JJCO Japanese Journal of Clinical Oncology

Jpn J Clin Oncol 2013;43(2)132–138
doi:10.1093/jjco/hys195
Advance Access Publication 29 November 2012

Practical Outcome of Adjuvant FOLFOX4 Chemotherapy in Elderly Patients with Stage III Colon Cancer: Single-center Study in Korea

Ji-Yeon Kim[1], Yu Jung Kim[1], Keun-Wook Lee[1], Jong Seok Lee[1], Duck-Woo Kim[2], Sung-Bum Kang[2], Hye Seung Lee[3], Na Young Jang[4], Jae-Sung Kim[4] and Jee Hyun Kim[1,*]

[1]Department of Internal Medicine, Seoul National University College of Medicine, Seoul National University Bundang Hospital, Seongnam, [2]Department of Surgery, Seoul National University College of Medicine, Seoul National University Bundang Hospital, Seongnam, [3]Department of Pathology, Seoul National University College of Medicine, Seoul National University Bundang Hospital, Seongnam and [4]Department of Radiation Oncology, Seoul National University College of Medicine, Seoul National University Bundang Hospital, Seongnam, Korea

*For reprints and all correspondence: Jee Hyun Kim, Department of Internal Medicine, Seoul National University Bundang Hospital, Seoul National University College of Medicine, 82, Gumi-ro 173 beon-gil, Bundang-gu, Seongnam 463-707, Korea. E-mail: jhkimmd@snubh.org

Received July 31, 2012; accepted October 22, 2012

Objective: Elderly patients derive similar benefits from 5-fluorouracil-based adjuvant chemotherapy in Stage III colon cancer; however, conflicting data exist regarding additional benefit from oxaliplatin, fluorouracil and leucovorin (FOLFOX) chemotherapy.
Methods: Single-center, retrospective analysis was performed to compare the safety and efficacy of adjuvant oxaliplatin, fluorouracil and leucovorin-4 chemotherapy in older patients (age $\geq$65 years) with younger patients with Stage III colon cancer after surgical resection.
Results: Among 391 patients with Stage III colon cancer, 229 patients received adjuvant oxaliplatin, fluorouracil and leucovorin chemotherapy (87 (43.5%) $\geq$65 years old versus 142 (74.3%) $<$65 years old). Older patients had similar clinico-pathological characteristics as younger patients except for higher Charlson-Age comorbidity score (median 3.44 versus 2.85, $P < 0.01$). The estimated 3-year disease-free survival (76.5 versus 80.0%, $P = 0.88$) and 3-year overall survival (90.9 versus 92.7%, $P = 0.98$) were similar. Grade 3–4 neutropenia was the only toxicity with higher frequency in the elderly patients (62.1 versus 46.5%, $P = 0.02$). Elderly patients received a lower relative dose intensity of oxaliplatin (0.76 versus 0.79) and 5-fluorouracil (0.75 versus 0.80, $P = 0.009$).
Conclusions: Adjuvant oxaliplatin, fluorouracil and leucovorin chemotherapy resulted in similar efficacy without significant increase in toxicity in older patients aged $\geq$65 when compared with younger patients with curatively resected Stage III colon cancer. Therefore, for colon cancer patients aged $\geq$65, oxaliplatin, fluorouracil and leucovorin chemotherapy can be recommended as safe and effective adjuvant chemotherapy after curative surgery in Asia.

Key words: aged – colon cancer – chemotherapy – adjuvant – FOLFOX4 protocol

INTRODUCTION

Colon cancer is the second leading cause of cancer-related death in the world and is one of the most prevalent solid malignancies in the elderly population worldwide. From 2004 to 2008, the median age at diagnosis for cancer of the colon and rectum in the United States was 71 years. Approximately 50% of patients were diagnosed over the age of 70 (1).

