Original Article

Colorectal cancer surgery in elderly patients 80 years and older: a comparison with younger age groups

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Background: A reduction in complications and mortality can be observed over the last few decades among elderly patients in the early postoperative period for colorectal cancer (CRC) surgery, but long-term outcomes are largely unknown. This study aimed to investigate the long-term outcomes of elderly patients 80 years and older after CRC surgery in comparison with younger age groups. The influence of clinical, oncological, and physical parameters on outcome were retrospectively analyzed.

Methods: A total of 346 patients underwent CRC surgery with curative intent between January 2013 and December 2017. Patients were divided into three age groups: younger than 60 (n=47), between 60 and 79 (n=218), and 80 and older (n=81). Clinicopathological variables including comorbidity, modified frailty index, prognostic nutrition index (PNI), operative/postoperative data, and outcome including cause of death were compared among age groups. To identify factors associated with death from CRC and other causes, univariate and multivariate analyses using the Cox proportional hazards model were performed.

Results: Immediate postoperative morbidity of patients with Clavien-Dindo grades of III or greater (16.0%) and the 30-day mortality rate (2.5%) of patients 80 years and older were not statistically different from those of younger age groups. Long-term disease-free survival was also similar among age groups, suggesting CRC surgery provides oncological benefit to patients irrespective of age. Multivariate analysis revealed that R1 resection, advanced tumor stage, carcinoembryonic antigen (CEA) level of >5 ng/mL, undifferentiated tumor, and longer postoperative hospital stay were risk factors for CRC death. Long-term overall survival was significantly reduced in comparison to younger age groups. Seventy percent of deaths in elderly patients during follow-up were primarily from respiratory failure and cardiovascular disease. Multivariate analysis demonstrated that advanced age, frailty, low PNI, and open procedure were risk factors for other causes of mortality.

Conclusions: Elderly patients undergoing CRC surgery appeared to enjoy similar oncological benefits as younger age groups. Since both modified frailty index and PNI were correlated with mortality unrelated to CRC, preoperative assessment of these factors can be important for predicting outcome and selecting patients for prehabilitation.

Keywords: Elderly patients 80 years and older; colorectal cancer surgery; other causes of death; colorectal cancer death; frailty

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Introduction

The number of people reaching old age is rapidly increasing worldwide. According to the World Population Prospects from the United Nations, people 65 years and older now comprise more than 20% of the world's population. In Japan, that figure has climbed to nearly 30% over the last three decades, with life expectancy reaching 81 for males and 87 for females. This increase in life expectancy is accompanied by a higher incidence of malignancies (1), one of which is colorectal cancer (CRC). In Japan, CRC is the most common type of cancer and the second highest cause of cancer-related death after lung cancer (2). More than 150,000 new CRC cases are diagnosed annually in Japan, 80% of which are over 60 and 20% are over 80 years old, and one-third of these patients are lost each year (3). The incidence of CRC in the elderly is increasing across Japan (1) at a rate similar to other countries (4).

Curative resection with adjuvant chemotherapy is the standard treatment for CRC, but there has been some debate on whether surgery with curative intent should be performed on elderly patients. This age group tends to receive either less aggressive treatment or palliative surgery due to the higher incidence of complications and mortality (4-6). However, an evolving trend over the last two decades has revealed a significantly improved short-term survival rate after CRC surgery in patients over 65 years. The 30-day mortality rate has also dropped from 6 times as high (4) to 3 times as high (7) as younger age groups. For patients 75 years and older, Ketelaers *et al.* (8) recently reported that the rate fell from 5.8% [2006–2012] to 1.2% [2013–2017], a figure similar to younger age groups. It appears that age per se is not a risk factor that affects short-term outcome in elderly patients undergoing CRC surgery (9-11). Improvement of surgical procedures (laparoscopic over open surgery), preoperative assessments, and perioperative management have contributed to these trends, and CRC surgery will remain an important treatment modality as the elderly population continues to expand.

