EJMI

DOI: 10.14744/ejmi.2025.155486
EJMI 2025;9(4):227–239

Research Article

Prognostic Factors and Real-World Outcomes in Patients Aged 65 Years and Older with Stage II and III Colon Cancer

Zeliha Birsin, Selin Cebeci, Seda Jeral, Vali Aliyev, Nebi Serkan Demirci, Özkan Alan

Department of Medical Oncology, Faculty of Medicine, Istanbul University-Cerrahpaşa, Istanbul, Türkiye

Abstract

Objectives: Colon cancer is common among older adults, yet this population is underrepresented in clinical trials. This study aimed to evaluate real-world outcomes and prognostic factors in patients aged ≥65 years with stage II and III colon cancer.

Methods: This retrospective cohort study included aged ≥65 years with stage II or III colon cancer who underwent curative-intent resection between 2010 and 2024. Clinical, pathological, and treatment-related variables were collected. Relapse-free survival (RFS) and overall survival (OS) were analyzed using Kaplan–Meier and Cox regression methods.

Results: Of the study population (n:218), 45% were younger than 70 years and 55% were aged ≥70 years (median age: 70). Adjuvant chemotherapy was administered to 66% overall, but less frequently in older patients (59% vs. 73%, p=0.027). Oxaliplatin-based regimens were rarely used in stage II disease (3%) but commonly given in stage III (68%, p<0.001). Treatment-related toxicity occurred in 52% of patients, without significant differences between age groups (p=0.937). In the overall cohort, age ≥70 was associated with significantly worse OS (median OS 8.95 vs. 13.3 years, log-rank p=0.021), while RFS did not differ significantly (5-year RFS 64% vs. 76%, p=0.067). In stage II disease, neither age nor receipt of adjuvant chemotherapy significantly influenced OS or RFS (both p>0.05), whereas T4 tumor stage independently predicted shorter OS (p=0.047). In stage III disease, older age (≥70; HR: 2.03, p=0.043), advanced nodal stage (HR: 2.21, p=0.013), and BMI <25 (HR: 2.14, p=0.002) were independent predictors of worse OS, while age was not independently associated with RFS (p>0.05). The addition of oxaliplatin did not provide a measurable survival benefit (p>0.05).

Conclusion: In elderly patients with colon cancer, age did not affect OS or RFS in stage II disease. In stage III, however, older age was an independent adverse factor for OS but not for RFS, while oxaliplatin did not provide additional survival benefit. These findings highlight the importance of individualized treatment decisions based on both tumor characteristics and patient factors.

Keywords: Adjuvant Chemotherapy, Colon Cancer, Elderly Oncology, Prognostic Factors, Real-world Data

Cite This Article: *Birsin Z, Cebeci S, Jeral S, Aliyev V, Demirci NS, Alan Ö. Prognostic Factors and Real-World Outcomes in Patients Aged 65 Years and Older with Stage II and III Colon Cancer. EJMI 2025;9(4):227–239.*

Address for correspondence: Zeliha Birsin, MD. Department of Medical Oncology, Faculty of Medicine, Istanbul University-Cerrahpaşa, Istanbul, Türkiye
Phone: +90 (212) 414 34 34 **E-mail:** zeliha.birsin@iuc.edu.tr

Submitted Date: October 27, 2025 **Revision Date:** December 27, 2025 **Accepted Date:** December 29, 2025

Colorectal cancer (CRC) is one of the most common cancers and a leading cause of cancer-related death worldwide(1). Although the incidence of colorectal cancer has been rising among younger individuals in recent years, it remains most common in older adults, with rates increasing with age.[1,2] The peak incidence is observed among individuals aged 65 to 74 years.[3]

The majority of newyl diagnosed colon cancer cases are identified at a local or regional stage, where surgical resection offers a potential cure(3). For these non-metastatic cases, the 5 year overall survival rates following surgery ara aproximately 68–83% in stage II and 45–65% in stage III. [4] Systemic recurrence following surgical resection remains a major cause of mortality. Therefore, adjuvant chemotherapy is essential to reducing the risk of recurrence and improving long-term outcomes, particularly in patients with high-risk stage II and all stage III colon cancer.[5,6] Several guideline-recommended regimens are available for this purpose, comprising various combinations and dosing schedules of fluorouracil, leucovorin, oxaliplatin, and capecitabine.[4,7]

However, the use of these regimens in older patients requires careful consideration, as this population faces unique challenges related to comorbidities, frailty, and age-associated declines in functional status and organ reserve.[8] Notably, although the majority of colon cancer cases occur in older adults, this population remains underrepresented in clinical trials.[9] As a result, existing evidence may not fully reflect the efficacy and safety of adjuvant chemotherapy in real-world elderly populations. Nevertheless, pooled analyses and cohort studies have suggested a survival benefit from adjuvant chemotherapy in this age group.[10] However, the addition of oxaliplatin to fluoropyrimidines appears to provide limited or no additional benefit for elderly patients with stage III disease.[11,12]

Given the the clinical complexity and the paucity of real-world data on older adults with colon cancer, this study aimed to evaluate survival outcomes and prognostic factors in patients aged 65 years and older with stage II and III colon cancer who underwent curative -intent surgical resection.

Materials and Methods

Study Design and Patient Inclusion Criteria

Between December 2010 and March 2024, a total of 1,780 patients with colon cancer who had undergone curative surgical resection were evaluated at the Department of Medical Oncology, Istanbul University-Cerrahpaşa Faculty of Medicine. Of these, 218 patients aged 65 years or older with stage II or III non-metastatic colon cancer who met the study eligibility criteria were included in the final analysis.

To be eligible for inclusion, patients had to be 65 years of age or older at the time of diagnosis, have pathologically confirmed stage II or III colon cancer, have undergone curative -intent surgical resection with no evidence of distant metastasis, and possess complete clinical and pathological data available for evaluation. Tumor staging was performed according to the 7th or 8th editions of the TNM classification system, based on the year of diagnosis. Patients were excluded if they were younger than 65 years, had a rectal cancer, had positive surgical margins, or lacked sufficient data that reliable survival assessment. Additionally, patients with secondary malignancies were excluded to avoid potential confounding effects on survival outcomes. Patients with a follow-up duration of less than one year were also excluded from the analysis.

