The Effect of Body Mass Index on the Feasibility of Surgery and Prognosis of Colorectal Cancer Patients Over 80 Years Old

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Abstract

Objective This study aimed to evaluate the safety and feasibility of radical surgery and explore prognostic factors affecting cancer-specific survival (CSS) in colorectal cancer (CRC) patients over 80 years old.

Methods From January 2010 to December 2020, a total of 372 elderly CRC patients who underwent curative resection at the National Cancer Center were enrolled and classified into a control group (BMI <24 kg/m²) and an overweight group (BMI ≥24 kg/m²). Preoperative clinical features, perioperative outcomes and postoperative pathological characteristics were collected and compared between the two groups.

Results The control group and overweight group comprised 219 and 153 patients, respectively. There was no significant difference between the two groups of patients in terms of operative time (153.0 vs 142.3 min, $P=0.226$), intraoperative bleeding (67.8 vs 69.3 ml, $P=0.873$) or other surgical outcomes or grade 3-4 postoperative complications (11.1% vs 14.6%, $P=0.326$). The 5-year CCS of patients in the overweight group was significantly worse than that of the control group (63.3% vs 80.0%, $P=0.046$). The multivariate analysis showed that CCS was significantly affected by BMI (HR: 2.30; 95% CI, 1.27-4.17; $P=0.046$) and N stage (HR: 2.97; 95% CI, 1.48-5.97; $P=0.002$).

Conclusion The results of this study demonstrated that radical resection for CRC is safe and feasible for patients over 80 years of age. The increase in BMI does not increase the difficulty of surgery or postoperative complications. BMI and N stage were independent prognostic factors for elderly CRC patients after radical resection.

Introduction

Colorectal cancer (CRC) is one of the most common causes of cancer death worldwide, and its morbidity and mortality are on the rise^[1, 2]. With the expansion of the population and the improvement of living standards, the ageing of the population continues to increase^[3]. Therefore, in clinical practice, the proportion of older patients receiving surgical treatment for colorectal cancer is increasing. Elderly patients with CRC have unusual clinicopathological features and genetic backgrounds^[4, 5]. In addition, these individuals often have comorbidities such as cardiovascular and cerebrovascular diseases and diabetes and often need more rigorous and prudent standardized management during the perioperative period^[6]. According to the clinical consensus and guidelines, adjuvant treatment such as chemotherapy and radiotherapy is not recommended for CRC patients older than 80 years of age regardless of TNM stage, but traditional prognostic indicators may not be suitable for elderly patients with CRC over 80 years old. Therefore, it is necessary to further investigate the perioperative safety and prognostic factors of elderly patients with CRC after curative resection.

Previous studies have only analysed the prognosis of elderly patients with CRC from a pathologico-anatomical tumour perspective^[8–15]. However, due to their unique clinicopathological characteristics and

lifestyle habits, some of the most common biological characteristics of elderly patients may be ignored, such as comorbidity, and body mass index (BMI), among other habits. In addition, for elderly patients over 80 years old, the proportion of deaths from non-tumour causes is relatively high, so simply calculating the overall survival rate is not sufficiently rigorous. Therefore, the main purpose of the present study was to demonstrate the safety and feasibility of radical surgery for CRC in elderly patients over 80 years of age, to evaluate the prognosis of elderly CRC patients without adjuvant therapy using the tumour-specific survival rate, and to comprehensively explore relevant prognostic factors.

Patients And Methods

From January 2010 to December 2020, all consecutive CRC patients older than 80 years of age who underwent curative resection at the National Cancer Center/National Clinical Research Center for Cancer/Cancer Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, were retrospectively collected and analysed. The inclusion criteria were as follows: (1) age 80 or above; (2) pathologically confirmed colorectal adenocarcinoma; (3) no evidence of distant metastasis; and (4) no adjuvant therapy, such as radiotherapy or chemotherapy, after the operation. Patients who underwent emergency surgery or had other malignant tumours were excluded from the analysis. The study was approved by the Ethics Committee of the Cancer Hospital, Chinese Academy of Medical Sciences and was conducted in accordance with the Declaration of Helsinki and Ethical Guidelines for Clinical Research. All patients provided written informed consent.

