

Original Paper

Mortality and Survival after Surgical Treatment of Colorectal Cancer in Patients Aged over 80 Years

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Keywords

Colorectal cancer · Elderly patients · Mortality · Surgery · Survival

Abstract

Objective: The purpose of this study was to identify the clinical factors and tumor characteristics that predict the outcome of colorectal cancer patients aged >80 years. **Materials and Methods:** The data of 186 patients aged >80 years with colorectal cancer were collected from a computer database, and the variables were analyzed by both uni- and multivariate analyses. **Results:** The 30-day mortality was 4% and the 90-day mortality 10%. The 1-year survival was 76%, and 27 (61%) of the 44 deaths were unrelated to cancer. The overall 5-year survival was 36%, the median survival 38 months, and the cancer-specific survival 40%. The recurrence rate after radical surgery was 22% and it was not affected by age. Kaplan-Meier estimates indicated that age, number of underlying diseases, radical operation, Union for International Cancer Control stage of the tumor, tumor size, number of lymph nodes involved, venous invasion, and recurrent disease were significant predictors of survival, but in the Cox regression model, only radical operation and venous invasion were independent prognostic factors for survival. **Conclusions:** After good surgical selection, low early mortality and acceptable long-term survival can be achieved even in the oldest old patients with colorectal cancer. However, low early mortality seems to underestimate the effects of surgery during the first postoperative year.

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Introduction

The population of Finland has aged over the past three decades, and this demographic change will even accelerate in the near future, as in many other Western societies. At the same time, with this longevity the higher overall incidence of colorectal cancer worldwide will be reflected in an even higher incidence of colorectal cancer in the elderly [1].

Colorectal cancer is the third most commonly diagnosed cancer in males and second in females, with an estimated 1.4 million cases and 693,000 deaths in 2012, and the highest incidence rates are seen in Australia/New Zealand, Europe, and North America [2]. The incidence of colorectal cancer increases with advancing age, 90% of patients being diagnosed after the age of 55 years, >70% in those aged ≥ 65 years and 30–40% aged ≥ 75 years [3]. The aging of the population will further increase the number of patients who have to be evaluated for surgery, and it has been forecasted that in 2025, in the United States there will be an expanded increase in the demand for colorectal procedures, and greatest growth will be seen in oncologic procedures [4].

Colorectal cancer in the elderly is nowadays managed, whenever possible, with surgical resection for cure, or even for palliation to avoid later complications. Although many elderly cancer patients have significant comorbidities which increase the risk of postoperative complications and mortality [5], many patients aged >80 years may still have 5–10 years of life expectancy if they are provided with the possibility to undergo cancer resection. The need for appropriate and safe surgical treatment does not diminish with age, and patient distress and anxiety concerning the prospects of survival would benefit greatly if precise data about prognosis were available. The elderly also want to know and understand their diagnosis and prognosis [6], and therefore it is of utmost importance for us to have relevant and reliable data for surgical decisions.

The aim of this study was to evaluate the risk factors of mortality and the predictors of survival. Therefore, we performed a systematic evaluation of the 10-year material of patients with colorectal cancer aged >80 years by collecting patient information from the database of Oulu University Hospital.

Materials and Methods

After approval by the local institutional review board, a computer-based analysis of all patients who had undergone resection for colorectal cancer during the 10-year period 2001–2010 at Oulu University Hospital at age >80 years was carried out. A total of 240 patients were identified from the computer database, which prospectively records data concerning diagnoses and procedures. The diagnoses were coded according to the International Classification of Diseases and the operations performed according to the Finnish Classification of Surgical Procedures.

Of the 240 patients evaluated for elective surgery; 203 were operated on, 190 undergoing laparotomy and 13 laparoscopy. The laparoscopic era in colorectal surgery began in our hospital at the end of the study period. The patients were evaluated for fitness to undergo general anesthesia and colorectal surgery, but were not preselected in any other way. Of the 203 patients evaluated for surgery, 186 underwent resection. These 186 patients constitute the study population, and the survival data of all other patients are presented separately.