Adjuvant Chemotherapy and Patient Follow-Up

Adjuvant chemotherapy was administered at the discretion of the treating oncologist, considering patient age, comorbidities, performance status, and pathological risk factors. In stage II patients, chemotherapy was generally reserved for those with high-risk features (e.g., T4 tumors, obstruction/perforation or inadequate lymph node sampling), and combination regimens with oxaliplatin were not routinely used. Stage III patients were more likely to receive combination chemotherapy when clinically indicated. The selection and duration of chemotherapy were individualized based on patient spesific factors. The chemotherapy regimens included FOLFOX (oxaliplatin 85 mg/m^2 IV on day 1; leucovorin 400 mg/m^2 IV on day 1; followed by 5-fluorouracil 400 mg/m^2 IV bolus on day 1 and 2400–3000 mg/m^2 46-48 hours continuous infusion every 14 days), CAPOX (oxaliplatin 130 mg/m^2 IV on day 1 plus capecitabine 1000 mg/m^2 orally twice daily on days 1–14, every 21 days), capecitabine monotherapy (1250 mg/m^2 orally twice daily on days 1–14 of a 21-day cycle), and 5-FU/LV (leucovorin 400 mg/m^2 IV followed by 5-fluorouracil 400 mg/m^2 IV bolus and 2400 mg/m^2 continuous infusion over 46-48 hours, every 14 days). Dose modifications were made as needed based on toxicity, renal function, and patient tolerability. Patients were followed according to standard institutional protocols. Computed tomography (CT) imaging of the chest and abdomen was performed every 3 to 6 months during the first two years, every 6 to 12 months between years 2 and 5, and annually thereafter.

Data Collection, Study Variables, and Outcome Definitions

Clinical, pathological, and treatment-related data were obtained from institutional electronic medical records

and archived patient files. Patients were categorized according to age (<70 vs. ≥70 years) and disease stage (stage II vs. stage III). Collected variables included demographic characteristics (age, sex), comorbidities, Eastern Cooperative Oncology Group Performance Status (ECOG) performance status, body mass index (BMI), tumor location (categorized as right-sided or left-sided colon), TNM stage, histological grade, lymphovascular invasion (LVI), perineural invasion (PNI), number of dissected lymph nodes, microsatellite instability (MSI) status, Caudal Type Homeobox Transcription Factor 2 (CDX2) expression, and adjuvant chemotherapy details (type of regimen, duration, initiation time after surgery, dose modifications, treatment-related toxicity, and discontinuation if applicable). Follow-up data included disease recurrence, last contact date, and survival status.

The primary endpoints of the study were overall survival (OS) and relaps-free survival (RFS). OS was defined as the duration from the date of curative-intent surgery to death from any cause. RFS was defined as the interval from the date of curative-intent surgery to the first radiologically or pathologically confirmed recurrence of disease. Patients who died without evidence of recurrence or were alive and relapse-free at the time of last follow-up were censored at the date of death or last contact, respectively.

Statistical Analysis

All statistical analyses were conducted using SPSS version 26.0 (IBM Corp., Armonk, NY, USA). Normality of continuous variables was assessed using with normality tests. Since the variables were not normally distributed, they were reported as median (minimum–maximum). Categorical variables were summarized using frequencies and percentages. Comparisons between groups were performed using the Chi-square or Fisher's exact test for categorical variables. Kaplan–Meier curves were used for survival analysis, and differences between groups were assessed using the Log-Rank test. Univariate and multivariate Cox proportional hazards regression analyses were performed to identify independent prognostic factors. A p-value of <0.05 was considered statistically significant.

Ethical Considerations

Access to patient information was restricted to the physicians involved in data analysis and report preparation, in line with institutional confidentiality policies. Ethical approval was obtained from the Ethics Committee of Istanbul University-Cerrahpaşa, Faculty of Medicine (Approval No: 2025/180, dated 05 March 2025). All procedures complied with the Declaration of Helsinki.

Results

Baseline Clinic and Demographic Findings

A total of 218 patients aged 65 years or older with stage II or III colon cancer were included in the study. The median age was 70 years (range: 65–90). In the overall cohort, 98 patients (45%) were aged <70 years, while 120 patients (55%) were aged ≥70 years. The gender distribution was balanced, with 106 (53.2%) female and 102 (46.8%) male patients. Most patients (85.8%) had at least one comorbidity, and the majority had an ECOG performance status of 1 (81.7%). Comorbidities were significantly more frequent in older patients (93% vs. 78%, p = 0.002). Regarding the surgical approach, 82.1% of patients underwent elective surgery, while 17.9% had urgent surgery. Based on TNM staging, 54.1% had stage II and 45.9% had stage III disease.

Baseline demographic and clinical characteristics of the study population are outlined in Table 1, stratified by disease stage (Stage II vs. Stage III), and in Table 2, according to age groups (<70 vs. ≥70 years)

Treatment characteristics, toxicities, and clinical outcomes

Among the overall cohort, 65.6% of patients received adjuvant chemotherapy, whereas 34.4% did not. The median interval between surgery to the initiation of chemotherapy was 8 weeks (range: 4–12 weeks). When stratified by stage, 44% of stage II patients and 91% of stage III patients underwent adjuvant chemotherapy (p<0.001). Oxaliplatin-based regimens were administered to only 3% of stage II patients, compared with a significantly higher proportion of stage III patients (68%, p<0.001). Capecitabine monotherapy was the most frequently used regimen overall (29.8%), followed by CAPOX (20.6%). The majority of patients (87.4%) completed a full six-month course of chemotherapy.

Treatment-related toxicity was observed in 52.4% of patients. The most frequently reported adverse effects included neutropenia (14%), neuropathy (10.5%) and diarrhea (7.7%). Grade 2 toxicity was most common (85.3%). Dose reduction due to toxicity was required in 39.9% of patients, while treatment discontinuation occurred in 5.6% of cases. Among those who discontinued treatment, the majority discontinued oxaliplatin.

Treatment characteristics were also evaluated by age group. Adjuvant chemotherapy was administered less frequently in patients aged ≥70 years compared to those aged <70 (59% vs. 73%, p=0.027). Although the use of oxaliplatin-based regimens was lower in the older group (25% vs. 43%), this difference approached statistical significance (p=0.054). There were no statistically significant differences between age groups in terms of treatment-related toxici-

Table 1. Baseline demographic and clinical characteristics of the overall cohort and by disease stage