All patients were divided into two groups according to BMI: the control group ($\text{BMI} < 24 \text{ kg/m}^2$) and the overweight group ($\text{BMI} \geq 24 \text{ kg/m}^2$). Clinical characteristics, perioperative variables, pathological results and survival outcomes for all patients were obtained from the medical records, operation records, and pathology records in our hospital database. Postoperative complications were assessed using the Clavien-Dindo classification (CD) categories and were defined as any condition that occurs within 30 days after surgery that affects the normal recovery process and requires conservative or surgical intervention^[16]. All procedures were performed by surgeons with more than 20 years of experience in colorectal surgery. The American Joint Committee on Cancer (AJCC, eighth edition) staging system was used for tumour staging.

Follow-up

The long-term outcome of the present study was the 5-year cancer-specific survival (CCS) rate. All patients received a follow-up survey every 2 months for the first 2 years and every 6 months for the next 3 years. The postoperative review examinations included physical examination, biomarkers (CEA and CA-199), CT scans of the chest, abdomen, and pelvis, and colonoscopy if necessary. CCS was defined as the time between the date of surgery and the date of death from cancer. The deadline for follow-up in this study was June 2021.

Statistical analysis

Quantitative data were analysed by the Mann-Whitney U test and are given as the mean $\pm$ standard deviation. Categorical variables were analysed by the chi-squared test and presented as frequencies and percentages. Univariate and multivariate Cox regression models were used to identify the factors predicting CSS. The Kaplan-Meier survival method was performed to analyse the 5-year CCS of the patients in different groups, and significant differences in CCS were compared using the log-rank test. The statistically significant variables ($P < 0.20$) in univariate analysis were subsequently tested by multivariate analysis through a Cox regression model, and the effect of each variable was assessed by the hazard ratio (HR) and 95% confidence interval (95% CI). A P value < 0.05 was considered statistically significant. Statistical analyses were performed using IBM SPSS Statistics software version 24.0 (IBM Corporation, Armonk, NY, USA).

Results

Short-term outcomes

Table 1 summarizes the baseline characteristics of the patients. Among the 372 elderly CRC patients included in this study, 219 were in the control group, and 153 were in the overweight group. In the overweight group, the proportion of patients with ASA grade III was significantly lower than that in the control group (36.6% vs 48.4%, $P = 0.024$). There was no statistically significant difference between the two groups in terms of sex, age, albumin level, HGB level, habits, comorbidities, previous abdominal surgery, or tumour location (all $P > 0.05$).

Table 1
Baseline characteristics

Variables	Overweight group (n = 153)	Control group (n = 219)	P
Gender			0.192
Male	99 (64.7)	127 (58.0)	
Female	54 (35.3)	92 (42.0)	
Age at operation (years old)			0.774
<85	139 (90.8)	197 (90.0)	
≥85	14 (9.2)	22 (10.0)	
ASA score			0.024
II	97 (63.4)	113 (51.6)	
III	56 (36.6)	106 (48.4)	
Preoperative albumin (g/L)			0.680
<35	32 (20.9)	42 (19.2)	
≥35	121 (79.1)	177 (80.8)	
Preoperative HGB (g/L)			0.664
<110	30 (19.6)	47 (21.5)	
≥110	123 (80.4)	172 (78.5)	
Habits			
Drinking	26 (17.0)	46 (21.0)	0.335
Smoking	36 (23.5)	54 (24.7)	0.803
Comorbidity	108 (70.6)	134 (61.2)	0.061
Hypertension	74 (48.4)	96 (43.8)	0.388
Diabetes mellitus	22 (14.4)	26 (11.9)	0.478
Coronary artery disease	18 (11.8)	18 (8.2)	0.255
Arrhythmia	24 (15.7)	46 (21.0)	0.197
Respiratory diseases	22 (14.4)	24 (11.0)	0.324
Other	8 (5.2)	14 (6.4)	0.640
Previous abdominal surgery	30 (19.6)	46 (21.0)	0.742

Variables	Overweight group (n = 153)	Control group (n = 219)	<i>P</i>
Tumor location			0.112
Right colon	36 (23.5)	68 (31.1)	
Left colon and rectum	117 (76.5)	151 (68.9)	

The perioperative outcomes and pathological results are listed in Table 2. More patients in the overweight group underwent laparoscopic surgery (64.7% vs 49.8%, $P = 0.004$). Both groups had similar operative times (153.0 vs 142.3 min, $P = 0.226$) and intraoperative blood loss (67.8 vs 69.3 ml, $P = 0.873$). There was no significant difference between the two groups in terms of overall postoperative complications (29.4% vs 25.1%, $P = 0.358$) or grade III-IV complications (11.1% vs 14.6%, $P = 0.326$). Regarding postoperative recovery, no significant difference was observed between the two groups. Regarding pathological outcome, there was no significant difference between the two groups in terms of T stage, N stage, tumour grade, tumour size, perineural invasion, lymphatic invasion, or number of LNs harvested.