Physical and nutritional impairments have a decidedly negative impact on outcome after surgery (12,13). Frailty, sarcopenia, hypoalbuminemia, and other comorbidities are often seen among elderly patients undergoing both general surgery and CRC resection. Dolan *et al.* reported that sarcopenia, found in 19.6% of CRC elderly patients, correlated with more postoperative complications and higher mortality (14). Comorbidity was also identified as an independent risk factor for morbidity and mortality (15). Although these features were important in predicting outcome after CRC surgery in the elderly, most of these studies included patients over 65 years and limited postoperative follow-up to within 1 year. Although a few studies reported on long-term outcome after CRC resection, they lacked detailed analyses on the causes of patient death and the correlation with preoperative conditions.

In the present study, we aimed to determine the long-term outcome of elderly patients 80 years and older after CRC surgery in comparison with younger age groups, as well as to clarify the influence of oncological and physical parameters on their outcome. We present the following article in accordance with the STROBE reporting checklist (available at https://jgo.amegroups.com/article/view/10.21037/jgo-21-627/rc).

Methods

The present study was performed retrospectively on 346 patients (median age 70.5 years; range, 29–103 years) who underwent elective colorectal resection with curative intent (R0 and R1 resection) for primary colon cancer (n=283) or rectal cancer (n=63) between January 2013 and December 2017 at St. Mary's Hospital. Patients with stage IV CRC (n=67) and those who underwent emergency surgery (n=23) were excluded from the study. Informed consent was obtained from individual patients and all data was collected retrospectively. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013) and was approved by the institutional review board of St. Mary's Hospital in Kurume, Japan (approval number 20-0701).

Patients were divided into three age groups: younger than 60 (n=47), between 60 and 79 (n=218), and 80 years and older (n=81), as younger age, elderly age, and very elderly age group, respectively, as previously reported (9,16-18). Preoperative data included gender, comorbidity (cardiovascular disease, hypertension, cerebral disease, renal disease, respiratory disease, diabetes mellitus, liver disease, cancer in other organs), American Society of Anesthesiologists Physical Status (ASA-PS) class, body mass index (BMI), and preoperative blood tests [hemoglobin, albumin, carcinoembryonic antigen (CEA), and prognostic nutrition index (PNI) calculated as 10 × serum albumin (g/dL) + 0.005 × total lymphocyte count (/mm^3)] (19). The modified frailty index was determined by four comorbid conditions and one

functional variable (13,20): a history of chronic obstructive pulmonary disease, congestive heart failure within 30 days of operation, diabetes mellitus requiring oral agents or insulin, hypertension requiring medication, and functional health status before operation (independent, partially independent, dependent). Each variable represents 1 point, for a total possible score of 5 points. A score of 2 or greater indicates frailty status (21). Intraoperative data included blood loss, operation time, and surgical method (open *vs.* laparoscopic). Tumor-related data included tumor location (right-sided/cecum to splenic flexure, left-sided/splenic flexure to sigmoid colon, or rectum), tumor margin status (R0/R1), tumor differentiation (well and moderate/poor and mucin), and tumor stage according to the 7th edition of the Union of International Cancer Control (UICC) (22). Immediate postoperative data included length of hospital stay, morbidity as denoted by a Clavien-Dindo class of III or greater (23), mortality within 30 days, and use of adjuvant chemotherapy. Parameters for postoperative outcome included mortality at 1 and 5 years in addition to cause of death, from which overall survival and disease-free survival rates were determined. Cause of death was categorized into CRC-related and "other", which encompassed respiratory disease, cardiovascular disease, other primary cancer, sepsis, etc. The median follow-up period was 45.6 months (range, 0.2–92.1 months).