Variables	Overall cohort		Stage 2		Stage 3		p
	n=218	%	n=118	%	n=100	%	
Age							
<70 years	98	45	52	44	46	46	0.775[1]
≥70 years	120	55	66	56	54	54	
Gender							
Male	102	46.8	66	56	50	50	0.382[1]
Female	106	53.2	52	44	50	50	
Comorbidity							
Absent	31	14.2	16	14	15	15	0.762[1]
Present	187	85.8	102	86	85	85	
ECOG							
0	35	16.1	19	16	16	16	
1	178	81.7%	96	81	82	82	0.964[1]
2	5	2.3	3	3	2	2	
BMI							
<25	89	40.8	50	42.3	39	39	0.614[1]
≥25	129	59.2	68	57.7	61	61	
Type of surgery							
Urgent	39	17.9	18	15	21	21	0.270[1]
Elective	179	82.1	100	85	79	79	
N stage							
N0	118	54.1	118	100	0	0	
N1	58	26.6	0	0	58	58	0.000[1]
N2	42	19.2	0	0	42	42	
T stage							
T2-T3	117	53.7	74	63	43	43	0.004[1]
T4	101	46.3	44	37	57	57	
<12 LN dissection							
Absent	217	99.5	117	99	100	100	1.000[1]
Present	1	0.5	1	1	0	0	
Lİ							
Absent	28	12.8	23	19	5	5	0.001[1]
Present	190	87.2	95	81	95	95	
Vİ							
Absent	73	33.5	46	39	27	27	0.062[1]
Present	145	66.5	72	61	73	73	
PNİ							
Absent	39	17.9	26	22	13	13	0.083[1]
Present	179	82.1	92	78	87	87	

Table 1. Continue

Variables	Overall cohort		Stage 2		Stage 3		p
	n=218	%	n=118	%	n=100	%	
Histology							
ADC	178	81.7	101	86	77	77	0.263[2]
Mucinous	33	15.1	14	12	19	19	
Signet ring cell	7	3.2	3	3	4	4	
Grade							
1	171	78.4	93	79	78	78	0.909[1]
2	25	11.5	14	12	11	11	
3	22	10.1	11	9	11	11	
Tumor location							
Left	131	60.1	71	60	60	60	0.980[1]
Right	87	39.9	47	40	40	40	
MMR							
pMMR	152	69.7	84	71	68	68	0.381[1]
dMMR	16	7.3	6	5	10	10	
Not available	50	22.9	28	24	22	22	
CDX2							
Negative	5	2.3	3	3	2	2	0.814[1]
Positive	159	72.9	84	71	75	75	
Not available	54	24.8	31	26	23	23	
Adjuvant CT							
Not Received	75	34.4	66	56	9	9	0.000[1]
Received	143	65.6	52	44	91	91	
Oxaliplatin-based CT							
Received	72	50.3	4	3	68	68	0.000[1]
Not received	71	49.7	48	41	23	23	
Recurrence							
Absent	155	71.2	96	82	59	59	0.000[1]
Present	63	28.8	22	18	41	41	
Current status							
Alive	157	72	97	82	60	60	0.000[1]
Exitus	61	28	21	18	40	40	

[1]Chi-Square Test, [2]Fisher›s Exact Test

CT: Chemotherapy; ADC: Adenocarcinoma; CDX2: Caudal type homeobox 2; LI: Lymphatic invasion; VI: Vascular invasion; PNI: Perineural invasion; MMR: Mismatch repair; pMMR; Proficient MMR; dMMR: Deficient MMR; NA: Not available.

ty (28% vs. 35%, p = 0.937), toxicity-related dose reduction (22% vs. 32%, p=0.432), or treatment discontinuation due to toxicity (5% vs. 2%). Patients aged <70 years were also numerically more likely to complete a full 6-month course of adjuvant chemotherapy compared to those aged ≥70 years (67% vs. 49%), although this difference did not reach statistical significance (p=0.222).

Recurrence was observed in 28.8% of patients during the follow-up period. At the time of the final analysis, 28% of patients had died, while 72% were remained alive. When stratified by age, recurrence rates did not differ significantly between patients aged <70 and those ≥70 years (p=0.058). Although mortality was numerically higher among patients aged ≥70 years compared to those <70 years (33% vs. 21%), the difference approached statistical significance (p=0.051). Treatment characteristics, associated toxicities, and clinical outcomes are summarized in Table 1 and Table S1.

Relaps-Free Survival Outcomes

The median follow-up time was 6.04 years. In the overall cohort, median RFS was not reached during the follow-up period. However, when stratified by age, the 5-year RFS rate was 76% in patients younger than 70 and 64% in those aged 70 and older. This difference did not reach statistical significance, although the p-value was borderline (Log-rank p=0.067) (Fig.1A).

The median RFS was not reached in the stage II subgroup. The 5-year RFS rate was 84% in patients younger than 70 and 78% in those aged 70 and older; however, this difference was not statistically significant (log-rank p=0.334) (Fig. 2A). Multivariate Cox regression analysis in stage II patients showed no significant association between RFS and variables including age, gender, surgery type, tumor grade or location, MMR status, or adjuvant chemotherapy. (Table-S2).

In patients with stage III colon cancer, median RFS was 7.38 years (95% CI not estimable). The 5-year RFS rate was significantly lower in those aged ≥70 and <70 years, at 48% and 66%, respectively (log-rank p=0.035) (Fig. 3A). In patients with stage III colon cancer, multivariate Cox regression analysis revealed that low BMI (<25) (HR: 3.05, 95% CI: 1.63–5.72, p=0.008) and higher N stage (HR: 1.99, 95% CI: 1.08–3.68, p=0.027) were significantly associated with decreased relaps-free survival. Other variables, including age, comorbidity, MMR status and receipt of adjuvant chemotherapy, were not independently associated with RFS (Table-S3).

Overall Survival Outcomes

The OS in the overall cohort was 12.75 years (95% CI: 8.48–17.03). When stratified by age, patients younger than 70 years had a median OS of 13.3 years (95% CI: 9.82–16.78), compared to 8.95 years (95% CI: 6.48–11.41) in those aged 70 and older. This difference was statistically significant (log-rank p = 0.021) (Figure 1B).

In the stage II group, the median OS was 12.75 years (95% CI: 11.38–14.12). The 5-year OS rate was 92% and 88% in those aged <70 and ≥70 years, respectively; this difference was not statistically significant (log-rank p = 0.438) (Fig. 2B). In multivariate Cox regression analysis of stage II patients, T4 tumor stage (HR: 2.36, 95% CI: 1.01–5.53, p=0.047) was found to be significantly associated with shorter overall survival. Other variables, including age, comorbidity, tumor grade, LVI, PNI, MMR status and adjuvant chemotherapy, were not independently associated with OS (Table 3).