Although the majority of the patients with colon cancer are elderly, most pivotal trials of adjuvant chemotherapy have involved young patients with colon cancer. Only 15.1% of the patients who were enrolled in 5-fluorouracil (5-FU)-based adjuvant chemotherapy trials were over 70 year of age (2–4). Pooled analyses of 5-FU-based adjuvant chemotherapy clinical trials have reported improved recurrence-free survival (hazard ratio (HR) = 0.68, $P < 0.001$) and overall survival (OS) (HR = 0.76, $P < 0.001$) in the chemotherapy arm compared with those in the surgery-alone control group. The degree of benefit was the same in younger (<70 years old) and older patients ($P = 0.33$ for the time to tumor recurrence and $P = 0.61$ for OS). In addition, there were no significant differences in adverse reactions between the two groups excluding neutropenia (5). However, many elderly patients are not offered adjuvant chemotherapy, or they opt not to be treated because of fears of increased toxicities (6).

Oxaliplatin, 5-FU and leucovorin (LV) (FOLFOX4) chemotherapy exhibited superior efficacy in terms of 3-year disease-free survival (DFS) compared with that of infusional 5-FU/LV in the Multicenter International Study of Oxaliplatin/5-Fluorouracil/Leucovorin in the Adjuvant Treatment of Colon Cancer (MOSAIC) trial, and the FOLFOX regimen has been considered the standard treatment option for Stage III colon cancer patients (7). However, there are conflicting data regarding the additional benefit of FOLFOX adjuvant chemotherapy in elderly patients with Stage III colon cancer. Pooled analyses of adjuvant and palliative FOLFOX chemotherapy reported improved DFS (HR = 0.69; 95% CI, 0.63–0.76; $P < 0.0001$) in the FOLFOX arm compared with that in the 5-FU/LV chemotherapy arm, and this did not differ by patient age (HR = 0.70; 95% CI, 0.63–0.77 for age <70; HR = 0.65; 95% CI, 0.52–0.81 for age ≥70; $P = 0.42$ for age-treatment interaction) (8). Conversely, analysis of the Adjuvant Colon Cancer Endpoints (ACCENT) database reported that the benefit of newer chemotherapy regimens may be restricted to patients <70 years old (9).

Most of the published reports on the efficacy and toxicity of FOLFOX4 chemotherapy are limited to Western patients, and scarce literature exists on the real-world outcome of FOLFOX adjuvant chemotherapy in elderly Asian populations. Therefore, we compared the efficacy and toxicity of FOLFOX4 adjuvant chemotherapy in older and younger colon cancer patients who received curative surgery for Stage III colon cancer in a community-based university hospital in Korea.

PATIENTS AND METHODS

Patients

Using a prospectively maintained colon cancer database, patients who met the eligibility criteria were retrospectively enrolled into this study. Before treatment, patients were given the option of treatment (FOLFOX versus capecitabine versus 5-FU/LV) by physicians and chose the regimen they preferred aided by information from physicians.

Patients were eligible if they (i) had histologically diagnosed colon cancer, (ii) underwent complete surgical resection (R0 resection) between May 2003 and March 2010 at Seoul National University Bundang Hospital, (iii) met the American Joint Committee on Cancer, 6th edition criteria for Stage III cancer (any T, N1 or N2, M0) (10) and (iv) received adjuvant FOLFOX4 chemotherapy. This study was reviewed and approved by the Institutional Review Board of Seoul National University Bundang Hospital (IRB No: B-1107/132-102).

Treatment

Eligible patients received FOLFOX4 adjuvant chemotherapy, consisting of a 2-h infusion of 85 mg/m^2 oxaliplatin given simultaneously with a 2-h infusion of 200 mg/m^2 LV, followed by a bolus of 400 mg/m^2 5-FU, and then a 22-h infusion of 600 mg/m^2 5-FU given on 2 consecutive days every 14 days for 12 cycles (7). Adverse effects were graded according to the Common Terminology Criteria for Adverse Effects version 3.0 (11). Dose reduction was based on the worst adverse event observed during the previous cycle. Regarding dose reduction, the oxaliplatin dose was reduced to 75 mg/m^2, the 5-FU bolus dose was reduced to 300 mg/m^2 and the 5-FU infusion dose was reduced to 500 mg/m^2, as described in the MOSAIC study (7). The relative dose intensities (RDIs) of the agents were calculated.