The clinical data included age, gender, coexistent diseases, operative procedures, tumor-related factors, results of pathologic examinations, morbidity, 30- and 90-day mortality, information regarding the length of hospital treatment, intensive care and discharge placement, chemo- and radiotherapy, recurrent disease, and overall 1- and 5-year survival. Coexistent diseases included diseases of the hearth (152), lungs (35), central nervous system (30), kidneys (25), liver (12), diabetes (34), and other diseases (74).

The mean age of the study population was 84 ± 3 years (81–95) (men [$n = 67$] 83 ± 3 years, women [$n = 119$] 84 ± 3 years). The age distribution was as follows: 134 patients 81–85 years, 42 patients 86–90 years, and 10 patients >90 years. In every case, the diagnosis was confirmed by biopsy in colonoscopy and

Table 1. The resective procedures in 186 patients

Procedure	Radical, n (%)	Palliative, n (%)	Total, n (%)
Right hemicolectomy	59 (32)	8 (4)	67 (36)
Anterior resection	50 (27)	4 (2)	54 (29)
Abdominoperineal resection	18 (10)	6 (3)	24 (13)
Sigmoid resection	12 (6)	1 (1)	13 (7)
Hartmann procedure	7 (4)	4 (2)	11 (6)
Left hemicolectomy	5 (3)	3 (2)	8 (4)
Other resections	5 (3)	4 (2)	9 (5)
Total	156 (84)	30 (16)	186 (100)

Six sigmoid resections, 3 right hemicolectomies, and 1 abdominoperineal resection were performed laparoscopically.

the extent of the disease by preoperative computed tomography examination of the abdomen and chest, and surgical findings and cancer growth in the surgical specimen by an experienced pathologist.

Tumors were staged according to the Union for International Cancer Control (UICC) TNM classification [7] and graded according to the World Health Organization histological classification system [8]. Pathologic factors included presence or absence of lymphatic spread and venous invasion. The number of lymph nodes sampled was recorded in every case.

Resection was radical when there was macroscopic removal of all cancer tissue with microscopic clearance of surgical margins. Resection was considered radical in 156 (84%) cases (Table 1). The Clavien-Dindo classification [9] was used in the evaluation of postoperative complications.

The follow-up of all patients resected radically was conducted in our outpatient clinic and health centers according to a new modification of the follow-up program of the Oulu University Hospital [10]. The patients were followed up every 3 months for the first 2 years, and thereafter every 6 months for 2–5 years or until their death. During each visit, the medical history was obtained, a clinical examination was performed, and CEA levels was checked. Colonoscopy was performed 3 months after surgery to ensure a clean colon if it had not been performed preoperatively and at 2 and 5 years. Computed tomography of the abdomen and chest was conducted at 1 and 3 years. The survival data of all patients and the date and cause of death were confirmed in every case in December 2015, when the last patient had been followed up for at least 5 years.

Five patients received preoperative radiotherapy of 25 Gy for T3 rectal cancer. Postoperatively, 19 patients received 5-fluorouracil-based adjuvant therapy for node-positive cancer.

Local recurrences were defined as recurrent lesions in the anastomotic area or tumor bed; others were defined as distant. Out of the cases with recurrent cancer, 10 patients underwent exploratory laparotomy, 8 received palliative chemotherapy, and 5 palliative radiotherapy.

Statistical analysis was performed using SPSS for Windows 2014. The association between categorical data was tested with the two-tailed χ^2 or the Fisher exact test, when appropriate, and continuous data with the Student *t* test. Survival rates were calculated from the time of primary surgery using the Kaplan-Meier method, and survivals were compared by the log-rank test. A multivariate analysis of the factors which influenced survival was carried out using the Cox proportional hazards regression model.

Results

All patient were symptomatic at the time of preoperative evaluation, intestinal bleeding (66), anemia (58), and changes in bowel habits (27) being the most frequent symptoms. At the time of surgery, the number of lymph nodes with metastasis differed significantly in relation to age groups (Table 2). Age had no influence on the number of radical resections.