Statistical analysis

Values were expressed as frequency and percentage. Differences in the categorical variables among the three age groups were compared using the Chi-square test or Fisher's exact test as appropriate. Overall and disease-free survival rates were analyzed with the Kaplan-Meier method using the log-rank test. Overall survival was defined as the period from the date of surgery to the date of last follow-up or death. Disease-free survival was defined as the duration from surgery to the date of CRC recurrence. Statistically significant variables from the univariate analysis were subsequently tested by multivariate analysis using the Cox proportional hazards model to determine the association between the individual determinants and death from CRC and other causes, and the effect of each variable was assessed by the hazard ratio (HR) and 95% confidence interval (95% CI). A P value of less than 0.05 was considered to be statistically significant. All statistical analyses were performed using the JMP software package (version 13.0, SAS Institute, Cary, NC, USA).

Results

Preoperative characteristics of CRC patients

Differences in preoperative features among the three age groups are shown in *Table 1*. Of the 346 patients, 47 (13.6%) were younger than 60 years, 218 (63.0%) were between 60 and 79 years, and 81 (23.4%) were 80 years and older, respectively. Female patients prevailed in the oldest age group, while males dominated in the two younger groups. There was no significant difference in BMI among the three groups. Patients in the 80+ age group had a higher occurrence of comorbidity and both a higher ASA-PS class and modified frailty index than the other age groups. In addition, laboratory studies revealed that this age group had significantly lower levels of PNI, hemoglobin, and albumin along with significantly higher levels of CEA than those in the younger groups.

Surgical achievements were similar among the three groups (*Table 2*). There were no statistical differences in laparoscopic *vs.* open surgery, amount of blood loss, or duration of operation. Investigation for tumor-related factors revealed that while rectal cancer saw a higher incidence among younger patients, CRC in patients 80 years and older was more often right-sided (male: 15/49 and female: 34/49). Pathological examination of resected specimens according to UICC classification showed no differences in tumor stage and differentiation among groups (*Table 2*). Although all patients underwent surgery with curative intent, 26 specimens revealed residual tumor cells on the tumor margin (R1) across all groups: 2 (4.3%), 17 (7.8%), and 7 (8.6%) respectively. R0 resection rates followed at 95.7%, 92.2%, and 91.4% respectively. There was no significant difference in R0 resection among groups.

Short-term outcome

Table 3 illustrates differences in the immediate postoperative course among the three age groups. The duration of hospital stay after surgery (mean ± standard deviation) was 17.2±15.6 days in the younger than 60 group, 20.9±17.7 days in the 60–79 group, and 21.8±17.1 days in the 80 and older group, revealing that the oldest age group required significantly longer hospital stays after surgery. Immediate postoperative morbidity in patients with a Clavien-Dindo class of III or greater (16.0%), and 30-day mortality (2.5%) in patients 80 years and older were not statistically different from those of younger age groups; however, elderly patients faced more complications and higher mortality than younger age groups. Two patients over 80 years died within

Table 1 Preoperative characteristics of colorectal cancer patients according to age group

Characteristic	N	<60 years (n=47), n (%)	60–79 years (n=218), n (%)	≥80 years (n=81), n (%)	P value
Gender					<0.001
Male	199	27 (57.4)	141 (64.7)	31 (38.3)	
Female	147	20 (42.6)	77 (35.3)	50 (61.7)	
Comorbidities					<0.001
No	87	31 (66.0)	50 (22.9)	6 (7.4)	
One or more	259	16 (34.0)	168 (77.1)	75 (92.6)	
ASA-PS class					<0.001
1	120	37 (78.7)	70 (32.1)	13 (16.0)	
≥2	226	10 (21.3)	148 (67.9)	68 (84.0)	
Modified frailty index					<0.001
0–1	208	44 (93.6)	128 (59.0)	36 (44.4)	
≥2	138	3 (6.4)	90 (41.0)	45 (55.6)	
BMI (kg/m^2)					0.524
<25	270	36 (76.6)	167 (76.6)	67 (82.7)	
≥25	76	11 (23.4)	51 (23.4)	14 (17.3)	
PNI					<0.001
<40	90	5 (10.6)	46 (21.1)	39 (48.1)	
≥40	256	42 (89.4)	172 (78.9)	42 (51.9)	
Hb (g/dL)					<0.001
<11	136	12 (25.5)	75 (34.6)	49 (60.5)	
≥11	210	35 (74.5)	143 (65.4)	32 (39.5)	
Alb (g/dL)					<0.001
<3.5	105	7 (14.9)	57 (26.1)	41 (50.6)	
≥3.5	241	40 (85.1)	161 (73.9)	40 (49.4)	
CEA (ng/mL)					0.038
<5	198	26 (55.3)	135 (61.9)	37 (45.7)	
≥5	148	21 (44.7)	83 (38.1)	44 (54.3)	