Follow-up

Patients were assessed every 2 weeks during treatment and then every 6 months for follow-up. The baseline assessment involved a medical history review, a physical examination, a comorbidity assessment according to the Charlson-Age comorbidity score (12, 13), measurements of carcinoembryonic antigen levels, and chest and abdominopelvic computed tomography (CT) scans. Patients underwent complete blood cell counts, liver and renal function tests at 2-week intervals and CT scans at 6-month intervals. Patients were monitored for adverse effects throughout the treatment period and for 28 days after the last cycle of FOLFOX4 chemotherapy. The diagnosis of recurrence was made on the basis of imaging and, if necessary, on biopsy.

Significant Toxicity

Significant toxicity was defined as febrile (>38.5°C) neutropenia, Grade 4 neutropenia, early treatment withdrawal because of Grade 3/4 toxicity or re-hospitalization for >7 days for Grade 3/4 toxicity, as outlined in the Groupe d'Investigateurs Nationaux pour l'Etude des Cancers Ovariens (GINECO) study (14).

Statistical Analysis

This study analyzed the outcomes in older patients (age ≥65 years) and younger patients. Efficacy analysis included 3-year DFS and OS. Safety analysis included all-grade and Grade 3/4 toxicities, significant toxicities and RDIs. DFS was defined as from the date of surgery to the date of tumor recurrence or death from any cause. OS was measured from the date of surgery to the date of death from any cause. Differences in baseline characteristics between elderly patients and younger patients were compared using a two-sided *t*-test, as was the difference in the incidence of Grade 3/4 toxicity. Kaplan–Meier estimates were used to assess 3-year DFS and OS. A log-rank probability value of <0.05 was considered statistically significant. Statistical analysis was performed using SPSS18.0K for Windows (SPSS, Chicago, IL, USA).

RESULTS

Study Population

Between May 2003 and March 2010, 2047 patients diagnosed with colorectal cancer were treated surgically at Seoul National University Bundang Hospital. Of these, 826 and 1221 patients were diagnosed with rectal cancer and colon cancer, respectively. Among 391 patients with Stage III colon cancer, 379 patients received curative resection. Of these 379 patients, 235 patients received FOLFOX4 chemotherapy. Six patients were lost to follow-up, leaving 229 patients included in the study overall (Fig. 1). A higher proportion of younger patients received FOLFOX chemotherapy than older patients (78.5 versus 46.1%, $P < 0.01$). Twenty-eight patients (14.5%) ≥65 years received no adjuvant chemotherapy, compared with 12 (6.5%) younger patients ($P = 0.015$) (Table 1).

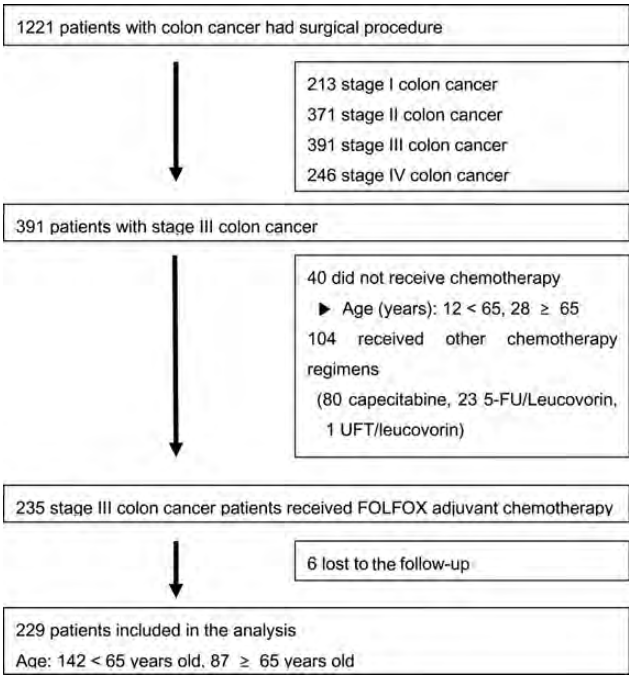

Figure 1. Flowchart of study participants with colon cancer.

