower BMI groups were 87.7% and 79.2%, respectively, the 5-year NCSS rates were 89.7% and 73.6%, and the 5-year OS rates were 78.6% and 58.2%. The log-rank test showed that there was no significant difference between the higher BMI and lower BMI groups in CSS ( $P = .097$ ; Figure 2a).

The log-rank test showed that there were significant differences between the higher BMI and lower BMI groups in NCSS and OS ( $P < .001$  and  $P < .001$ , respectively; Figure 2b, 2c).

### Analysis of the risk factors

To investigate the risk factors associated with CSS, NCSS and OS, univariate and multivariate Cox regression hazards analyses of all elderly CRC patients were performed (Table 2). Lower BMI (HR 1.862,  $P = .027$ ), stage III (HR 4.443,  $P < .001$ ), and presence of postoperative complications (HR 2.215,  $P = .002$ ) were significantly associated with poor CSS in a univariate analysis. Lower BMI (HR 2.588,  $P < .001$ ), male sex (HR 1.606,  $P = .008$ ), ASA3-5 (HR 1.971,  $P < .001$ ), open approach (HR 1.653,  $P = .018$ ), and absence of adjuvant chemotherapy (HR 5.749,  $P < .001$ ) were significantly associated with poor NCSS in a univariate analysis. Lower BMI (HR 2.279,  $P < .001$ ), male sex (HR 1.449,  $P = .009$ ), ASA3-5 (HR 1.718,  $P < .001$ ), stage III (HR 1.476,  $P = .009$ ), open approach (HR 1.456,  $P = .021$ ), and the presence of postoperative complications (HR 1.676,  $P = .001$ ) were significantly associated with poor OS in a univariate analysis.

An additional multivariate analysis showed that lower BMI was the only independent risk factor for all types of survival as follows: CSS (HR 1.867; 95% CI 1.069-3.496;  $P = .027$ ), NCSS (HR 2.331; 95% CI 1.451-3.949;  $P < .001$ ), and OS (HR 2.230; 95% CI 1.541-3.324;  $P < .001$ ).

