

Outcomes of colorectal cancer surgery in nonagenarian patients: a multicenter retrospective study

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Background: The use of surgery in patients with colorectal cancer (CRC) aged \geq 90 years remains controversial. This study aimed to evaluate the short-term postoperative and long-term oncologic outcomes of CRC surgery in patients within this age group.

Methods: A total of 151 consecutive nonagenarian patients who underwent CRC surgery were included from 3 different hospitals. The Comprehensive Complication Index (CCI) was used to grade postoperative complications. Univariate and multivariate analyses were conducted to identify factors associated with CCI and overall survival (OS).

Results: The patients had a mean age of 92.8 years (standard deviation \pm 1.9 years). Forty-six patients (30.5%) underwent emergency surgery, and 105 patients (69.5%) underwent elective surgery. The postoperative complications rate was 66.2% (100/151), and the mean CCI was 26.3 (\pm 30.8). Twenty-three patients (15.2%) died postoperatively, and the perioperative mortality rates for elective surgery and emergency surgery were 7.6% (8/105) and 32.6% (15/46), respectively (P<0.001). The 1-, 3-, and 5-year survival rates were 77.5%, 53.9%, and 38.6%, respectively. Multivariate analysis revealed emergency surgery and American Society of Anesthesiologists (ASA) score to be predictors of postoperative complications. Advanced tumor stage, palliative surgery, ASA score \geq 4, and CCI >17 were associated with poor OS.

Conclusions: CRC surgery should not be denied to nonagenarian patients. Surgical treatment can be performed with acceptable morbidity and mortality, and achieves long-term survival in a select group.

Keywords: Colorectal cancer (CRC); nonagenarian; elderly; survival; mortality

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Introduction

Life expectancies are rising globally, and the number of people who reach the age of 90 and beyond is increasing. However, with age, the incidence of cancer increases. For instance, age is an important risk factor for colorectal cancer (CRC), which is the third most common cancer in the world (1,2). Older people are increasingly being diagnosed with

CRC, with a median age at diagnosis of about 70 years (3). Further, in patients aged \geq 90 years, CRC accounts for more than one-fifth of new cancer diagnoses (4).

Surgical treatment remains the mainstay for resectable CRC. However, surgery is not always performed on nonagenarians with CRC due to the risk of complications relating to age, comorbidity, and reduced functional

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reserve. It has even been considered that the best treatment option for nonagenarians with CRC is no treatment (5). However, to date, data on the outcomes of CRC surgery in nonagenarians are limited.

The present study aimed to evaluate the short-term postoperative results and long-term survival following CRC surgery in patients aged ≥ 90 years, and to define factors associated with the Comprehensive Complication Index (CCI) and overall survival (OS).

We present the following article in accordance with the STROBE reporting checklist (available at https://dx.doi. org/10.21037/jgo-21-324).

Methods

Patients

From January 2000 to December 2019, 151 consecutive patients with CRC aged ≥90 years from 3 individual hospitals were enrolled. Patients were excluded if they did not undergo surgery, had CRC concurrent with another type of cancer, or had incomplete clinical records.

Before surgery, patients underwent a series of examinations, including: colonoscopy with biopsies, CT of the abdominal pelvic cavity, and chest X-ray or CT. For patients undergoing elective surgery, mechanical bowel preparation was administered 1 day before surgery. All patients were given intravenous antibiotics 30 minutes before surgery, and the antibiotics lasted for 48 hours after surgery.

Different surgical procedures were performed depending on the patient's tumor site, tumor stage, and condition. Surgical procedures performed within 24 hours after hospital admission were defined as emergency surgery. The surgical procedures have been described in detail previously (6,7). For laparoscopic surgery, multiple trocars (4 or 5 trocars) were used.

Data on postoperative complications were collected, and the CCI was used to classify complications (8). Operative mortality was defined as any death related to surgery or surgical complications. Tumor specimens were examined by at least 2 pathologists. Tumors were staged according to the American Joint Committee on Cancer (8th edition) staging system.

Data collection

The following patient data were prospectively collected:

sex, age, Eastern Cooperative Oncology Group (ECOG) performance status score, body mass index (BMI), patient comorbidities, American Society of Anesthesiologists (ASA) score, tumor location, and tumor stage. Patient comorbidities were recorded and graded according to the Charlson Comorbidity Index (9). OS was defined as the time from the date of surgery to the date of death.