ASA-PS, American Society of Anesthesiologists Physical Status; BMI, body mass index; PNI, prognostic nutrition index; Hb, hemoglobin; Alb, albumin; CEA, carcinoembryonic antigen.

30 days after surgery from heart failure and aspiration pneumonia. Adjuvant chemotherapy was administered postoperatively to patients across all age groups who were eligible for treatment: 26 (81.3%), 84 (58.3%), and 4 (6.5%).

Long-term outcome

The median follow-up period was 45.6 months, with a range of 0.2–92.1 months. The breakdown by group is as follows: 46.7 months for the younger than 60 group, 48.3 months for the 60–79 group, and 33.3 months for the 80 years and older group. During follow-up, 59 patients (17.1%) developed local or distant metastases: 19.1% in the younger than 60 group, 17.4% in those between 60 and 79, and 14.8% in the 80 and older group. Of the 346 patients, a total of 60 patients died: 8.5% of those younger than 60, 11.9% of those between 60 and 79, and 37.0% of those 80 and older. Of the 30 deaths in the oldest group, 9 were directly from CRC and the remaining 21 were from other causes. These causes included respiratory disease (30.0%),

Table 2 Surgical data and tumor characteristics of colorectal cancer according to age group

Characteristic	N	<60 years (n=47), n (%)	60–79 years (n=218), n (%)	≥80 years (n=81), n (%)	P value
Surgical procedure					0.538
Laparoscopic surgery	271	34 (72.3)	174 (79.8)	63 (77.8)	
Open surgery	75	13 (27.7)	44 (20.2)	18 (22.2)	
Blood loss (mL)					0.529
<150	239	32 (68.1)	147 (67.4)	60 (74.1)	
≥150	107	15 (31.9)	71 (32.6)	21 (25.9)	
Operation time (min)					0.189
<270	154	23 (48.9)	89 (40.8)	42 (51.9)	
≥270	192	24 (51.1)	129 (59.2)	39 (48.1)	
Tumor location					0.001
Right side (C-T)	139	14 (29.8)	76 (34.9)	49 (60.5)	
Left side (D-Rs)	144	21 (44.7)	99 (45.4)	24 (29.6)	
Rectal	63	12 (25.5)	43 (19.7)	8 (9.9)	
UICC stage					0.259
I/II	219	28 (59.6)	145 (66.5)	46 (56.8)	
III	127	19 (40.4)	73 (33.5)	35 (43.2)	
Tumor differentiation					0.185
Well and moderate	327	44 (93.6)	209 (95.9)	74 (91.4)	
Poor and mucin	19	3 (6.4)	9 (4.1)	7 (8.6)	
Tumor margin status					0.604
R0	320	45 (95.7)	201 (92.2)	74 (91.4)	
R1	26	2 (4.3)	17 (7.8)	7 (8.6)	

UICC, Union of International Cancer Control.

cardiovascular disease (23.8%), other primary cancer (9.5%), sepsis (14.3%), and others such as senility, renal failure or suicide (19.0%). Seventy percent of deaths encountered in patients 80 years and older during the follow-up period were primarily from respiratory failure and cardiovascular disease, not cancer. As shown in *Table 3* and *Figure 1*, there was no significant difference among age groups in disease-free survival, while overall survival was significantly lower in patients 80 years and older (*Table 3*, *Figure 2*).