Table 2
Pathological data and perioperative outcome

Variables	Overweight group (n = 153)	Control group (n = 219)	<i>P</i>
T stage			0.395
T1-T2	28 (18.3)	48 (21.9)	
T3-T4	125 (81.7)	171 (78.1)	
N stage			0.133
N0	91 (59.5)	113 (51.6)	
N1-N2	62 (40.5)	106 (48.4)	
Tumor grade			0.087
I	69 (3.9)	22 (10.1)	
II	111 (72.5)	147 (67.1)	
III	36 (23.6)	50 (22.8)	
Tumor size (cm, mean $\pm$ SD)	4.5 $\pm$ 2.2	4.9 $\pm$ 2.2	0.292
Perineural invasion	44 (28.8)	62 (28.3)	0.925
Lymphatic invasion	48 (31.4)	62 (28.3)	0.524
LN harvest (days, mean $\pm$ SD)	17.2 $\pm$ 8.3	18.9 $\pm$ 8.6	0.158
Surgical procedure			0.004
Open	54 (35.3)	110 (50.2)	
Laparoscope	99 (64.7)	109 (49.8)	
Operative time (min, mean $\pm$ SD)	153.0 $\pm$ 58.1	142.3 $\pm$ 59.9	0.226
Estimated intraoperative blood loss (ml, mean $\pm$ SD)	67.8 $\pm$ 35.4	69.3 $\pm$ 31.2	0.873
Postoperative complications	45 (29.4)	55 (25.1)	0.358
Grade 3–4 postoperative complications	17 (11.1)	32 (14.6)	0.326
Time to first flatus (days, mean $\pm$ SD)	5.1 $\pm$ 2.2	4.8 $\pm$ 2.5	0.383
Postoperative hospital stay (days, mean $\pm$ SD)	11.0 $\pm$ 5.6	10.2 $\pm$ 4.9	0.268
Re-operation	5 (3.3)	10 (4.6)	0.531
Mortality	1 (0.7)	0 (0)	0.857

Table 3 lists the postoperative complications of the 372 elderly CRC patients. The incidence rates of overall complications, grade 1–2 complications and grade 3–4 complications were 40.1%, 26.9% and 13.2, respectively. Among the overall complications, abdominal abscess (8.6%), anastomotic leakage (7.5%) and ileus (7.5%) were the most common. The most common grade 3–4 complication was urinary retention (2.4%), followed by pleural effusion (2.2%) and abdominal abscess (1.9%).

Table 3
Overall and grade 3–4 postoperative complications of 372 elderly patients

Complications	Grade 1–2 complications		Grade 3–4 complications		All complications	
	n	%	n	%	n	%
Total	100	26.9	49	13.2	149	40.1
Cardiac disorders						
Arrhythmia	11	3.0	6	1.6	17	4.6
Cardiac failure	6	1.6	1	0.2	7	1.8
Acute coronary syndrome	2	0.5	2	0.5	4	1.0
Hypertensive emergencies	2	0.5	0	0	2	0.5
Respiratory disorder						
Pneumonia	7	1.9	6	1.6	13	3.5
Pleural effusion	4	1.1	8	2.2	12	3.3
Atelectasis	6	1.6	5	1.3	11	2.9
Gastrointestinal disorders						
Anastomotic leakage	22	5.9	6	1.6	28	7.5
Ileus	22	5.9	6	1.6	28	7.5
Gastrointestinal hemorrhage	7	1.9	2	0.5	9	2.4
Renal and urinary disorders						
Urinary infection	13	3.5	1	0.2	14	3.7
Renal failure	0	0	1	0.2	1	0.2
Urinary retention	6	1.6	9	2.4	15	4.0
Other disorders						
Abdominal abscess	25	6.7	7	1.9	32	8.6
Rectovaginal fistula	0	0	1	0.2	1	0.2
Intra-abdominal hemorrhage	5	1.3	4	1.1	9	2.4
Wound infection	24	6.5	2	0.5	26	7.0
Pulmonary embolism	0	0	2	0.5	2	0.5

Survival Analysis

The mean follow-up period for the whole group was 51.3 months (range, 11–132 months; overweight group: 48.3 months; control group: 54.2 months). During this period, 130 of the 372 patients died (34.9%). Among them, 102 died from tumour recurrence or metastasis (27.4%). The Kaplan curves showed that the CCS rate of patients in the overweight group was significantly inferior to that of the control group ($P=0.046$). In addition, the 3- and 5-year CCS rates in the overweight group were 71.0% and 63.3%, respectively, and those in the control group were 87.3 and 80.0%, respectively (Fig. 1).