Statistical analysis

Quantitative variables were expressed as means and standard deviations (SDs), and the Student's t-test was used for comparisons. Categorical variables were expressed as frequencies and percentages, and comparisons were analyzed by the chi-square test, when one or more of the cell counts in a 2×2 table was less than 5, Fisher's exact test was used. All comparisons were two-sided, and P<0.05 was considered to indicate statistical significance.

Linear regression was adopted to analyze the clinicopathological factors associated with the CCI. The Kaplan-Meier method was employed to calculate survival, and the survival curves were compared by the log-rank test. The Cox proportional-hazards model was applied to analyze survival-associated factors, and adjusted hazard ratios (HRs) and their 95% confidence intervals (CIs) were calculated. Variables with significant associations in univariate analysis, as defined by a P value <0.1, were included in multivariate analysis. SPSS 25.0 for Windows (IBM Corporation, Armonk, NY, USA) was used to perform the data analyses.

All procedures performed in this study involving human participants were in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by institutional ethics board of three hospitals (No.:2014ke-161-1). Individual consent for this retrospective analysis was waived.

Results

Clinical factors

This study included 151 patients with CRC aged ≥90 years, among whom 89 patients (58.9%) were women. The patients had a mean age of 92.8 years (SD ±1.9 years), and their mean Charlson Comorbidity Index score was 7.7 (±2.6). Colon cancer was more common than rectal cancer (66.9% vs. 33.1%, Table 1).

There were 105 cases (69.5%) and 46 cases (30.5%) of elective surgery and emergency surgery, respectively.

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Table 1 General features of nonagenarian patients who received colorectal cancer surgery

Characteristic	Total (n=151)	Emergency surgery (n=46)	Elective surgery (n=105)	P value
Male/female	62/89	17/29	45/60	0.498
Age (years)	92.8 (±1.9)	92.6 (±2.2)	92.9 (±1.8)	0.350
ЗМI	21.5 (±3.0)	20.8 (±2.7)	21.9 (±3.0)	0.051
Tumor location (%)				0.002
Colon	101 (66.9)	39 (84.8)	62 (59.0)	
Rectum	50 (33.1)	7 (15.2)	43 (41.0)	
ECOG score (%)				0.517
2	44 (29.1)	11 (23.9)	33 (31.4)	
3	88 (58.3)	30 (65.2)	58 (55.2)	
4	19 (12.6)	5 (10.9)	14 (13.3)	
ASA score (%)				0.429
2	49 (32.5)	13 (28.3)	36 (34.3)	
3	86 (57.0)	26 (56.5)	60 (57.1)	
4	16 (10.6)	7 (15.2)	9 (8.6)	
Tumor stage (%)				0.004
1	12 (7.9)	0 (0.0)	12 (11.4)	
2	59 (39.1)	13 (28.3)	46 (43.8)	
3	69 (45.7)	28 (60.9)	41 (39.0)	
4	11 (7.3)	5 (10.9)	6 (5.7)	
Charlson Comorbidity Index	7.7 (±2.6)	8.4 (±3.0)	7.4 (±2.4)	0.048
Radiotherapy (%)	5 (3.3)	2 (4.3)	3 (2.9)	0.641
Chemotherapy (%)	20 (13.2)	3 (6.5)	17 (16.2)	0.107
Surgical approach (%)				<0.001
Laparoscopic	41 (27.2)	2 (4.3)	39 (37.1)	
Open	110 (72.8)	44 (95.7)	66 (62.9)	
Surgical intent (%)				0.141
Curative	128 (84.8)	36 (78.3)	92 (87.6)	
Palliative	23 (15.2)	10 (21.7)	13 (12.4)	
Operative procedure (%)				0.025
Right/extended right colectomy	54 (35.8)	19 (41.3)	35 (33.3)	
Hartmann's procedure	25 (16.6)	8 (17.4)	17 (16.2)	
Left hemicolectomy/sigmoidectomy	24 (15.9)	10 (21.7)	14 (13.3)	
Anterior resection	21 (13.9)	1 (2.2)	20 (19.0)	
Trans-anal excision	3 (2.0)	0 (0.0)	3 (2.9)	
Subtotal colectomy	5 (3.3)	0 (0.0)	5 (4.8)	

Table 1 (continued)

Table 1 (continued)