Postoperative 30-day mortality was 4% (7/186) and 90-day mortality 10% (19/186). Both 30- and 90-day mortality were associated with the number of coexistent diseases ($p =$

Table 2. Clinical variables of patients undergoing surgical resection according to age group

Variable	Age, years			p value
	81–85	86–90	>90	
Gender				
Male	49	16	2	0.546
Female	85	26	8	
Number of coexistent diseases				
0	7	0	2	0.229
1	36	10	2	
2	61	22	2	
3	30	10	4	
Tumor location				
Right	49	17	6	0.329
Left	85	25	4	
UICC stage				
I	12	4	1	0.612
II	58	24	5	
III	44	7	3	
IV	20	7	1	
Tumor differentiation				
I	30	10	2	0.729
II	78	21	7	
III	26	11	1	
Metastasized disease				
No	116	37	10	0.458
Yes	18	5	0	
Tumor size				
<20 mm	26	4	0	0.357
20–50 mm	67	23	6	
>50 mm	41	15	4	
Number of lymph nodes				
0	77	30	6	0.037
1–3	38	9	2	
4–6	15	3	0	
>6	4	0	2	

UICC, Union for International Cancer Control.

0.0001) and the presence of postoperative complications ($p = 0.001$), and 30-day mortality was especially related to pulmonary complications ($p = 0.008$). During the 30 postoperative days, 4 patients died of intra-abdominal infection, 2 of cardiac infarction, and 1 of pulmonary embolus. There were no significant differences between the age groups in 30-day mortality: 81–85 years 3% (4/134), 86–90 years 7% (3/42), and >90 years 0% (0/10). Mortality according to UICC stage was as follows: stage I 0% (0/17), stage II 2% (2/87), stage III 6% (3/54), and stage IV 7% (2/28).

Postoperative morbidity was 30% (56/186), divided according to Clavien-Dindo classification as follows: 7 grade V, 17 grade IV, 15 grade III, 11 grade II, and 6 grade I complication. Morbidity was 30% (40/134) in patients aged 81–85 years, 29% (12/42) in patients aged 85–90 years and 30% (3/10) in patients aged >90 years. Wound infection (10), intestinal obstruction (8), and anastomotic leak (6) were the most common complications, and reoperation had most frequently to be performed for leakage (5), wound dehiscence (4), and abdominal bleeding (3).

The mean length of hospitalization was 11 ± 7 days, without any difference between age groups, but the hospital stay was prolonged if the patients experienced postoperative complications ($p = 0.029$). The need for intensive care treatment was related to the number of coexistent diseases ($p = 0.001$) and the presence of postoperative complications ($p = 0.004$). The majority of patients (65% [121/186]) were discharged to other hospitals, and this discharge was not related to age, but to postoperative complications ($p = 0.0001$).

The recurrence rate after radical resection was 22% (35/156) in 2 years and 27% (42/156) in 5 years. The median asymptomatic time until recurrence was 21 months. According to UICC stage, recurrences developed as follows: stage I 12% (2/17), stage II 18% (16/87), stage III 42% (22/53), and stage IV 66% (2/3). The recurrence rate was not affected by age in the patient groups aged >80 years. Of the recurrences, 12 were local and 30 distant. Distant recurrences included 12 patients with liver metastases, 10 with peritoneal seeding, 6 with lung metastases, and 2 with metastases of the brain.

Five radical re-resections were performed, 3 colonic resections, 1 hepatic resection, and 1 abdominoperineal resection. In addition, 1 palliative resection, 3 colostomies, and 1 bypass procedure had to be undertaken after radical primary surgery. Five patients received palliative radiotherapy of 40 Gy for pelvic recurrence and 8 chemotherapy for abdominal seeding.