In the univariate analysis, sex, age, BMI, preoperative HGB, lifestyle habits, surgical procedure, T stage, N stage, perineural invasion, lymphatic invasion, and reoperation significantly affected both OS and DFS ($P < 0.02$). These variables were thus incorporated into the multivariate analysis, and the results revealed that the CCS was significantly affected by BMI (HR: 2.30; 95% CI, 1.27–4.17; $P=0.046$) and N stage (HR: 2.97; 95% CI, 1.48–5.97; $P=0.002$) (Table 4) (Fig. 1–3).

Table 4
Univariate and multivariate Cox regression analysis of cancer specific survival in 372 elderly patients after curative resection

Variables	Cancer specific survival			
	Univariate analysis		Multivariate analysis	
	HR(95%CI)	P	HR(95%CI)	P
Gender: male/female	1.63 (0.88–3.02)	0.118	1.18 (0.60–2.29)	0.636
Age at operation: ≥85/<85	1.84 (0.83–4.08)	0.137	1.57 (0.65–3.83)	0.317
ASA score: III/II	1.08 (0.62–1.90)	0.779		
BMI: ≥24/<24	1.76 (1.01–3.05)	0.046	2.30 (1.27–4.17)	0.006
Preoperative albumin: ≥35/<35	0.74 (0.40–1.35)	0.322		
Preoperative HGB: ≥110/<110	0.63 (0.34–1.19)	0.158	0.70 (0.35–1.42)	0.326
Habits: drinking	1.46 (0.79–2.70)	0.233		
Habits: smoking	1.49 (0.83–2.69)	0.184	1.55 (0.80–3.00)	0.193
Comorbidity: yes/no	0.78 (0.45–1.36)	0.382		
Previous abdominal surgery:yes/no	0.69 (0.33–1.48)	0.342		
Tumor location: left colon and rectum/ right colon	1.09 (0.58–2.04)	0.797		
Surgical procedure: open/laparoscope	1.46 (0.83–2.57)	0.185	1.20 (0.65–2.22)	0.564
Operative time: ≥135/<135	1.12 (0.65–1.94)	0.688		
T stage: T3-T4/T1-T2	2.28 (0.97–5.35)	0.058	1.34 (0.54–3.35)	0.528
N stage: N1-N2/N0	2.90 (1.63–5.18)	< 0.001	2.97 (1.48–5.97)	0.002
Tumor grade				
I	Reference	-		

Variables	Cancer specific survival			
	Univariate analysis		Multivariate analysis	
	HR(95%CI)	P	HR(95%CI)	P
II	0.71 (0.28–1.83)	0.483		
III	0.94 (0.33–2.67)	0.904		
Perineural invasion: yes/no	1.74 (0.95–3.19)	0.074	1.19 (0.59–2.42)	0.627
Lymphatic invasion	1.99 (1.14–3.47)	0.016	1.03 (0.53–1.98)	0.939
Grade 3–4 complications: yes/no	0.82 (0.35–1.92)	0.641		
Re-operation: yes/no	3.21 (0.77–13.37)	0.109	1.67 (0.35–8.03)	0.523

Discussion

One of the biggest challenges in healthcare is the ageing population; in 2015, the life expectancy at birth was 82.9 years, with males expected to live to 80.5 years old and females expected to live to 85.1 years old. Elderly CRC patients are regarded as a special population with unique clinicopathological characteristics, and the increase in comorbidities typically observed in this population tend to increase the potential risk during the perioperative period. In addition, BMI has been previously reported to be associated with the incidence of postoperative complications and even the prognosis of colorectal cancer^[17–20]. In the present study, to clarify the effect of BMI on the technical feasibility and oncological safety of radical surgery and the prognosis of CRC in elderly patients, we compared the short- and long-term outcomes between elderly patients in the control group and overweight group.