Characteristic	Total (n=151)	Emergency surgery (n=46)	Elective surgery (n=105)	P value
Defunctioning stoma/bypass	19 (12.6)	8 (17.4)	11 (10.5)	
Postoperative complications (%)	100 (66.2)	40 (87.0)	60 (57.1)	<0.001
CCI	26.3 (±30.8)	39.7 (±35.1)	20.4 (±26.8)	<0.001
Postoperative hospital stay (days)	17.0 (±11.8)	20.9 (±16.4)	15.3 (±8.7)	0.007
Reoperation (%)	8 (5.3)	3 (6.5)	5 (4.8)	0.700
Operative mortality (%)	23 (15.2)	15 (32.6)	8 (7.6)	<0.001

BMI, body mass index; ECOG, Eastern Cooperative Oncology Group; ASA, American Society of Anesthesiologists; CCI, Comprehensive Complication Index.

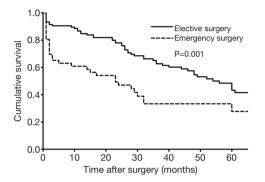


Figure 1 Cumulative survival after elective and emergency surgery.

Most patients underwent open resection (72.8%), which was performed with curative intent in 84.8% of such cases. The most common surgical procedures included right colectomy (35.8%), Hartmann's procedure (16.6%), left hemicolectomy/sigmoidectomy (15.9%), and anterior resection (13.9%). Primary anastomosis was performed in 95 patients (62.9%).

Operative outcomes

The postoperative complications rate was 66.2%. The median CCI was 17.3 (range, 0–100), and the mean CCI was 26.3 (±30.8). The most frequently observed complications were confusion (23.8%), pneumonia (22.5%), ileus (19.2%), and renal failure (17.2%). Two patients (2.1%) experienced anastomotic leakage, both of whom underwent emergency surgery (1 right colectomy and 1 left hemicolectomy).

A total of 23 patients (15.2%) died postoperatively, from causes including pneumonia or respiratory failure (n=9), sepsis (n=5), stroke (n=3), acute myocardial infarction (n=3), multiple organ failure (n=2), and intracranial hemorrhage (n=1).

Patients who underwent emergency surgery and those who underwent elective surgery displayed significant differences in demographics and operative outcomes. Significant differences were detected in tumor site (P=0.002), tumor stage (P=0.004), Charlson Comorbidity Index (8.4 vs. 7.4, P=0.048), surgical approach (P<0.001), surgical procedure (P=0.025), postoperative complications (87.0% vs. 57.1%, P<0.001), CCI (39.7 vs. 20.4, P<0.001), postoperative hospital stay (20.9 days vs. 15.3 days, P=0.007), and operative mortality (32.6% vs. 7.6%, P<0.001) between the emergency surgery group and elective surgery group.

Oncologic outcomes

The median follow-up was 30 months (range, 1–106 months). The 1-, 3-, and 5-year survival rates were 77.5%, 53.9%, and 38.6%, respectively. The estimated 5-year OS rate was 43.3% (95% CI, 32.1–54.5) in the elective surgery group, and 27.8% (95% CI, 12.1–43.5) in the emergency surgery group (*Figure 1*, P=0.001).

Univariate and multivariate analysis

In univariate analysis, ASA score (P<0.001), ECOG score (P=0.002), emergency surgery (P<0.001), and open surgery (P=0.059), were significantly associated with CCI (*Table 2*). In multivariate analysis with a linear regression model, only ASA score (P<0.001) and emergency surgery (P=0.004) retained their significance as independent prognostic factors for postoperative complications.

Univariate analysis showed that palliative surgery (P<0.001), advanced tumor stage (P=0.001), ASA score \geq 4 (P<0.001), ECOG score \geq 4 (P=0.027), emergency surgery

Table 2 Univariate and multivariate anal	vses of the effects of covari	ates on Comprehensive Comp	lications Index

Factor –	Univariate	Multivariate		
	B (95% CI)	P value	B (95% CI)	P value
Age	-0.195 (-4.505 to 0.606)	0.134	-	_
Female/male	-0.207 (-10.298 to 9.884)	0.968	-	-
BMI	-0.099 (-1.780 to 1.582)	0.908	-	-
Rectum/colon	-2.552 (-13.093 to 7.988)	0.633	-	-
ECOG score	12.212 (4.510 to 19.913)	0.002	-2.161 (-9.713 to 5.391)	0.573
ASA score	27.063 (20.340 to 33.786)	<0.001	27.185 (19.543 to 34.827)	<0.001
Tumor stage	4.922 (-1.699 to 11.543)	0.144	-	-
Palliative/curative	7.583 (-6.117 to 21.344)	0.278	-	-
Charlson Comorbidity Index	1.016 (-0.867 to 2.898)	0.288	-	-
Open/laparoscopic	10.696 (-0.419 to 21.812)	0.059	4.433 (-5.492 to 14.358)	0.379
Emergency surgery	19.274 (8.949 to 29.98)	<0.001	14.249 (4.702 to 23.797)	0.004