The overall survival rates at 1 and 2 years were 76 and 63%, and 27 (61%) of the 44 deaths occurring during the first postoperative year were unrelated to cancer. Of those 27 patients who succumbed during the first postoperative year without evidence of recurrent cancer, 9 died within 3 months, 6 between 3 and 6 months, and 12 after 6 months. The 1-year survival was not related to the need for intensive care treatment during hospital treatment or to discharge to home or other hospitals.

The overall 5-year survival after radical surgery was 36% and median survival 38 months. The following 5-year survivals according to UICC stage were detected: stage I 40%, stage II 34%, stage III 26%, and stage IV 20%. The overall 5-year survival rates according to age group were 36% in patients aged 80–85 years, 38% in patients aged 86–90 years, and 10% in patients aged >90 years. The overall cancer-specific 5-year survival was 40%, and according to the above-mentioned age groups is was 38, 43, and 0%, respectively.

A total of 37 patients were treated nonoperatively, and they all died within 1 year, with a median survival of 4 months. The 17 patients who underwent laparotomy, but not resective surgery, all died within 2 years, with a median survival of 6 months.

The distribution of prognostic features possibly affecting survival were analyzed by Kaplan-Maier analysis (Table 3). To determine independent survival factors, a Cox regression proportional hazards model was used, which revealed that only radical operation and venous invasion were independent predictors of survival (Table 4).

Discussion

Life expectancy after qualified surgery increases even in the oldest old patients because inadequate treatment is associated with poor survival [11]. Thus, surgical resection should not be denied of the elderly, because despite of higher postoperative mortality, favorable long-term outcome can be achieved by surgical therapy alone [12]. Our policy has been to resect the primary tumor whenever possible, but preoperative selection has been conducted in terms of fitness to undergo general anesthesia. Fifteen percent (37/249) of our patients were considered unable to undergo general anesthesia, but all others underwent exploration for resection.

Sixty-five percent of our patients and 77% of who those underwent laparotomy and exploration had radical resection, which is in line with the experiences of Sunouchi et al. [13]

Table 3. Kaplan-Meier (univariate) analysis considering the most important factors of 5-year survival

Variable	5-year survival, n (%)	Median survival, months	95% CI	p value (log rank test)
Gender				
Male	29 (43)	39	27.971–50.029	0.151
Female	35 (31)	34	25.450–42.550	
Age				
81–85 years	48 (36)	39	29.808–48.192	0.048
86–90 years	16 (38)	38	17.888–58.112	
>90 years	1 (10)	24	0.0000–59.639	
Underlying diseases				
0–1	23 (40)	56	36.040–58.560	0.027
2	29 (34)	37	33.131–40.548	
3	12 (27)	30	23.135–36.954	
Operation				
Radical	63 (40)	45	35.337–54.663	0.0001
Palliative	1 (3)	8	4.422–11.578	
Postoperative morbidity				
Yes	19 (34)	31	14.650–47.350	0.230
No	46 (36)	39	31.926–50.214	
UICC stage				
I	23 (40)	49	22.109–75.891	0.0001
II	29 (34)	52	35.751–68.249	
III	10 (26)	34	24.998–43.002	
IV	1 (20)	8	4.897–11.1	
Histological grade				
I	18 (43)	47	24.771–69.229	0.085
II	36 (34)	38	29.353–46.647	
III	10 (26)	17	4.918–29.082	
Tumor size				
<20 mm	14 (47)	50	45.580–54.420	0.0001
21–50 mm	40 (42)	40	25.161–54.839	
>50 mm	10 (17)	23	11.078–34.922	
Number of lymph nodes				
0	47 (42)	47	35.281–58.719	0.0001
1–3	16 (33)	31	18.655–43.345	
4–6	1 (6)	15	4.679–25.230	
>6	0 (0)	8	0.000–20.002	
Venous invasion				
Yes	2 (4)	17	8.450–25.550	0.0001
No	62 (48)	56	53.704–58.296	
Recurrence				
Yes	3 (7)	31	22.749–39.251	0.0001
No	60 (53)	60	57.766–62.234	

CI, confidence interval; UICC, Union for International Cancer Control.