For the stage III group, the median OS was 7.91 years (95% CI: 5.28–10.54). The 5-year OS rate was significantly lower in those aged ≥70 and <70 years, at 54% and 71%, respectively (log-rank p = 0.014), with a median OS of 6.67 years (95% CI: 4.21–9.13) versus not reached in the

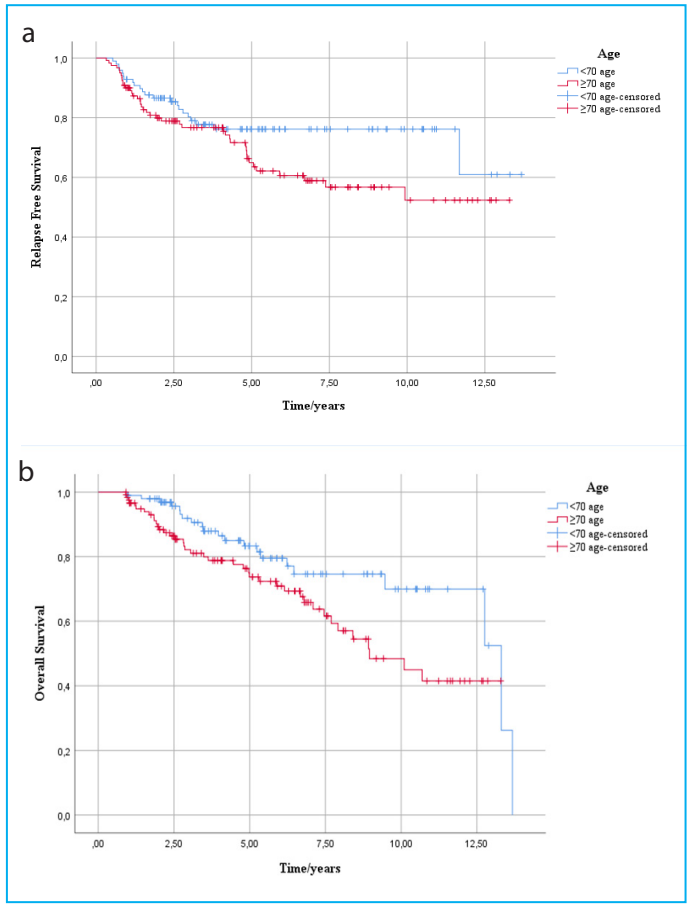

Figure 1. Kaplan–Meier curves showing **(a)** relapse-free survival (RFS) and **(b)** overall survival (OS) in patients aged <70 years versus those aged ≥70 years. While RFS was not significantly different between the two groups (log-rank p=0.067), OS was significantly worse in older patients (log-rank p=0.021).

younger group (Fig. 3B).In multivariate Cox regression analysis, older age (≥70 years) (HR: 2.03, 95% CI: 1.02–4.04, p = 0.043), advanced nodal stage (HR: 2.21, 95% CI: 1.18–4.16, p=0.013), and lower BMI (<25) (HR: 2.14, 95% CI: 1.12–4.16, p=0.002) were independently associated with worse overall survival. Neither the receipt of adjuvant chemotherapy (HR: 0.58, 95% CI: 0.22–1.49, p = 0.260) nor the use of oxaliplatin-based regimens (HR: 1.57, 95% CI: 0.77–3.18, p=0.207) showed a statistically significant impact on OS. Similarly, other variables such as MMR status, comorbidity, and tumor grade were not independently associated with overall survival in the multivariate analysis (Table 4).

Discussion

In this retrospective cohort of 218 elderly patients (age≥65) with stage II–III colon cancer, we evaluated survival outcomes and prognostic factors. In the overall cohort, there was no significant difference in relapse-free survival (RFS) between patients younger and older than 70 years, whereas OS was significantly worse in those aged ≥70 years. In stage II disease, neither age nor adjuvant chemotherapy significantly influenced outcomes. In contrast, in stage III patients, age ≥70 was an independent adverse prognostic factor for OS. While Kaplan–Meier analysis suggested worse RFS in older patients, multivariate analysis demonstrated that age was not an independent predictor of RFS in stage III disease.

As life expectancy gradually increases, a growing number of older adults are being diagnosed with colon cancer(3, 9, 13). Given both the higher incidence of colon cancer in older adults and the unique clinical challenges they face—such as comorbid conditions, functional impairment, and decreased tolerance to treatment—there is a clear need to deepen our understanding of the disease in this population.

The prognostic impact of age at colon cancer onset remains uncertain, as previous studies have yielded conflicting results. While some reports indicate that elderly

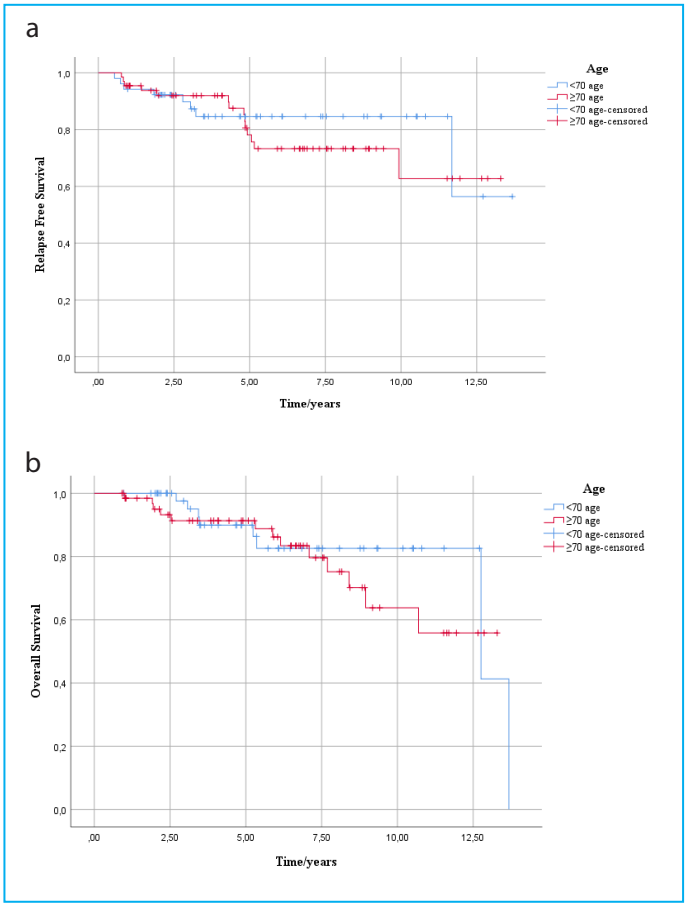

Figure 2. Kaplan–Meier curves showing **(a)** relapse-free survival (RFS) and **(b)** overall survival (OS) in patients with stage II colon cancer, stratified by age group (<70 vs. ≥70 years). No statistically significant differences were observed in RFS (log-rank p=0.334) or OS (log-rank p=0.438) between the two age groups.