B, regression coefficient; CI, confidence interval; BMI, body mass index; ECOG, Eastern Cooperative Oncology Group.

(P=0.002), and CCI >17 (P=0.001) were significantly associated with poor survival (*Table 3*). Multivariate analysis identified advanced tumor stage (HR =2.024; 95% CI, 1.254–3.268; P=0.004), palliative surgery (HR =1.876; 95% CI, 1.011–3.481; P=0.046), ASA score \geq 4 (HR =2.638; 95% CI, 1.132–6.148; P=0.025), and CCI >17 (HR =1.784; 95% CI, 1.127–2.823; P=0.013) as factors associated with poor OS.

Discussion

Data on the operative and oncologic outcomes of nonagenarians with CRC are scarce. Several retrospective studies with a small number of patients have reported that CRC surgery appeared to be safe for select patients aged \geq 90 years, with acceptable morbidity and mortality, although the results were conflicting (10-15). Therefore, we conducted a multicenter study with a larger number of patients aged \geq 90 years, and investigated their operative and oncologic outcomes.

In the present study, 66.2% patients experienced some type of complication; however, the median CCI was 17.3, and many of the complications were minor. Although the overall operative mortality rate was relatively high (15.2%), the mortality rate of elective surgery was lower, at 7.6%, which is similar to the results reported by other authors (8-10,13). The 5-year survival rate was 38.6%. Based on our results, we believe that surgical treatment can achieve acceptable short-term postoperative and long-term oncologic outcomes for patients with CRC aged \geq 90 years; therefore, it should not be denied to this population.

We found that pneumonia or respiratory failure was the first cause of death. Chan *et al.* (11) also demonstrated that pneumonia with respiratory failure as the most common postoperative complication and the leading cause of mortality. Yap *et al.* (14) reported that by incorporating a physician's input into the perioperative care, the 30-day mortality could be as low as 2.1%, patients in the study had a much lower (2%) incidence of pneumonia. These encouraging results demonstrated the importance of multidisciplinary collaborative care in the extreme elderly.

Emergency surgery was found to be an independent risk factor for complications among the patients in our study, and the rate of operative mortality was high (32.6%) in patients who underwent emergency resection. Therefore, it is reasonable to avoid urgent surgery and to offer therapeutic alternatives, such as self-expanding metallic stents for patients with colonic obstructions (16). Turning emergency surgery into elective surgery would aid in decreasing morbidity and mortality. For the inevitable emergency operation, multidisciplinary collaborative care was of great important. More attention should be paid to their breathing, because respiratory failure was the first cause of death.

In contrast, laparoscopic surgery was found to be

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Table 3 Univariate and multivariate	analysis of the	e effects of	covariates on s	urvival

Factor —	Univariate	Multivariate		
	HR (95% CI)	P value	HR (95% CI)	P value
Age	0.941 (0.839–1.055)	0.291	-	_
Sex				
Male	Reference			
Female	1.089 (0.719–1.650)	0.687	-	-
BMI	1.018 (0.951–1.089)	0.616	-	-
Tumor location				
Colon	Reference			
Rectum	0.830 (0.534–1.288)	0.406	-	-
Surgical intent				
Curative	Reference		Reference	
Palliative	3.165 (1.789–5.599)	<0.001	1.876 (1.011–3.481)	0.046
ASA score				
<4	Reference		Reference	
≥4	3.318 (1.849–5.956)	<0.001	2.638 (1.132–6.148)	0.025
ECOG score				
<4	Reference		Reference	
≥4	1.874 (1.073–3.273)	0.027	0.869 (0.403–1.872)	0.720
Stage				
I–II	Reference		Reference	
III–IV	2.069 (1.356–3.157)	0.001	2.024 (1.254–3.268)	0.004
Charlson Comorbidity Index				
≤7	Reference			
>7	0.911 (0.682–1.535)	0.911	-	-
Surgical approach				
Laparoscopic	Reference			
Open	1.172 (0.722–1.902)	0.521	-	-
CCI				
≤17	Reference		Reference	
>17	1.962 (1.301–2.959)	0.001	1.784 (1.127–2.823) 0.0	
Chemotherapy	0.989 (0.524–1.866)	0.989	-	-
Type of surgery				
Elective	Reference			
Emergency	2.033 (1.310–3.156)	0.002	1.545 (0.963–2.478)	0.071