Along with the increase in material wealth, the incidence of obesity has increased and become a medical and social problem. It has been previously confirmed that obesity increases the difficulty of CRC surgery and the incidence of postoperative complications^[17, 19, 21]. A study involving 792 patients with low rectal cancer conducted by Zhang et al. showed that the operation time and length of postoperative hospital stay in the overweight group were significantly longer than those in the control group, and the increase in BMI was closely related to the incidence of postoperative complications such as pneumonia, anastomotic leakage, allergy and incisional hernia^[21]. However, the results of the present study show that the increase in BMI does not affect the surgical results, such as the operation time (153.0 vs 142.3, $P=0.226$) and intraoperative blood loss (67.8 vs 69.3, $P=0.873$). At the same time, the incidence of overall postoperative complications (29.4% vs 25.1%, $P=0.358$) and grade 3–4 complications (11.1% vs 14.6%, $P=0.326$) in the overweight group did not increase significantly, which differs from that reported in the

literature. This may be because a higher proportion of patients in the obesity group underwent laparoscopic surgery (64.7% vs 49.8%, $P = 0.004$), thus speeding up postoperative recovery and reducing the possibility of complications.

The safety of radical surgery for elderly patients with colorectal cancer is a concern for surgeons. Prior works have reported that the incidence of overall complications in elderly patients with CRC after radical surgery is 9.9%-25.4%, and the incidence of grade 3–5 complications is 6.5%-20.1%^[22–25]. Our study showed that the incidence rates of overall complications, grade 1–2 complications and grade 3–4 complications were 40.1%, 26.9% and 13.2%, respectively, which were consistent with previous reports in the literature. In addition, this study revealed that the most common overall complication after radical resection of elderly patients with CRC is abdominal abscess (8.6%), and the most common grade 3–4 postoperative complication is urinary retention (2.4%). Therefore, in view of the above complications, more attention should be given to aseptic operation and the appropriate prolongation of antibiotic use after radical resection of CRC in elderly patients.

Obesity is clearly associated with the incidence of CRC^[26], and the relationship between obesity and colorectal cancer has been previously reported but remains controversial. Several studies believe that a high BMI is associated with a poor prognosis in patients with CRC^[18, 27], while some studies believe that a high BMI is not related to prognosis^[28, 29] or even related to a better prognosis^[30, 31]. This study explores the prognostic factors related to elderly patients with CRC after curative resection, and the results show that BMI (HR: 2.30; 95% CI, 1.27–4.17; $P = 0.046$) and N stage (HR: 2.97; 95% CI, 1.48–5.97; $P = 0.002$) were independent prognostic factors affecting CCS. Scarpa et al. grouped 595 CRC patients based on BMI and conducted postoperative follow-up. Multivariate analysis showed that BMI > 30 kg/m² was an independent risk factor for prognosis and recurrence after surgery (HR: 2.2; 95% CI, 1.3–3.9; $P = 0.003$)^[32]. Doria-Rose et al. obtained similar results: those with a high BMI, especially BMI > 35 kg/m², had a higher recurrence rate and poorer overall survival than those with a normal BMI^[33]. The results of the above studies were basically consistent with our findings.

The most significant limitation of the present study is its retrospective nature, and only 372 patients were included, which may have caused some inherent selection bias. In addition, compared to rectal cancer, colon cancer is more likely to cause systemic consumption and lower BMI, and we did not calculate colon and rectal cancer separately. Therefore, multicentre, large-scale, prospective studies are warranted to verify our results.

In conclusion, the results of our study demonstrated that radical resection for CRC is safe and feasible for patients over 80 years of age. An increase in BMI does not increase the difficulty of surgery or postoperative complications. BMI and N stage were independent prognostic factors for elderly CRC patients after radical resection.

Abbreviations

cancer-specific survival (CSS)

colorectal cancer (CRC)

body mass index (BMI)

Clavien-Dindo classification (CD)

cancer-specific survival (CCS)

Declarations

Ethics approval and consent to participate

The ethics committee of the National Cancer Center/Cancer Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College approved this study. Prior written informed consent was obtained from all study participants.

Consent for publication

Not Applicable.

Availability of data and materials

The datasets generated and/or analysed during the current study are not publicly available due to the data is confidential patient data but are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

Contributions: (I) conception and design: JWL, SCZ, and WP; (II) administrative support: JWL and ZXZ; (III) provision of study materials or patients: YJJ and WP and MW; (IV) collection and assembly of data: SCZ; (V) data analysis and interpretation: SCZ and JWL and GDR. All authors read and approved the final manuscript.

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Figures

Figure 1

Cancer specific survival curve of overweight group and control group.

Figure 2

Cancer specific survival curve of N0 group and N1-2 group.

Figure 3

Forest plots for Cancer specific survival of elderly CRC patients after curative resection based on multivariable COX proportional hazard model.