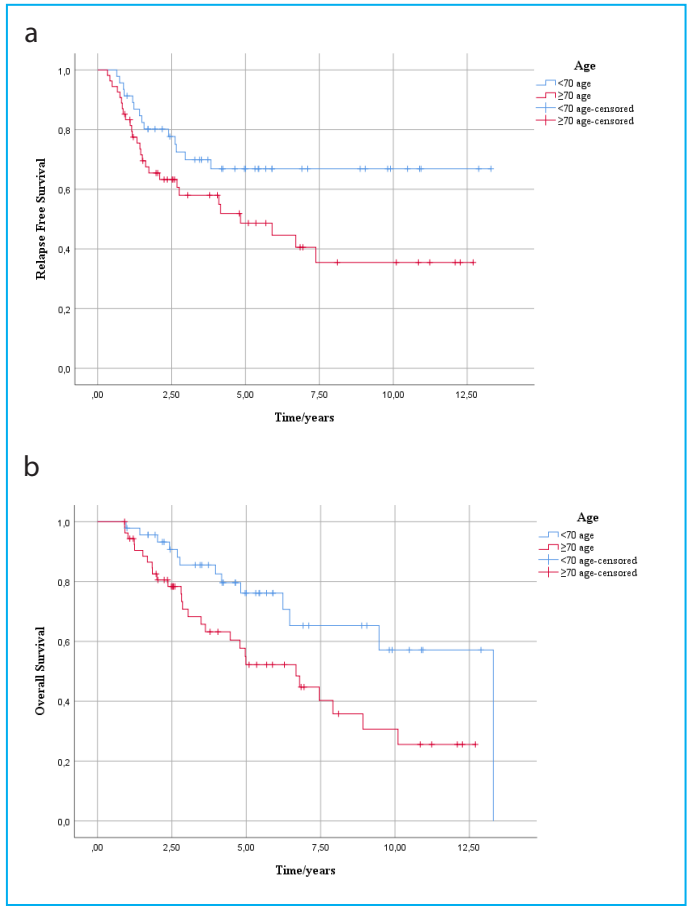

Figure 3. Kaplan–Meier curves showing **(a)** relapse-free survival (RFS) and **(b)** overall survival (OS) in patients with stage III colon cancer, stratified by age group (<70 vs. ≥70 years). Both RFS and OS were significantly worse in older patients (RFS: log-rank p=0.035; OS: log-rank p=0.014).

Table S1. Treatment characteristics, toxicities, and clinical outcomes

	n (%)
Adjuvant CT, n (%)	
Received	143 (65.6)
Not received	75 (34.4)
Adjuvant CT, n (%)	
None	75 (34.4)
Capesitabine	65 (29.8)
CAPOX	45 (20.6)
FOLFOX	27 (12.4)
5-FU/FA	6 (2.8)
Oxaliplatin-based CT, n (%)	
Received	72 (50.3)
Not received	71 (49.7)
Median time to CT initiation / week	8 (min4-max12)
Duration of treatment, n (%)	
<3 months	8 (5.6)
3 months	10 (7)
6 months	125 (87.4)
Treatment-related Toxicity, n (%)	
Present	68 (52.4)
Absent	75 (47.6)
Types of toxicity, n (%)	
None	75 (52.4)
Neuropathy	15 (10.5)
Mucostis	3 (2.1)
Neutropenia	20 (14)
Thrombocytopenia	10 (7)
Hand-foot syndrome	7 (4.9)
Diarrhea	11 (7.7)
AKI	1 (0.7)
AMI	1 (0.7)
Toxicity grade, n (%)	
1	3 (4.4)
2	58 (85.3)
3	7 (10.3)
Dose reduction due to toxicity, n (%)	
Yes	57 (39.9)
No	83 (60.1)
Treatment discontinuation due to ti, n (%)	
No	135 (94.4)
Capecitabine/5FU discontinuation	1 (0.7)

Table S1. Continue

	n (%)
Treatment discontinuation due to ti, n (%)	
Oxaliplatin discontinuation	7 (4.9)
Recurrence, n (%)	
Present	63 (28.8)
Absent	155 (71.2)
Recurrence site, n (%)	
Liver	32 (50.7)
Lung	5 (7.9)
Peritoneal implants	12 (19.3)
Local recurrence	6 (9.5)
Liver and peritoneal implants	8 (12.6)
Current status, n (%)	
Exitus	61 (28)
Alive	157 (72)

CT: Chemotherapy, AKI: Acute Kidney Injury, AMI: Acute Myocardial Infarction, FOLFOX: 5-Fluorouracil, Leucovorin, and Oxaliplatin, CAPOX: Capecitabine and Oxaliplatin.

patients experience poorer survival outcomes.[14,15]—often attributed to increased comorbidities, postoperative complications, and reduced tolerance or omission of chemotherapy—other studies have shown comparable survival rates between older and younger patients undergoing curative treatment.[10,16] In our study, patients aged 70 years and older had significantly poorer OS compared to younger patients (p=0.021), whereas the difference in RFS did not reach statistical significance (p=0.067) in the overall cohort. When analyzed by stage, this age-related difference in OS was evident only in stage III patients, whereas no significant prognostic difference by age was observed among stage II patients. In contrast, RFS could not be associated with age in either stage II or stage III disease.

In our study, the use of adjuvant chemotherapy did not result in a significant improvement in OS or RFS among patients with stage II colon cancer. Similar to the findings reported by Lee et al., adjuvant treatment did not appear to provide a survival benefit in elderly patients with stage II disease.[17] In the stage III group, the vast majority of patients (91%) received adjuvant chemotherapy, and only a small subset (9%) did not. Therefore, a direct comparison between treated and untreated patients in this group is limited by the imbalance in group sizes. Notably, most of the patients who did not receive adjuvant chemotherapy were aged 70 years or older (p=0.027). This finding is consistent with existing literature, which consistently demonstrates a decline in the use of adjuvant chemotherapy with

Table 2. Baseline demographic and clinical characteristics of the cohort stratified by age group (<70 vs. ≥70 years)