Baseline Characteristics

The median age of all enrolled patients was 61.0 years (range, 28–80 years). There were no significant differences in the baseline characteristics between the age groups, with the exception of a higher Charlson-Age comorbidity score (3.44 versus 2.85) in older patients ($P < 0.01$) (Table 2).

Chemotherapy

The median number of chemotherapy cycles received was 11.5 in younger patients and 11.0 in older patients ($P = 0.57$). The planned 12 cycles were received by 89.4% of patients in the younger group and 81.6% of patients in the older group (Table 3).

The RDI of oxaliplatin was 0.76 in the older group and 0.79 in the younger group ($P = 0.65$). In contrast, the RDI of 5-FU was lower in older patients than in younger patients (0.75 versus 0.80, $P = 0.009$) (Table 4).

In total, 154 of 229 patients (67.7%) received chemotherapy within 4 weeks of surgery, but 75 patients (32.3%) received delayed chemotherapy because of postoperative complications, poor performance status or at their request. More patients in the older group ($n = 57$, 65.5%) received delayed chemotherapy than younger patients ($n = 98$, 69.0%) with marginal significance ($P = 0.08$).

DFS and OS

At the time of analysis, the median follow-up duration was 49.7 months. The 3-year DFS estimates for younger and older patients were 80.0 and 76.5%, respectively ($P = 0.88$), and the estimated 3-year OS estimates in younger and older patients were 92.7 and 90.9%, respectively ($P = 0.98$) (Fig. 2). As of July 2012, 16 and 10 patients died in the younger and older groups, respectively. Cancer-specific

Table 1. Adjuvant chemotherapy use in older (≥65) and young (<65) patients

	Age ≥65 ($n = 193$)[a]	Age <65 ($n = 186$)[a]
Chemotherapy regimen		
FOLFOX	89 (46.1%)	146 (78.5%)
Capecitabine	66 (34.2%)	14 (7.5%)
5-FU/LV	9 (4.7%)	14 (7.5%)
UFT/LV	1 (0.5%)	0 (0%)
No adjuvant treatment	28 (14.5%)	12 (6.5%)

[a]379 (193 and 186) patients received curative resection.

Table 2. Baseline characteristics of patients

	Age ≥65 ($n = 87$)	Age <65 ($n = 142$)	P value
Age	Median: 61.0	(28–80)	
Median	68.0	55.0	
Sex, *n* (%)			
Male	55 (64.1)	79 (56.8)	0.26
Female	32 (35.9)	63 (43.2)	
MDRD GFR (ml/min), *n* (%)			
>60	82 (94.2)	141 (99.7)	0.13
50–60	4 (4.6)	1 (0.6)	
30–50	1 (1.1)	0 (0)	
Serum albumin (g/dl), *n* (%)			
>3.5	82 (94.4)	135 (94.4)	0.43
2.5–3.5	5 (5.6)	7 (5.6)	
<2.5	0 (0)	0 (0)	
ECOG PS, *n* (%)			
0–1	85 (97.7)	141 (99.3)	0.16
2	2 (2.3)	1 (0.7)	
Charlson-Age comorbidity score, *n* (%)			
Median	3.44	2.85	<0.01
2	21 (23.0)	68 (47.9)	
3	27 (31.0)	43 (30.3)	
4	24 (27.6)	19 (13.4)	
5	14 (16.1)	10 (7.0)	
6	2 (2.3)	1 (0.7)	
7	0 (0.0)	1 (0.7)	
BMI			
Average	23.11	23.30	0.47
<20	14 (16.1)	13 (9.2)	
20–25	51 (58.6)	95 (66.9)	
≥25	22 (25.3)	34 (23.9)	