(64% for patients >80 years of age) and Papamichael et al. [14] (67% for patients >89 years). The rate of palliative surgery still remained proportionally high in our series, but the reduction in palliative procedures in the very elderly should be important as one way to decrease operative mortality and increase treatment efficacy [15].

Older age is independently associated with worse short-term outcome after major oncologic resections [16], and although most oldest-old colon cancer patients do well after elective colectomy, a noteworthy proportion of them die within 90 postoperative days, outside the immediate postoperative period [17], which was also seen here. Postoperative mortality is

Table 4. Results of Cox regression proportional hazards analysis

Variable	<i>p</i> value	95% CI
Age	0.306	0.877–1.520
Underlying diseases	0.182	0.913–1.611
Radical operation	0.0001	1.581–4.845
UICC stage	0.681	0.694–1.269
Tumor size	0.695	0.810–1.371
Lymph nodes	0.407	0.837–1.553
Venous invasion	0.001	0.283–0.739

CI, confidence interval; UICC, Union for International Cancer Control.

reported to increase with age [18], but we were unable to confirm this finding in patients aged >80 years. This difference is caused by selection bias because elderly patients have to be selected for major colorectal surgery.

Mortality can be considerable, and this fact may have important implications when determining the management of this group of patients [19]. Therefore, the use of risk-based treatment decision-making has been recommended [16]. All of our patients selected to have conservative treatment died within 1 year after decision-making, and most of them from causes unrelated to cancer, reflecting good surgical selection.

The effects of older age extend to other important outcome measures after colorectal cancer surgery, and increased morbidity in the oldest old has been reported [20]. Elderly patients with significant comorbidity more frequently die due to complications, and excess 1-year mortality indicates a prolonged impact of surgery [21], so the 30-day mortality rate may underestimate the risk of dying during the first year after surgery. When the patients survive the immediate postoperative phase and the first postoperative year, they seem to have nearly the same cancer-related survival as their younger counterparts.

The problem is that too many of these patients succumb after referral to home or health centers, and moreover, 61% of our deaths during the first postoperative year were unrelated to cancer. The fragility of the patients, their reduced postoperative functional status, and their limited physiological resources presumably play an important role in this excess mortality during the first year after surgery [22, 23]. Although a substantial improvement in the care of colorectal cancer in the elderly has been achieved by increasing the proportion of patients resected for cure, developing perioperative care and decreasing operative mortality [24], this is not enough. The deaths during the first postoperative period need special attention in the future.

Overall survival is reduced in elderly patients, but the cancer-specific survival differences related to age are much less striking [3]. Older patients have a greater probability to die without evidence of recurrence [25]. Our recurrence rate after radical surgery was 27% in patients aged >80 years, which was lower than in our 5-year study (41%), in which we evaluated all colorectal cancer patients [11]. This finding was mainly caused by differences in UICC staging and differentiation of the tumors.

Eighty-two percent of the recurrences of the oldest old manifested within 2 years, which corresponds to 60–85%, as documented by Devesa et al. in 1988 [26].

Although age was a predictor of long-term survival in our series, it was not an independent risk factor in Cox regression analysis. Vascular and lymphatic invasion represent crucial steps in the formation of micrometastases and eventually macroscopic tumor growth at a secondary site, and both these features have been identified to be independent adverse prognostic factors [27]. Extramural venous invasion is a poor prognostic factor for overall

survival and local recurrence and is independent of tumor stage [28]. In patients aged >80 years, vascular invasion was an independent prognostic factor influencing 5-year survival.

In conclusion, after sensible selection for surgery of colorectal cancer, a good long-term survival can be achieved even in the very elderly, but there is an excess mortality unrelated to cancer during the first postoperative year. This problem is caused by the prolonged impact of surgical treatment, and an exact evaluation of these surgical factors is needed.

Disclosure Statement

The authors report no conflicts of interest.

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