Variables	Age				p
	<70 (n=98)		≥70 (n=120)		
Gender, n (%)					
Male	51	52	65	54	0.754[1]
Female	47	48	55	46	
Comorbidty, n (%)					
Absent	22	22	9	8	0.002[1]
Present	76	78	111	93	
ECOG, n (%)					
0	28	29	7	6	-
1	69	70	109	91	
2	1	1	4	3	
BMI, n (%)					
<25	36	37	53	44	0.267[1]
≥25	62	63	67	56	
T stage, n (%)					
T2-T3	54	55	63	53	0.702[1]
T4	44	45	57	48	
N stage, n (%)					
N0	53	54	66	55	0.897[1]
N1	27	28	30	25	
N2	18	18	24	20	
Stage, n (%)					
2	52	53	66	55	0.775[1]
3	46	47	54	45	
Tumor location, n (%)					
Left	65	66	66	55	0.089[1]
Right	33	34	54	45	
Adjuvant CT, n (%)					
Received	72	73	71	59	0.0027[1]
Not received	26	27	49	41	
Oxaliplatin-based CT, n (%)					
Received	42	43	30	25	0.054[1]
Not received	30	31	41	34	
Treatment-related toxicity, n (%)					
Absent	38	39	37	31	0.937[1]
Present	34	35	34	28	
Toxicity-related discontinuation, n (%)					
Absent	70	71	65	54	-
Oxaliplatin stop	1	1	6	5	
Capesitabine stop	1	1	0	0	
Dose reduction due to toxicity, n (%)					
Absent	41	42	45	38	0.432[1]
Present	31	32	26	22	
Duration of treatment, n (%)					
<3 months	2	2	6	5	0.222 [1]
3 months	4	4	6	5	
6 months	66	67	59	49	
Recurrence, n (%)					
Absent	80	82	90	75	0.240[1]
Present	18	18	30	25	
Current status, n (%)					
Alive	77	79	80	67	0.051[1]
Exitus	21	21	40	33	

[1]Chi-Square Test; CT: Chemotherapy; BMI: Body Mass index; ECOG: Eastern Cooperative Oncology Group.

advancing age.[18,19] Previous studies have identified older age as a strong negative predictor for the receipt of chemotherapy.[20]

The addition of oxaliplatin to adjuvant chemotherapy has been shown to improve outcomes in patients with high-risk stage II and stage III colon cancer.[21] However, its efficacy in patients aged 70 years and older remains unclear. While some studies suggest that clinically fit older adults may derive a survival benefit from oxaliplatin-containing regimens,[22] others have reported conflicting results,[11,23] highlighting ongoing uncertainty in this population. In our cohort, oxaliplatin-based chemotherapy was administered to only 3% of patients with stage II disease, whereas 68% of patients with stage III colon cancer treated with such regimen. Given the very low rate of oxaliplatin use in stage II, meaningful comparisons regarding survival outcomes in this subgroup are limited. Hoewever, among elderly patients with stage III disease, the use of oxaliplatin-based chemotherapy did not show a significant impact on either OS or RFS in multivariate Cox regression analysis, suggesting that the addition of oxaliplatin may provide limited benefit in this age group.

Within our study group, chemotherapy-related toxicity, toxicity-related dose reduction, and treatment discontinuation rates did not significantly differ between patients aged below and above 70 years. However, treatment discontinuation due to toxicity occurred numerically more often in patients

Table S2. Univariate and multivariate cox regression analysis for relapse-free survival in patients with stage 2 colon cancer

	Univariate Analiz		Multivariate Analiz	
	HR (95%CI)	p	HR (95%CI)	P
Age				
<70	1.66 (0.71-3.87)	0.233		
≥70				
Gender				
Female	0.77 (0.34-1.73)	0.540		
Male				
Comorbidty				
Absent	1.19 (0.40-3.56)	0.745		
Present				
BMI				
<25	0.98 (0.44-2.17)	0.971		
≥25				
T stage				
T2-T3	1.90 (0.91-3.98)	0.076	1.94 (0.92-4.07)	0.077
T4				
Lİ				
Absent	0.96 (0.32-2.81)	0.946		
Present				
Vİ				
Absent	1.05 (0.45-2.26)	0.895		
Present				
PNİ				
Absent	0.85 (0.31-2.27)	0.747		
Present				
Tumor location				
Right	1.06 (0.48-2.36)	0.871		
Left				
Grade				
1				
2	1.13 (0.64-2.02)	0.659		
3				
Type of surgery				
Emergency	0.65 (0.24-1.74)	0.396		
Elective				
MMR				
pMMR				
dMMR	0.94 (0.70-1.27)	0.703		
NA				
Adjuvant CT				
Received	1.05 (0.47-2.31)	0.903		
Not received				
Oxaliplatin-based CT				
Received	0.75 (0.09-6.04)	0.790		
Not received				

CT: Chemotherapy, LI: Lymphatic invasion, VI: Vascular invasion, PNI: Perineural invasion, CEA: Carcinoembryonic antigen, MMR: Mismatch repair, pMMR: proficient MMR, dMMR: deficient MMR, NA: Not available.

aged 70 and older, and was predominantly associated with oxaliplatin-based regimens. These findings suggest that adjuvant chemotherapy may be generally tolerable in elderly patients; however, the use of oxaliplatin in this population should be approached with greater caution, and clinicians may consider limiting its use to fit elderly individuals following careful geriatric and toxicity risk assessment.

Our multivariate analysis showed that in stage II elderly patients, T4 tumor stage was the only independent predictor of poorer survival, whereas age itself was not prognostically significant. Similary, comorbidity, tumor grade, and receipt of adjuvant chemotherapy were not independently predictive. This finding underscores that in clinical decision-making for stage II disease, advanced age alone should not be considered a limiting factor; rather, treatment planning should be guided by tumor characteristics, performance status, and frailty assessment.

In the stage III cohort, older age (≥70 years), advanced nodal involvement and lower BMI (<25) emerged as independent predictors of poorer survival. These findings highlight the prognostic signifance of both tumor-related and host-related factors in colon cancer. Notably, higher preoperative BMI has been associated with more favorable outcomes in elderly patients, possibly reflecting better nutritional and physiological reserve.[24,25] Therefore, in this population, nutritional status should be carefully assessed and deficits corrected, as adequate nutritional reserve may directly translate into improved survival outcomes.