Factors influencing cause of death

A univariate analysis of CRC death revealed that tumor margin status, UICC stage, CEA, tumor differentiation, postoperative hospital stay, morbidity, BMI, and operative blood loss were significant factors influencing cause of death. Multivariate analysis showed that margin status, UICC stage, CEA, tumor differentiation, and postoperative hospital stay were found to be important risk factors (*Table 4*). Age was not a significant factor for CRC death. A univariate analysis of other causes of death revealed that age, modified frailty index, PNI, surgical procedure, operation time, morbidity, and postoperative hospital stay were significant factors. Age, modified frailty index, PNI, and surgical procedure were found to be significant risk factors for mortality from causes other than CRC through the multivariate analysis.

Discussion

This study aimed to determine the long-term outcome,

Table 3 Short-term outcome, long-term outcome and cause of death in colorectal cancer patients according to age group

Variables	N	<60 years (n=47), n (%)	60–79 years (n=218), n (%)	≥80 years (n=81), n (%)	P value
Short-term outcome					
Postoperative mortality within 30 days	2	0 (0)	0 (0)	2 (2.5)	0.072
Postoperative morbidity within 30 days (Clavien-Dindo ≥ III)	33	2 (4.3)	18 (8.3)	13 (16.0)	0.068
Postoperative hospital stay					0.028
<21 days	254	41 (87.2)	159 (72.9)	54 (66.7)	
≥21 days	92	6 (12.8)	59 (27.1)	27 (33.3)	
Survival at 1 year post-surgery					0.001
Alive	327	46	212	69	
Dead	19	1	6	12	
Long-term outcome					
5-year survival	92	90.8%	86.6%	52.1%	<0.001
5-year disease-free survival	77	78.4%	81.9%	81.7%	0.875
Recurrence at 5 years	59	9	38	12	0.797
Number of deaths at 5 years	60	4	26	30	
Cause of death					<0.001
Colorectal cancer	30	3 (75.0)	18 (69.2)	9 (30.0)	
Other	30	1 (25.0)	8 (30.8)	21 (70.0)	
Cause of other deaths					
Respiratory disease	10		3	7	
Cardiovascular disease	8		3	5	
Other primary cancer	3		1	2	
Sepsis	3			3	
Other	6	1	1	4	

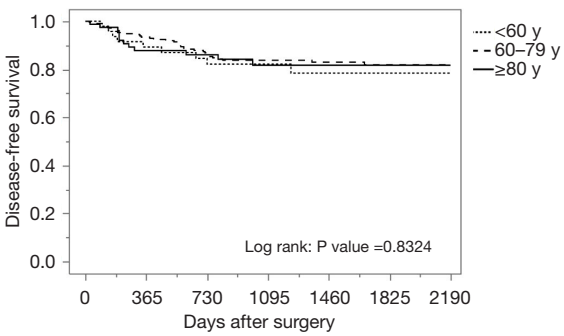

Figure 1 Disease-free survival in patients with colorectal cancer surgery according to age group. There was no significant difference among the three age groups in disease-free survival (P value =0.8324).

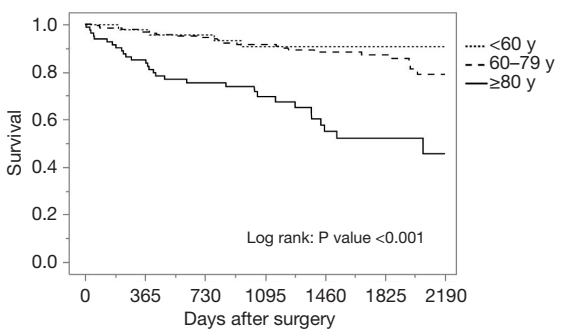

Figure 2 Survival in patients with colorectal cancer surgery according to age group. Overall survival was significantly lower in patients 80 years and older compared to the other age groups (P value <0.001).