Table 3. Tumor characteristics of the patients

	Age ≥65 ($n = 87$)	Age <65 ($n = 142$)	P value
Stage, *n* (%)			
IIIA	0 (0)	4 (2.8)	0.18
IIIB	55 (63.2)	78 (54.9)	
IIIC	32 (36.8)	60 (42.3)	
Depth of invasion, *n* (%)			
T1	0 (0)	2 (1.4)	0.52
T2	3 (3.4)	2 (1.4)	
T3	65 (74.7)	106 (74.6)	
T4	19 (21.8)	32 (22.5)	
No. of nodes involved, *n* (%)			
N1	56 (64.4)	82 (57.7)	0.32
N2	31 (35.6)	60 (42.3)	
Pathology, *n* (%)			
Adenocarcinoma	84 (96.6)	132 (93.0)	0.54
Well differentiated	1 (1.1)	4 (2.8)	
Moderate differentiated	75 (86.2)	117 (82.4)	
Poorly differentiated	8 (9.2)	11 (7.7)	
Mucinous	3 (3.4)	10 (7.0)	

Table 4. Timing of chemotherapy, cycles, and relative dose intensity

	Age ≥65 ($n = 87$)	Age <65 ($n = 142$)	P value
Time from surgery to chemotherapy initiation (weeks)	4.0 (2.7–10.3)	4.2 (2.1–7.3)	0.08
≤4, *n*(%)	57 (65.5)	98 (69.0)	
>4	30 (34.5)	44 (31.0)	
Chemotherapy cycles			
Average, *n*	11.0	11.5	0.06
Completed cycles, *n* (%)			
≤6	8 (9.2)	6 (4.2)	0.57
7–11	8 (9.2)	9 (6.4)	
12	71 (81.6)	127 (89.4)	
Relative dose intensity			
Oxaliplatin	0.76	0.79	0.65
5-Fluorouracil	0.75	0.80	0.01

death was reported in 13 younger and 9 older patients (9.2 and 10.3% of patients, respectively). Three younger patients and one older patient died from causes unrelated to cancer (two deaths from traffic accidents and one from high-grade burns in younger patients; one patient died from myocardial infarction in the elderly group).

Toxicity

Neutropenia, nausea, vomiting and neuropathy were the most common all-grade adverse events in both groups (Table 5). The frequencies of all-grade nausea and stomatitis were higher in older patients (65.5 versus 50% $P < 0.01$; 42.5 versus 33.4% $P = 0.03$). The frequencies of Grade 3/4 toxicity were similar in both groups, and Grade 3/4 neutropenia was the only severe toxicity that occurred significantly more frequently in older patients (62.1 versus 46.5%, $P = 0.02$). In addition, Grade 3/4 diarrhea occurred more frequently in elderly patients over 70 years old (12.9 versus 4.0%, $P = 0.03$) (Supplementary data, Table S4).

Significant toxicities, as described in the GINECO study, occurred in 9.1% of younger patients and 14.9% of older patients as follows: 4 cases of febrile neutropenia (2.8%) in younger