This study has several limitations. Its retrospective, single-center design may introduce selection bias and limit generalizability. The relatively small sample size, particularly in subgroups such as stage III patients without adjuvant therapy, may have reduced statistical power. Additionally, the lack of cause-specific mortality data limited

Table S3. Univariate and multivariate cox regression analysis for relapse-free survival in patients with stage 3 colon cancer

	Univariate Analiz		Multivariate Analiz	
	HR (95%CI)	p	HR (95%CI)	P
Age				
<70	2.02 (1.04-3.90)	0.036	1.45 (0.72-2.93)	0.296
≥70				
Gender				
Female	0.92 (0.50-1.71)	0.814		
Male				
Comorbidty				
Absent	3.63 (0.87-15.05)	0.076	4.07 (0.95-7.35)	0.057
Present				
BMI				
<25	2.27 (1.29-4.14)	0.056	3.05 (1.63-5.72)	0.008
≥25				
T stage				
T2-T3	0.78 (0.50-1.23)	0.298		
T4				
N stage				
N1	2.01 (1.11-3.68)	0.023	1.99 (1.08-3.68)	0.027
N2				
N3				
Lİ				
Absent	0.85 (0.20-3.57)	0.831		
Present				
Vİ				
Absent	1.22 (0.58-2.58)	0.587		
Present				
PNİ				
Absent	0.95 (0.40-2.28)	0.925		
Present				
Tumor location				
Right	1.02 (0.65-1.60)	0.256		
Left				
Grade				
1	1.02 (0.65-1.60)	0.923		
2				
3				
Type of surgery				
Emergency	0.61 (0.30-1.23)	0.169		
Elective				
MMR				
pMMR	0.91 (0.71-1.17)	0.481		
dMMR				
NA				
Adjuvant CT				
Received	0.67 (0.26-1.73)	0.420		
Not received				
Oxaliplatin-based CT				
Received	1.51 (0.75-3.03)	0.239		
Not received				

CT: Chemotherapy; LI: Lymphatic invasion; VI: Vascular invasion; PNI: Perineural invasion; CEA: Carcinoembryonic antigen; MMR: Mismatch repair; pMMR: proficient, MMR; dMMR: deficient MMR; NA: Not available.

cancer-specific survival analysis. Nonetheless, the study offers valuable real-world insights into outcomes and prognostic factors in older patients with non-metastatic colon cancer.

Conclusions

Based on our findings, age did not significantly influence outcomes in stage II disease. In stage III disease, however, older age (≥70) was identified as an independent adverse prognostic factor for OS, whereas it was not independently associated with RFS. The use of oxaliplatin-based chemotherapy in older adults should be careully considered, given its potential toxicity and uncertain benefit in this population. Additionally, nutritional status appears to play a critical role in treatment tolerance and overall prognosis, underscoring the importance of comprehensive geriatric assessment. These findings emphasize the need for a personalized approach when considering adjuvant treatment in older adults, taking into account both tumor characteristics and individual patient factors.

Disclosures

Ethics Committee Approval: This retrospective study was approved by the Ethics Committee of Istanbul University-Cerrahpaşa, Cerrahpaşa Faculty of Medicine (Approval Number: 2025/180; Date of Approval: 05 March 2025). The study was conducted in accordance with the principles of the Declaration of Helsinki and the Good Clinical Practice Guidelines of the Turkish Medicines and Medical Devices Agency.

Informed Consent: As this was a retrospective study based on

Table 3. Univariate and multivariate cox regression analysis for relapse-free survival in patients with stage 3 colon cancer

	Univariate Analiz		Multivariate Analiz	
	HR (95%CI)	p	HR (95%CI)	P
Age				
<70	1.43 (0.57-3.60)	0.441		
≥70				
Gender				
Female	0.85 (0.51-1.43)	0.558		
Male				
Comorbidty				
Absent	1.16 (0.36-3.73)	0.792		
Present				
BMI				
<25	0.82 (0.34-1.98)	0.662		
≥25				
T stage				
T2-T3	2.32 (0.99-5.44)	0.050	2.36 (1.01-5.53)	0.047
T4				
Lİ				
Absent	0.71 (0.23-2.15)	0.554		
Present				
Vİ				
Absent	0.82 (0.32-2.06)	0.677		
Present				
PNİ				
Absent	0.58 (0.21-1.61)	0.302		
Present				
Tumor location				
Right	1.36 (0.56-3.28)	0.489		
Left				
Grade				
1	1.07 (0.55-2.05)	0.840		
2				
3				
Type of surgery				
Emergency	0.51 (0.18-1.42)	0.199		
Elective				
MMR				
dMMR	0.99 (0.71-1.37)	0.969		
pMMR				
NA				
Adjuvant CT				
Received	1.42 (0.59-3.44)	0.429		
Not received				
Oxaliplatin-based CT				
Received	0.58 (0.07-4.79)	0.615		
Not received				

CT: Chemotherapy; LI: Lymphatic invasion; VI: Vascular invasion; PNI: Perineural invasion; MMR: Mismatch repair; pMMR: Proficient MMR; dMMR: Deficient MMR; NA:Not available.

Table 4. Univariate and multivariate cox regression analysis for overall survival in patients with stage 3 colon cancer

	Univariate Analiz		Multivariate Analiz	
	HR (95%CI)	p	HR (95%CI)	P
Age				
<70	2.29 (1.16-4.54)	0.017	2.03 (01.02-4.04)	0.043
≥70				
Gender				
Female	0.86 (0.46-1.62)	0.654		
Male				
Comorbidty				
Absent	3.38 (0.81-14.06)	0.094	3.82 (0.88-16.05)	0.073
Present				
BMI				
<25	0.46 (0.24-0.88)	0.020	2.14 (1.12-4.16)	0.002
≥25				
T stage				
T2-T3	0.81 (0.52-1.28)	0.379		
T4				
N stage				
N1	2.30 (1.24-4.28)	0.008	2.21 (1.18-4.16)	0.013
N2				
N3				
Lİ				
Absent	0.58 (0.13-2.47)	0.468		
Present				
Vİ				
Absent	1.17 (0.54-2.57)	0.679		
Present				
PNİ				
Absent	1.08 (0.42-2.78)	0.864		
Present				
Tumor location				
Right	1.40 (0.74-2.64)	0.295		
Left				
Grade				
1	1.00 (0.62-1.61)	0.976		
2				
3				
Type of surgery				
Emergency	0.50 (0.25-1.03)	0.061	0.66 (0.31-1.40)	0.290
Elective				
MMR				
pMMR	0.85 (0.66-1.09)	0.214		
dMMR				
NA				
Adjuvant CT				
Received	0.58 (0.22-1.49)	0.260		
Not received				
Oxaliplatin-based CT				
Received	1.57 (0.77-3.18)	0.207		
Not received				

CT: Chemotherapy; LI: Lymphatic invasion; VI: Vascular invasion; PNI: Perineural invasion; MMR: Mismatch repair; pMMR: Proficient MMR; dMMR: Deficient MMR; NA:Not available.

medical record review, informed consent was waived in accordance with the approval of the institutional ethics committee.

Peer-review: Externally peer reviewed.

Conflicts of Interest: The authors declare that there are no conflicts of interest related to this study.

Funding: This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Author Contributions: Concept – Z.B., Ö.A.; Design – N.S.D., V.A.; Supervision – Z.B., Ö.A.; Materials – Z.B., Ö.A.; Fundings – N.S.D., Ö.A.; Data collection &/or processing –S.J.; Analysis and/or interpretation – V.A., S.C.; Literature search – Z.B., Ö.A.; Writing – Z.B.; Critical review – Z.B., Ö.A.