Table 4 Univariate and multivariate analyses for deaths after colorectal cancer surgery

Variables	Deaths from colorectal cancer				Deaths from causes other than colorectal cancer			
	Univariate analysis		Multivariate analysis		Univariate analysis		Multivariate analysis	
	HR (95% CI)	P value	HR (95% CI)	P value	HR (95% CI)	P value	HR (95% CI)	P value
Age		0.165				<0.001		<0.001
<60 years	Reference	–			Reference	–		–
60–79 years	1.38 (0.46–5.95)	0.593			2.14 (0.39–39.61)	0.431	0.75 (0.11–14.77)	0.802
≥80 years	2.85 (0.85–12.83)	0.929			16.82 (3.51–301.60)	<0.001	4.93 (0.84–93.78)	0.081
Gender, male	0.88 (0.42–1.89)	0.746			1.56 (0.75–3.48)	0.239		
Modified frailty index ≥2	1.94 (0.92–4.12)	0.081			5.77 (2.60–14.55)	<0.001	3.44 (1.50–9.13)	0.003
PNI <40	1.60 (0.66–3.51)	0.278			4.26 (2.07–8.88)	<0.001	2.48 (1.11–5.61)	0.026
Hb <11 g/dL	1.11 (0.51–2.35)	0.783			1.67 (0.81–3.44)	0.165		
BMI <25 kg/m^2	4.30 (1.29–26.69)	0.014	1.02 (0.25–6.99)	0.976	1.35 (0.59–3.64)	0.503		
CEA ≥5 ng/mL	4.47 (1.87–12.34)	0.001	5.88 (2.05–20.06)	<0.001	1.32 (0.56–3.06)	0.521		
Tumor margin R1	13.13 (6.06–27.72)	<0.001	10.59 (3.97–29.20)	<0.001	3.43 (0.82–9.73)	0.084		
Open procedure	2.12 (0.93–4.55)	0.072			2.97 (1.42–6.15)	0.005	2.44 (1.02–5.91)	0.045
Tumor location		0.533				0.080		
Right side	Reference	–			Reference	–		
Left side	0.75 (0.30–1.80)	0.512			0.68 (0.31–1.42)	0.301		
Rectal	1.28 (0.50–3.18)	0.593			0.24 (0.04–0.86)	0.026		
UICC stage III	5.62 (2.56–13.62)	<0.001	6.00 (2.32–17.14)	<0.001	1.87 (0.89–3.86)	0.098		
Tumor differentiation poor and mucin	4.53 (1.52–11.00)	0.010	7.01 (1.85–25.43)	0.005	0.83 (0.05–3.86)	0.847		
Postoperative hospital stay ≥21 days	3.63 (1.72–7.76)	0.001	5.36 (1.70–17.11)	0.005	2.70 (1.30–5.55)	0.009	1.91 (0.76–4.71)	0.167
Clavien-Dindo class ≥ III	3.16 (1.24–7.10)	0.018	1.05 (0.32–3.55)	0.939	2.71 (1.00–6.22)	0.049	2.45 (0.74–7.70)	0.139
Operation time ≥270 min	1.29 (0.61–2.72)	0.450			3.36 (1.59–7.73)	0.001	2.37 (0.99–6.04)	0.054
Operative blood loss ≥150 mL	3.58 (1.70–7.89)	0.001	1.01 (0.38–2.69)	0.989	1.07 (0.47–2.27)	0.866		

HR, hazard ratio; CI, confidence interval; PNI, prognostic nutrition index; BMI, body mass index; Hb, hemoglobin; CEA, carcinoembryonic antigen; UICC, Union of International Cancer Control.

cause of death, and risk factors in elderly patients 80 years and older undergoing CRC surgery. The results showed that there were no significant differences in short-term morbidity, mortality, or 5-year disease-free survival between elderly patients 80 years and older and patients in younger age groups. R1 resection, advanced cancer stage, presence of pathological undifferentiated tumor, elevated CEA, and longer postoperative hospital stay were identified as risk factors for CRC deaths. In contrast, long-term overall survival was significantly reduced in elderly patients 80 years and older compared to younger age groups. Seventy percent of deaths encountered in patients 80 years and older were primarily from respiratory failure and cardiovascular diseases. Advanced age, frailty, low PNI, and open procedures were important risk factors for deaths from causes other than CRC.