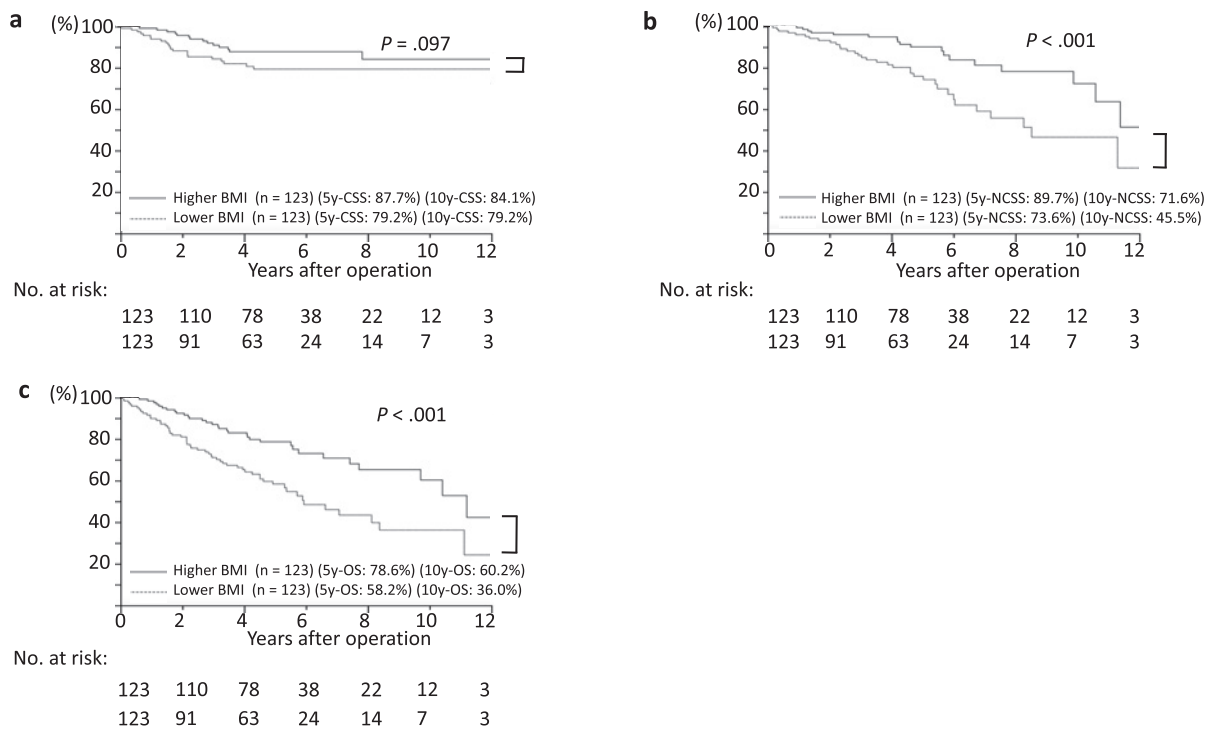
### Causes of death

Table 3 shows the causes of death after surgery. Before matching, significant differences were observed in the total number of deaths between the higher BMI and lower BMI groups ( $P < .001$ ). There were no significant differences in causes of death (e.g., death from primary cancer or death from other disease) between the groups ( $P = .433$ ). Among stage I patients, no significant differences were observed in the total number of deaths between the groups ( $P = .098$ ), and no significant difference was observed in the causes of death between the groups ( $P = 1.000$ ). Among stage II patients, a significant difference was observed in the total number of deaths between the groups ( $P = .004$ ), but no

**Table 1.** Patient Baseline Data before and after Propensity Score Matching.

Characteristic	Overall cohort			After matching		
	Higher BMI (n = 129)	Lower BMI (n = 342)	P Value	Higher BMI (n = 123)	Lower BMI (n = 123)	P Value
BMI, mean (IQR)	24.5 (23.8-25.5)	20.1 (18.4-21.5)	<.001***	24.5 (23.8-25.5)	20.1 (18.4-21.9)	<.001***
Age, mean (IQR)	83 (81-85)	84 (81-87)	.017*	83 (81-85)	82 (81-85)	.847
Sex						
Male, n (%)	64 (49.6)	157 (45.9)	.535	60 (48.8)	55 (44.7)	.609
Female, n (%)	65 (50.4)	185 (54.1)		63 (51.2)	68 (55.3)	
Approach						
Laparoscopic	66 (51.2)	114 (33.3)	<.001***	61 (49.6)	59 (48.0)	.899
Open	63 (48.8)	228 (66.7)		62 (50.4)	64 (52.0)	
CEA, median (IQR)	4.5 (2.5-7.6)	4.4 (2.6-9.2)	.858	4.3 (2.5-7.6)	3.9 (2.4-6.4)	.329
ASA						
1, n (%)	13 (10.1)	45 (13.2)	<.001***	13 (10.6)	13 (10.6)	1.000
2, n (%)	94 (72.9)	179 (52.3)		89 (72.4)	89 (72.4)	
3, n (%)	21 (16.3)	111 (32.5)		20 (16.3)	20 (16.3)	
4, n (%)	1 (0.8)	6 (1.8)		1 (0.8)	1 (0.8)	
5, n (%)	0	1 (0.3)		0	0	
Tumor Location						
Right-sided colon, n (%)	60 (46.5)	171 (50.0)	.789	57 (46.3)	57 (46.3)	1.000
Left-sided colon, n (%)	35 (27.1)	87 (25.4)		34 (27.6)	34 (27.6)	
Rectum, n (%)	34 (26.4)	84 (24.6)		32 (26.0)	32 (26.0)	
Histological type						
Tub	108 (83.7)	296 (86.5)	.460	104 (85.5)	100 (81.3)	.612
Non-tub	21 (16.3)	46 (13.5)		19 (15.5)	23 (18.7)	
UICC 8 <sup>th</sup> Stage						
I, n (%)	28 (21.7)	66 (19.3)	.429	27 (22.0)	27 (22.0)	.811
IIA, n (%)	57 (44.2)	127 (37.1)		53 (43.1)	48 (39.0)	
IIB, n (%)	4 (3.1)	21 (6.1)		4 (3.3)	5 (4.1)	
IIC, n (%)	1 (0.8)	10 (2.9)		1 (0.8)	2 (1.6)	
IIIA, n (%)	26 (20.2)	78 (22.8)		25 (20.3)	26 (21.1)	
IIIB, n (%)	8 (6.2)	20 (5.9)		8 (6.5)	5 (4.1)	
IIIC, n (%)	5 (3.9)	20 (5.9)		5 (4.1)	10 (8.1)	
Present, n (%)	6 (4.7)	19 (5.6)	.820	5 (4.1)	6 (4.9)	1.000
Absent, n (%)	123 (95.3)	323 (94.4)		118 (95.9)	119 (95.1)	
Postoperative complication						
Absent, n (%)	86 (66.7)	251 (73.4)	.169	84 (68.3)	86 (69.9)	.890
Present, n (%)	43 (33.3)	91 (26.6)		39 (31.7)	37 (30.1)	