References

1. Siegel RL, Giaquinto AN, Jemal A. Cancer statistics, 2024. CA Cancer J Clin 2024;74(1):12–49.
2. Angelakas A, Christodoulou T, Kamposioras K, Barriuso J, Braun M, Hasan J, et al. Is early-onset colorectal cancer an evolving pandemic? Real-world data from a tertiary cancer center. Oncologist 2024;29(12):e1680–e91.
3. Institute SDotNC. Cancer Stat Facts: Colorectal Cancer n.d. Available at: https://seer.cancer.gov/statfacts/html/colorect.html Accessed on Jan 07, 2026.
4. Argilés G, Tabernero J, Labianca R, Hochhauser D, Salazar R, Iveson T, et al. Localised colon cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol 2020;31(10):1291–305.
5. Wolmark N, Rockette H, Mamounas E, Jones J, Wieand S, Wickerham DL, et al. Clinical trial to assess the relative efficacy of fluorouracil and leucovorin, fluorouracil and levamisole, and fluorouracil, leucovorin, and levamisole in patients with Dukes' B and C carcinoma of the colon: results from National Surgical Adjuvant Breast and Bowel Project C-04. J Clin Oncol 1999;17(11):3553–9.
6. André T, Boni C, Mounedji-Boudiaf L, Navarro M, Tabernero J, Hickish T, et al. Oxaliplatin, fluorouracil, and leucovorin as adjuvant treatment for colon cancer. N Engl J Med 2004;350(23):2343–51.
7. Benson AB, Venook AP, Adam M, Chang G, Chen YJ, Ciombor KK, et al. Colon Cancer, Version 3.2024, NCCN Clinical Practice Guidelines in Oncology. J Natl Compr Canc Netw 2024;22(2D):e240029.
8. Ioffe D, Dotan E. Guidance for treating the older adults with colorectal cancer. Curr Treat Options Oncol 2023;24(6):644–66.
9. Kim JH. Chemotherapy for colorectal cancer in the elderly. World J Gastroenterol 2015;21(17):5158–66.
10. Sargent DJ, Goldberg RM, Jacobson SD, Macdonald JS, Labianca R, Haller DG, et al. A pooled analysis of adjuvant chemotherapy for resected colon cancer in elderly patients. N Eng J Med 2001;345(15):1091–7.
11. Tournigand C, André T, Bonnetain F, Chibaudel B, Lledo G, Hickish T, et al. Adjuvant therapy with fluorouracil and oxaliplatin in stage II and elderly patients (between ages 70 and 75 years) with colon cancer: subgroup analyses of the Multicenter International Study of Oxaliplatin, Fluorouracil, and Leucovorin in the Adjuvant Treatment of Colon Cancer trial. J Clin Oncol 2012;30(27):3353–60.
12. Haller DG, Cassidy J, Tabernero J, Maroun JA, Braud FGD, Price TJ, et al. Efficacy findings from a randomized phase III trial of capecitabine plus oxaliplatin versus bolus 5-FU/LV for stage III colon cancer (NO16968): Impact of age on disease-free survival (DFS). Journal of Clinical Oncology. 2010;28(Suppl 15):3521.
13. Christensen K, Doblhammer G, Rau R, Vaupel JW. Ageing populations: the challenges ahead. Lancet 2009;374(9696):1196–208.
14. Lee SM, Shin JS. Colorectal Cancer in Octogenarian and Nonagenarian Patients: Clinicopathological Features and Survivals. Ann Coloproctol 2020;36(5):323–9.
15. Patel SS, Nelson R, Sanchez J, Lee W, Uyeno L, Garcia-Aguilar J, et al. Elderly patients with colon cancer have unique tumor characteristics and poor survival. Cancer 2013;119(4):739–47.
16. Mulcahy HE, Patchett SE, Daly L, O'Donoghue DP. Prognosis of elderly patients with large bowel cancer. Br J Surg 1994;81(5):736–8.
17. Lee Y, Park I, Cho H, Gwak G, Yang K, Bae BN. Effect of adjuvant chemotherapy on elderly stage II high-risk colorectal cancer patients. Ann Coloproctol 2021;37(5):298–305.
18. Khalil L, Gao X, Switchenko JM, Alese OB, Akce M, Wu C, et al. Survival outcomes of adjuvant chemotherapy in elderly patients with stage III colon cancer. Oncologist 2022;27(9):740–50.
19. Pinter C, Sharma S, Abid A, Ahmed O, Le D, Kanthan R, et al. Outcomes of elderly patients with node-positive colon cancer: A multicenter population-based cohort study. Clinical Colorectal Cancer 2025;24(2):143–52.
20. van den Berg I, van de Weerd S, van Klaveren D, Coebergh van den Braak RRJ, van Krieken JHJM, Koopman M, et al. Daily practice in guideline adherence to adjuvant chemotherapy in stage III colon cancer and predictors of outcome. Eur J Surg Oncol 2021;47(8):2060–8.
21. André T, de Gramont A, Vernerey D, Chibaudel B, Bonnetain F, Tijeras-Raballand A, et al. Adjuvant fluorouracil, leucovorin, and oxaliplatin in stage II to III colon cancer: Updated 10-year survival and outcomes according to BRAF mutation and mismatch repair status of the MOSAIC study. J Clin Oncol 2015;33(35):4176–87.
22. Lund CM, Nielsen D, Dehlendorff C, Christiansen AB, Rønholt F, Johansen JS, et al. Efficacy and toxicity of adjuvant chemotherapy in elderly patients with colorectal cancer: the AC-

CORE study. ESMO Open 2016;1(5):e000087.
23. Yothers G, O'Connell MJ, Allegra CJ, Kuebler JP, Colangelo LH, Petrelli NJ, et al. Oxaliplatin as adjuvant therapy for colon cancer: updated results of NSABP C-07 trial, including survival and subset analyses. J Clin Oncol 2011;29(28):3768–74.
24. Takeyama H, Noura S, Suzuki Y, Odagiri K, Yanagimoto Y, Yamashita M, et al. Higher body mass index is a simple favorable non-cancer prognostic marker for Japanese elderly colorectal cancer patients after curative resection. J Anus Rectum Colon 2022;6(2):134–42.
25. Adachi T, Hinoi T, Kinugawa Y, Enomoto T, Maruyama S, Hirose H, et al. Lower body mass index predicts worse cancer-specific prognosis in octogenarians with colorectal cancer. J Gastroenterol 2016;51(8):779–87.