There is an evolving trend demonstrating significant improvement in short-term survival rates after CRC surgery over the last 2 decades. In a systematic review of 34,194 patients conducted in 2000, the Colorectal Cancer Collaborative Group (4) reported that 30-day mortality of patients over 85 years old was 6.2 times higher than that of patients under 65. Eleven years later, an analysis of 19,375 patients by Al-Refaie *et al.* (7) using the American College of Surgeons National Surgical Quality Improvement Program (ACS NSQIP) reported that 30-day mortality of patients over 80 years was only three times higher compared to those in the 40–55 age range. Most recently, Ketalaers *et al.* (8) described improvement in 30-day mortality of patients over 75 years from 5.8% [2006–2012] to 1.2% [2013–2017]. Surgical procedure (laparoscopic *vs.* open surgery), anesthesia, and postoperative management have contributed to this decrease, but CRC surgery for the elderly remains a significant concern as the demographic continues to grow.

Our data showed that patients 80 years and older frequently presented with comorbidity, higher ASA-PS class, advanced modified frailty index, and lower levels of PNI, albumin and hemoglobin. Those between 60–79 years exhibited a similar trend to those under 60 years. Of interest was the female patient population presenting with more right-sided colon cancer and less rectal cancer—a finding similar to previous reports (24). In addition, a higher CEA level in patients 80 years and older might be caused by more right-sided cancer with malignant potential (25,26). Since these characteristics often distinguish elderly patients from their younger counterparts, careful preoperative geriatric assessments including comorbidity, physical activity, and nutritional impairment are important for elderly patients undergoing CRC surgery.

There was no significant difference among age groups in 30-day morbidity. Postoperative morbidity in patients with a Clavien-Dindo class of III or greater, and mortality in patients 80 years and older within 30 days after surgery were 16.0% and 2.5%, respectively—findings that appear relatively low when compared to the 11–31.7% morbidity rate (27-29) and 2–7% mortality rate (28,30). As described by Ketelaers *et al.* (8), these results suggest that short-term outcome after CRC surgery has nearly equalized for older and younger CRC patients, although prolonged length of postoperative stay is required. Despite the absence of significant difference in the frequency of morbidity among age groups, the incidence of anastomotic leakage, paralytic ileus, and pneumonia tended to be higher in patients 80 years and older (data not shown). The frequency of dysphagia, decline of ADLs, and delirium after surgery were also encountered more frequently in the oldest patient group.

There were no statistically significant differences in disease-free survival and recurrence rate among the three age groups. Our study showed that risk factors for CRC death were R1 resection, advanced tumor stage, a CEA level of >5 ng/mL, pathological undifferentiated tumor and longer postoperative hospital stay, all of which were findings similar to previous reports (27,31-33). These results demonstrate that elderly patients undergoing CRC surgery receive oncological benefit. As Papamichael *et al.* previously described (34), radical curative surgery for elderly patients with CRC should not be withheld solely due to advanced age. Virk *et al.* reported the 10-year survival rate for patients undergoing surgery for CRC was 25.45% in the 80–89 age group, while the rate for those who did not receive treatment or surgery was a dismal 0.96% (16).