BMI, body mass index; IQR, interquartile range; CEA, carcinoembryonic antigen; ASA, American Society of Anesthesiologists; Tub, tubular adenocarcinoma.  
\* P-value <.05, \*\* P-value <.01, \*\*\* P-value <.001



**Figure 2.** Kaplan–Meier curves of the higher body mass index (BMI) and lower BMI groups for (a) cancer-specific survival (CSS), (b) non-cancer-specific survival (NCSS), and (c) overall survival (OS) after propensity score matching. Using a log-rank test, significant differences were identified between the higher BMI and lower BMI groups’ NCSS and OS ( $P < .001$  and  $< .001$ , respectively).

significant difference was observed in the causes of death between the groups ( $P = .542$ ). Among stage III patients, a significant difference was observed in the total number of deaths between the groups ( $P = .009$ ), while no significant difference was observed in the causes of death ( $P = .344$ ).

After matching, significant differences were observed in the total number of deaths between the higher BMI and lower BMI groups ( $P = .003$ ). There were no significant differences in the causes of death between the groups ( $P = .655$ ). Among stage I patients, no significant difference was observed between the groups in the total number of deaths ( $P = .148$ ), and no significant difference was observed in the causes of death ( $P = 1.000$ ). Among stage II patients, there were no significant differences in the total number of deaths between the groups ( $P = .070$ ), and no significant difference was observed in the causes of death ( $P = .713$ ). Among stage III patients, there were no significant differences in the total number of deaths between the groups ( $P = .169$ ), and no significant difference was observed in the causes of death ( $P = 1.000$ ).

### Discussion

In elderly CRC patients, decision-making regarding the indication of surgery is difficult in some cases. A previous study recommended that age should not detract from offer-

ing optimal therapy to patients with good risk factors[16]. In contrast to young patients, elderly patients require careful preoperative assessment, which considers not only CSS but also NCSS. In elderly CRC patients, non-cancer death (e.g., death from cardiovascular disease, lung disease, or cerebrovascular disease) stably increases and the impact of non-cancer death on OS is significant[7]. The impact of NCSS on OS makes it more difficult to make a correct preoperative assessment in elderly patients.

Considering the impact of age on CRC patients, although several studies have addressed the prognosis of elderly CRC patients, whether age is a definitive independent prognostic factor in CRC remains controversial[6,8,14,17]. These controversies might be due to the variation of patient characteristics that could be confounding factors for age[8]. In addition to the variable distribution of patient characteristics, the impact of NCSS is expected to have an effect on the analysis of the prognosis. While, NCSS in elderly CRC patients who receive curative surgery is rarely studied. In this study, to evaluate the prognosis in elderly CRC patients more precisely, we included CSS, NSCC, and OS in our prognostic evaluation.