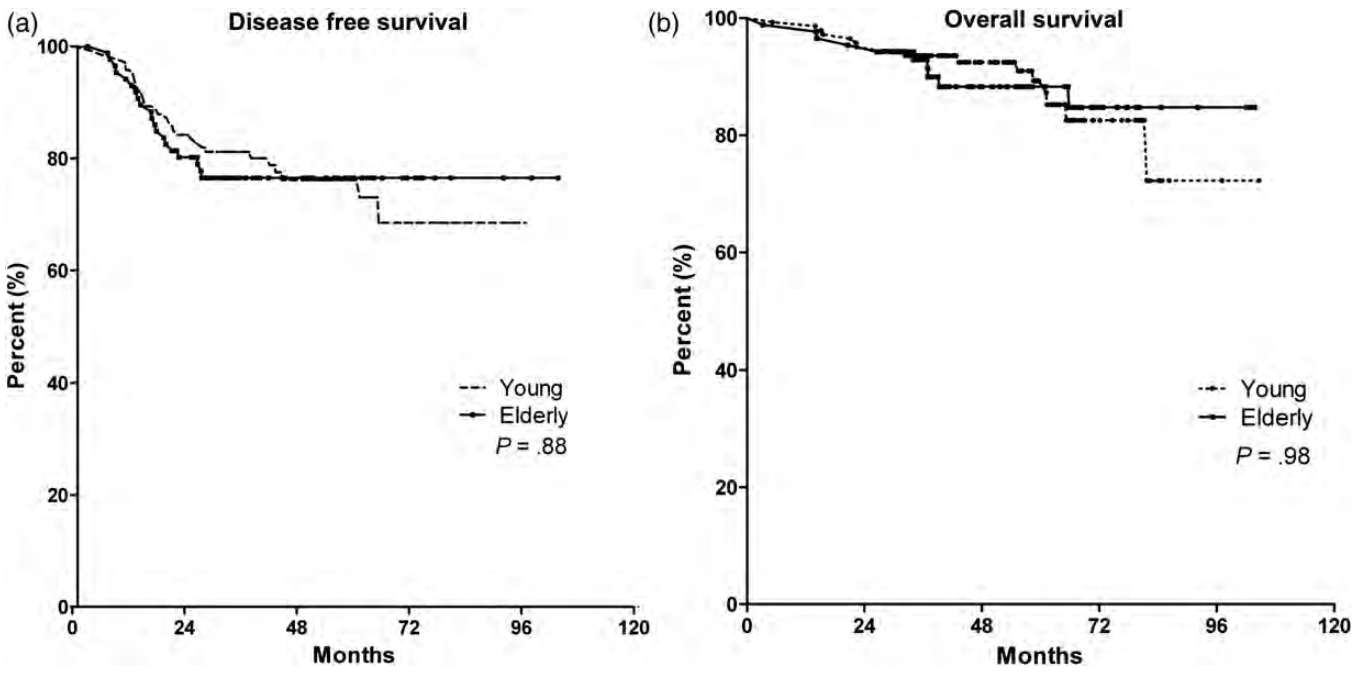

Figure 2. Kaplan–Meier curves of (a) disease-free survival and (b) overall survival in the elderly and younger patients.

Table 5. Adverse events in younger and elderly patients

	Age ≥65 ($n = 87$)	Age <65 ($n = 142$)	*P* value
Neuropathy (all grade), *n* (%)	63 (72.4)	102 (71.8)	0.27
(Grade 3–4)	4 (4.6)	6 (4.2)	0.89
Neutropenia (all grade), *n* (%)	69 (79.3)	104(73.2)	0.48
(Grade 3–4)	54 (62.1)	66 (46.5)	0.02
Anemia (all grade), *n* (%)	28 (32.1)	34 (23.9)	0.23
(Grade 3–4)	0	0	NA
Thrombocytopenia (all grade), *n* (%)	30 (34.5)	44 (31.0)	0.50
(Grade 3–4)	3 (3.4)	3 (2.1)	0.55
Nausea (all grade), *n* (%)	57 (65.5)	71 (50)	0.00
(Grade 3–4)	1 (1.1)	0	0.16
Vomiting (all grade), *n* (%)	6 (6.9)	3 (2.1)	0.16
(Grade 3–4)	0	0	NA
Diarrhea (all grade), *n* (%)	31 (35.6)	41 (28.9)	0.13
(Grade 3–4)	6 (6.9)	6 (4.2)	0.38
Stomatitis (all grade), *n* (%)	37 (42.5)	46 (33.4)	0.03
(Grade 3–4)	1 (1.1)	0	0.16
Mucositis (all grade), *n* (%)	3 (3.4)	2 (1.4)	0.40
(Grade 3–4)	0	0	NA
LFT abnormality (all grade), *n* (%)	27 (31.0)	69 (48.6)	0.01
(Grade 3–4)	0	3 (2.1)	0.09
Infection, *n* (%)	5 (5.7)	4 (2.8)	0.27
Hospitalization, *n* (%)	2 (1.4)	1 (1.1)	0.73

patients versus 5 (5.7%) cases in older patients ($P = 0.27$); 10 cases of Grade 4 neutropenia in younger patient (7.0%) versus 9 cases in older patients (10.3%) ($P = 0.38$); 1 case of re-hospitalization in younger patients versus 2 cases in older patients; and 2 cases of early treatment withdrawal in younger patients (1.4%) versus 5 cases in older patients (5.7%) ($P = 0.06$). Infection ($n = 3$) and Grade 4 diarrhea ($n = 3$) were the most common causes of early treatment withdrawal.