In our study, the 5-year overall survival rate was 52.1% in patients 80 years and older, which was similar to the 40–58% survival rates reported by others (17,27,33). Based on these results, we believe that advanced age is not a contraindication for surgery in patients with CRC. However, our study showed that seventy percent of deaths encountered in patients over 80 years died of causes not related to CRC during the follow-up period. Major reasons for other causes of death were respiratory failure, especially by aspiration pneumonia, followed by cardiovascular disease and sepsis. A large-scale analysis (4) found a that the incidence of respiratory failure in patients over 85 years was 3 times higher than those under

65 years. Previous studies indicated that aspiration pneumonia is caused by impairments of the swallowing and cough reflexes after experiencing a decrease of muscle strength in swallowing and respiration (18,29). Poor oral health in frail older patients increased the incidence of aspiration pneumonia (35). Furthermore, dysphagia is associated with oral, physical, cognitive and psychological frailty in elderly patients (36,37). In this study, 55.6% of patients 80 years and older who met the criteria for modified frailty experienced dysphagia at a rate of 2.5% (2/81) before surgery and 18.5% (15/81) after surgery (data not shown). Ten (83.3%) of the 12 patients 80 and older who died within 1 year after surgery had experienced difficulty with mobility. Postoperative dysphagia was found in 6 patients (50.0%), modified frailty in 9 patients (75.0%), and low PNI in 7 patients (58.3%) (data not shown). Preoperative frailty, postoperative dysphagia, and deficits in nutritional status are all factors likely establishing aspiration pneumonia as the first leading cause of non-cancer death (38). Emphasis on oral health care and swallowing training might be useful for prevention of aspiration pneumonia in elderly frail patients. A population-based study reported that patients with CRC are associated with an increased risk of cardiovascular death, especially during the first year after diagnosis (39). In this study, 5 of the 8 deaths from cardiovascular disease (62.5%) occurred within 1 year. CRC patients should be screened early after diagnosis for cardiovascular disease.

We found that advanced age, frailty, low PNI, and open procedure were independent risk factors for other causes of death after CRC surgery; however, there are only a few reports that analyze these risk factors. Next to age, modified frailty index was found to be the second most important risk factor for mortality from non-CRC causes. Frailty is a state of vulnerability characterized by an age-associated decline in physiological and functional reserve across multiple organ systems and is associated with a greater risk of adverse postoperative outcomes such as severe complications, decreased long-term survival, higher readmission rates, and longer hospital stays (19), all of which are similar to outcomes in patients with sarcopenia (40,41). Preoperative evaluation of frailty could be a promising risk stratification tool for older patients undergoing general surgery (20). A low preoperative PNI level was found to be the third risk factor for survival and is significantly associated with the incidence of postoperative complications and poor prognosis in patients with CRC after laparoscopic surgery (15). Preoperative assessment of modified frailty index and PNI may help reliably predict both non-CRC related deaths after surgery as well as postoperative complications, which could prove useful when selecting elderly patients undergoing CRC surgery. Those with a higher risk may benefit from prehabilitation therapy before surgery (42). Our data also indicated that a laparoscopic approach to CRC surgery was beneficial for elderly patients, even those with comorbidities and decreased physical activity. This finding was corroborated in a previous report (43,44).

The present study has several limitations. It is a retrospective study that lacks assessment of postoperative quality of life. Patients with stage IV CRC and those who underwent emergency surgery were excluded, which further reduced the relatively small sample size. This limitation may have contributed to the lack of statistical difference in morbidity and mortality among the three age groups. Strengths of this study include the availability of detailed perioperative information on the population undergoing CRC surgery, as well as the promising long-term outcomes identified. In addition, the study highlighted the potential for preoperative evaluation to become a powerful tool in understanding which elderly patients might benefit the most from surgery.

Many elderly patients 80 years and older who undergo CRC surgery experience oncological benefits similar to younger patients, and this holds true even for those near the age of life expectancy. Appropriate preoperative assessment of certain indices such as modified frailty index and PNI can be an important step in selection of patients for CRC surgery and improvement of outcome during recovery. Higher-risk patients may find benefit in prehabilitation therapy, a mode of ancillary treatment currently utilized at our institute.

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Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at https://jgo.amegroups.com/article/view/10.21037/jgo-21-627/rc

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Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://jgo.amegroups.com/article/view/10.21037/jgo-21-627/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. Informed consent was obtained from individual patients and all data was collected retrospectively. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013) and was approved by the institutional review board of St. Mary's Hospital in Kurume, Japan (approval number 20-0701).

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