Regarding the impact of NCSS on the prognosis in elderly CRC patients, our findings showed that NCSS had a greater impact on OS than CSS had in elderly CRC patients underwent curative surgery (Figure 2). Furthermore, al-

**Table 2.** Univariate and Multivariate Cox Regression Hazards Analyses of Risk Factors for Overall Survival.

Factors	Univariate				Multivariate			
	CSS	NCSS	OS	OS	CSS	NCSS	OS	OS
	HR (95% CI)	HR (95% CI)	HR (95% CI)	HR (95% CI)	HR (95% CI)	HR (95% CI)	HR (95% CI)	P Value
Higher BMI (≥23)	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	<.001***
Lower BMI (<23)	1.862 (1.070-3.473)	2.588 (1.628-4.348)	2.279 (1.590-3.369)	2.230 (1.541-3.324)	1.867 (1.069-3.496)	2.331 (1.451-3.949)	2.230 (1.541-3.324)	<.001***
Female	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	.017*
Male	1.209 (0.760-1.924)	1.606 (1.132-2.288)	1.449 (1.096-1.917)	1.408 (1.064-1.866)	Ref.	1.651 (1.162-2.357)	1.408 (1.064-1.866)	.005***
CEA levels ≤5 ng/ml	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	.392
>5 ng/ml	1.580 (0.988-2.533)	0.946 (0.644-1.335)	1.133 (0.850-1.504)	1.133 (0.850-1.504)	Ref.	Ref.	Ref.	.027*
ASA 1-2	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	.021*
3-5	1.330 (0.802-2.149)	1.971 (1.383-2.798)	1.718 (1.289-2.277)	1.453 (1.069-1.969)	Ref.	1.563 (1.069-2.284)	1.453 (1.069-1.969)	.017*
Colon	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	.209
Rectum	1.259 (0.742-2.062)	1.201 (0.806-1.752)	1.222 (0.892-1.653)	1.222 (0.892-1.653)	Ref.	Ref.	Ref.	.126
Tub	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	.382
Non-tub	1.445 (0.739-2.593)	1.334 (0.771-2.173)	1.378 (0.909-2.015)	1.378 (0.909-2.015)	Ref.	Ref.	Ref.	.265
Stage I-II	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	<.001***
III	4.443 (2.760-7.327)	0.719 (0.470-1.068)	1.476 (1.105-1.961)	1.363 (1.018-1.815)	4.042 (2.501-6.690)	Ref.	Ref.	.009**
Approach Lap	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	.021*
Open	1.219 (0.7493-2.041)	1.653 (1.086-2.600)	1.456 (1.058-2.036)	1.088 (0.768-1.560)	Ref.	1.268 (0.804-2.051)	1.088 (0.768-1.560)	.313
Adjuvant chemotherapy (+)	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	<.001***
(-)	1.465 (0.610-2.980)	5.749 (1.828-34.96)	1.795 (0.974-3.791)	1.717 (1.260-2.318)	6.172 (1.955-37.45)	Ref.	Ref.	.062
Post-operative complication (-)	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	.001**
(+)	2.215 (1.362-3.543)	1.406 (0.970-2.059)	1.676 (1.234-2.252)	1.676 (1.234-2.252)	2.370 (1.244-3.283)	Ref.	Ref.	.005***

CSS, cancer specific survival; NCSS, non cancer specific survival; OS, overall survival; CI, confidence interval; BMI, body mass index; CEA, carcinoembryonic antigen; ASA, American Society of Anesthesiologists; Tub, tubular adenocarcinoma; Lap, laparoscopic