HR, hazard ratio; CI, confidence interval; BMI, body mass index; ASA, American Society of Anesthesiologists; ECOG, Eastern Cooperative Oncology Group; CCI, Comprehensive Complication Index.

associated with a low risk of postoperative complications in univariate analysis, although its statistical significance was lost in multivariate analysis. The benefits of laparoscopic colorectal resection have been widely studied in randomized controlled trials (17-20). However, all of these trials excluded elderly patients. Elderly patients are associated with higher rate of comorbidities and reduced functional reserve compared with younger patients, and increasing age itself is an important risk factor for postoperative morbidity and mortality. The usage of laparoscopic surgery in the very elderly patient remains controversial, the haemodynamic changes secondary to the increased intra-abdominal pressure caused by the pneumoperitoneum can be associated with perioperative complications which may be most marked in the nonagenarians. Because of safety considerations, most patients underwent open resection (72.8%). However, we found that laparoscopic surgery could be performed safely in nonagenarians and was associated with a low rate of complications. Laparoscopic surgery might be a better choice for colorectal cancer patients over 90 years old, especially for patients with palliative surgery. Further studies with larger sample sizes are needed to confirm these results.

Few studies have reported on the risk of anastomotic leakage in nonagenarians. In the present study, the rate of anastomotic leakage was low, with only 2 patients (2.1%) developing this complication. This observation is consistent with those of other authors. For instance, Roque-Castellano *et al.* (10) performed 18 anastomoses, with no cases of leakage reported, and Yap *et al.* (14) reported only 1 case of anastomotic leakage after right hemicolectomy. On the basis of these results, anastomosis should not be denied to patients aged \geq 90 years.

ASA score was identified as an independent risk factor for both postoperative complications and survival. Surgeons should be extremely cautious in deciding whether to perform surgery on patients with an ASA score of \geq 4, due to the association with a poor prognosis following surgery. Higher disease stages and palliative surgery were also associated with poor OS, indicating that the biological behavior of tumors is similar between nonagenarians and younger patients. However, for nonagenarian patients with an ASA score <4, curative surgery should be considered, especially for those in the early stages of cancer.

In most previous studies, postoperative morbidity was assessed using the Clavien-Dindo classification, which grades the severity of postoperative complications according to the most severe complication when the patient has more than 1 complication (21). The CCI is a novel metric of postoperative complications. It shows an improvement on the CDC because it is calculated as the sum of all complications and is connected to clinical outcomes (8,22). Previously, only one study had used the CCI to evaluate postoperative complications in patients with CRC aged \geq 90 years. Roque-Castellano *et al.* (10) found that the mean CCI score was 28.7 and that the mortality rate reached 100% in patients with a CCI score \geq 60. We also found that CCI was an independent prognostic factor for OS. These results demonstrate that CCI should be used to assess postoperative complications and survival in patients with CRC aged \geq 90 years.

Although this is a multicenter study involving a larger number of patients than previous studies, it still has some limitations. Firstly, owing to the study's retrospective nature, potential bias may exist. Secondly, the patients who received surgery were regarded as having a low risk of complications. Thirdly, data on patients who did not receive surgery were not available. Finally, we only reported the results of morbidity and mortality, as information about the patients' quality of life and functional outcomes was not available.

Conclusions

CRC surgery should not be denied to nonagenarian patients. Surgical treatment can be performed with acceptable morbidity and mortality, and achieves long-term survival in a select group (e.g., elective surgery, ASA score <4, early-stage cancer) of these patients.

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Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at https://dx.doi. org/10.21037/jgo-21-324

Data Sharing Statement: Available at https://dx.doi. org/10.21037/jgo-21-324

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://dx.doi. org/10.21037/jgo-21-324). 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. All procedures performed in this study involving human participants were in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by institutional ethics board of three hospitals (No.:2014-ke-161-1). Individual consent for this retrospective analysis was waived.

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