\* P-value <.05, \*\* P-value <.01, \*\*\* P-value <.001



**Table 3.** Causes of Death after Surgery before and after Propensity Score Matching.

	Overall cohort			After matching		
	Higher BMI (n = 129)	Lower BMI (n = 342)	<i>P</i> value	Higher BMI (n = 123)	Lower BMI (n = 123)	<i>P</i> value
Total number of deaths, n (%)	33 (25.6)	166 (48.5)	<.001***	32 (26.0)	55 (44.7)	.003**
Death from primary cancer	14	58	.433	14	21	.655
Death from other diseases	19	108		18	34	
Other cancer death	7	25	N.A.	7	8	N.A.
Respiratory disease	0	14		0	8	
Heart disease	1	10		1	2	
Gastroenterological disease	0	6		0	1	
Renal and urinary disease	0	5		0	0	
Brain-related disease	1	3		0	1	
Sudden death	1	3		1	0	
Aortic rupture	1	1		1	1	
Senile decay	0	2		0	0	
Unknown other than cancer	8	39		8	13	
Stage I (n = 94)	28	66		27	27	
Total number of deaths	6	27	.098	6	12	.148
Death from primary disease	0	1	1.000	0	1	1.000
Death from other disease	6	26		6	11	
Stage II (n = 220)	62	158		58	55	
Total number of death	15	73	.004**	14	23	.070
Death from primary disease	5	19	.542	5	6	.713
Death from other disease	10	54		9	17	
Stage III (n = 157)	39	118		38	41	
Total number of deaths	12	66	.009**	12	20	.169
Death from primary disease	9	38	.344	9	14	1.000
Death from other disease	3	28		3	6	

BMI, body mass index; N.A., not analyzed.

\* *P*-value <.05, \*\* *P*-value <.01, \*\*\* *P*-value <.001

though cancer-related death rarely occurred at more than 5 years after surgery, non-cancer-related death occurred constantly over time (Figure 2). Global epidemiological data suggest that the ratio of non-cancer-related death is higher than that of cancer-related death[18]. As for epidemiology in Japan, cancer is the leading cause of death among people of 45-94 years of age[19]. However, the ratio of cancer-related death to all-cause death decreases in people of ≥85 years of age[19]. These results may support our finding that NSCC had a large impact on the prognosis of elderly CRC patients who received curative surgery. Although few previous reports described NCSS, OS is affected by NCSS because OS represents the combination of CSS and NSCC. In a previous study, the Kaplan-Meier curves for OS and CSS in elderly CRC patients resembled those of our study, and this result implied that the balance of the impact of NCSS and CSS on OS was consistent with our results[14].

BMI is an indicator of the physical condition and among Japanese healthy people 65-79 years of age, those with a BMI of ≥20 have a better prognosis compared with those with a BMI of <20 have[13]. In this study, our results

showed that lower BMI was associated with significantly worse OS and NCSS in elderly CRC patients who received curative surgery. A previous multicenter study of elderly CRC patients also showed that BMI is a useful prognostic factor and that lower BMI is associated with worse OS and CSS[14]. Therefore, our finding that elderly CRC patients with higher BMI values had a better prognosis than those with lower BMI values was thought to be reasonable. Furthermore, in this study, to precisely evaluate the impact of BMI on prognosis, we included NCSS in the analysis of elderly CRC patients who received curative surgery. Although-as described above-the impact of BMI on OS and CSS in elderly CRC patients was previously reported, there have been no studies on the impact of BMI on NCSS in elderly CRC patients[14]. In the present study, the hazard ratio of higher BMI for NCSS was 2.588 (*P* < .001) and that for CSS was 1.862 (*P* = .027). The log-rank test after PSM showed that lower BMI tended to be associated with worse CSS, but not significantly, whereas lower BMI was associated with significantly worse NCSS. These results also implied that BMI has a greater impact on NSCC than on

CSS in elderly CRC patients after curative surgery.

In this study, both the analysis with PSM and the multivariate analysis showed the tendency to be an independent association between lower BMI and poor CSS in elderly CRC patients. This result was similar to that of a previous study that found that lower BMI is independently associated with poor CSS in elderly CRC patients[14]. Although the result that lower BMI was associated with worse CSS is not definitive in this study and is difficult to interpret, we considered that one possible explanation was the association with sarcopenia. Sarcopenia is significantly and progressively associated with the risk of advanced colorectal neoplasia, and this association may be explained by metabolic factors that could be potential mediators of the effect of sarcopenia and cancer progression[20]. Another hypothesis is that treatment after cancer recurrence might have impacted CSS. Although we analyzed the impact of adjuvant chemotherapy, we did not analyze treatment after recurrence. Moreover, tolerability of treatment after recurrence might have been associated BMI status. Our finding, that a high BMI was preferable for CSS, NCSS, and OS may suggest that preoperative interventions to improve BMI values, such as rehabilitation and nutritional support, have the potential to improve the CSS, NSCC, and OS in elderly CRC patients.

Analyses of the causes of death showed that the number of deaths among patients with lower BMI was significantly greater than that among patients with higher BMI. The causes of death in the lower BMI and higher BMI groups did not differ to a statistically significant extent, although the ratio of the death from CRC in comparison to that from other diseases in the higher BMI group tended to be slightly greater than that in the lower BMI group. Regardless of the BMI, the analyses of the causes of death according to stages showed that the rate of non-CRC death was greater than that of CRC death in stages I-II and that the rate of CRC death was greater than that of non-CRC death in stage III. When planning the follow-up after curative surgery in elderly patients with stage I-II CRC, it may be effective to focus on non-CRC disease over CRC recurrence.

The present study had several limitations. First, this was a single-center retrospective study, although PSM was used to balance the variables that may influence the outcomes. However, our results were compatible with a previous multicenter study that also used PSM and we believe our results were reasonable[14]. Second, the present investigation was based on data from Japanese elderly patients. In general, Japanese individuals have lower BMI values in comparison to Europeans and North and South Americans[21]. Although there are few Japanese people with severe obesity (BMI  $\geq$  35) and there were no patients with severe obesity in this study, the rate of severe obesity is greater in other countries[22]. Severe obesity could have an adverse impact on

the prognosis, and we hypothesize that our results would not be directly applicable to non-Asian patients[23]. Our results may imply that relatively higher BMI that does not exceed the threshold for the definition of severe obesity is preferable to low BMI in terms of prognosis. The desirable threshold would vary in each country and race. Although the mean BMI of Japanese people is 22.7 and the threshold of the present study in Japanese elderly patients was 23, a higher threshold, such as 25 or more, may be favorable in Western countries[21,24]. The adaptation of the findings of the present study to other countries requires further studies in other countries and with other ethnicities. Third, in the present study we did not evaluate other reported prognostic factors, such as the prognostic nutritional index or the risk analysis index[25,26]. However, while these factors require complicated calculations, the calculation and evaluation of preoperative BMI is very simple[25,26]. Fourth, the median follow-up period was 4.03 (IQR: 1.80-5.49) years and the follow-up period was not long enough to discuss 5-year survival rate. Based on the Japanese Society for Cancer of the Colon and Rectum guidelines, we followed up patients for up to 5 years after surgery in principle[27]. However, some patients were censored or died and the median follow-up period was shorter than 5 years. Furthermore, there were a certain number of patients who did not wish to be followed up due to their old age. To discuss long-term prognosis, a longer follow-up period is desirable.

In conclusion, we found that higher BMI was a strong and independent favorable prognostic factor, especially for OS and NCSS. Preoperative BMI can be a simple and useful tool for predicting prognosis after curative surgery in elderly patients with CRC.

#### Conflicts of Interest

There are no conflicts of interest.

#### Author Contributions

HT contributed to the conception, the design, the acquisition, analysis, and interpretation of data, drafting and revising of the work. SN, YS, KO, YY, MY, JS, TK, HI, TI, NT, and KD contributed to the acquisition and analysis of data, and drafting or revising the work. All authors approved the final manuscript.

#### Approval by Institutional Review Board (IRB)

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Approved by the IRB of the Toyonaka Municipal Hospital

This study was performed in accordance with the Declaration of Helsinki.

#### Disclaimer

Naohiro Tomita is the Deputy Editor-in-Chief of Journal of the Anus, Rectum and Colon and on the journal's Edito-



rial Board. He was not involved in the editorial evaluation or decision to accept this article for publication at all.

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