DISCUSSION

In the current study, adjuvant FOLFOX4 chemotherapy demonstrated similar efficacy in terms of 3-year DFS in patients at least 65 years old and younger (76.5 and 80.0%, respectively). Regarding the toxicity profile, there were no significant differences between younger and older patients excluding a higher incidence of Grade 3/4 neutropenia in the older group. Hospitalization rates were similar in both groups. In older patients, early treatment withdrawal rates were higher than in younger patients, although not statistically significant due to small numbers (9.2 in elderly versus 4.2% in young patients; $P = 0.57$).

FOLFOX has been widely used as standard adjuvant chemotherapy for colon cancer; however, there are few reports on the efficacy and safety of FOLFOX chemotherapy in Asian population, even more so for elderly patients. Although a small number of patients limit the power of this study to prove equivalence or non-inferiority of FOLFOX4 in older patients compared with younger patients, 3-year DFS of 76.5% shown in the older group (≥65 years) compare favorably with those of the MOSAIC trial (median

age = 61), which reported a 3-year DFS rate of 72.2% in the Stage III patients in FOLFOX arm (7) (Fig. 2).

Toxicity profile in the current study are similar to those of the pooled analyses of the safety and efficacy of FOLFOX chemotherapy by Goldberg et al., except for Grade 3/4 neutropenia which occurred more frequently in our population (62.1 versus 49.0%). In Goldberg study, Grade 3/4 neutropenia (43 versus 49%; $P = 0.04$) and thrombocytopenia (2 versus 5%; $P = 0.04$) were significantly more common in older patients, but 60-day mortality and the overall incidence of Grade $\geq$3 adverse events were not associated with older age (8). Higher incidence of Grade 3/4 neutropenia in the current study may explain the lower RDI of 5-FU compared with that in Western countries (in elderly patients, 0.75 in our study versus 0.83–1.00 in Western studies) (7, 8). In our study, grade $\geq$3 neuropathy was reported in 4.6% of older patients and 4.2% of younger patients ($P = 0.89$). The incidences of Grade $\geq$3 diarrhea were 6.9% in older patients and 4.2% in younger patients. Our results are similar to those of the MASCOT trial, an Asian study of adjuvant FOLFOX4 chemotherapy for colon cancer patients (4.3 versus 5.7% for Grade $\geq$3 neurotoxicity, 5.2 versus 6.3% for Grade $\geq$3 diarrhea) (15). In contrast to Asian data, the incidence of Grade $\geq$3 neurotoxicity and Grade $\geq$3 diarrhea in Western colorectal cancer patients who received adjuvant FOLFOX4 chemotherapy were 12.4 and 10.8%, respectively (7). This trend that Grade $\geq$3 neurotoxicity and diarrhea occurs less commonly in Asian patients than in Western patients (4.4 versus 12%; 6.3 versus 11%) was also reported by Sugihara et al. (16).

Kahn et al. (17) revealed that older patients were less likely to receive adjuvant chemotherapy, especially oxaliplatin-containing regimens. They found that only 50% of patients over 75 years old received adjuvant chemotherapy and that the adjuvant chemotherapy withdrawal rate is higher in elderly patients than in younger patients (40 versus 25% at 150 days after the start of adjuvant chemotherapy). Our data also revealed similar results. In total, 93.5% of younger patients received adjuvant chemotherapy, and 78.5% of younger Stage III colon cancer patients chose adjuvant FOLFOX4 chemotherapy. Conversely, 14.5% of older Stage III colon cancer patients who underwent curative surgery did not receive adjuvant chemotherapy ($P = 0.02$). Only 46.5% of older patients received adjuvant FOFOX-4 chemotherapy, and 34.2% of older patients received capecitabine as an adjuvant chemotherapy.

Capecitabine, an oral fluoropyrimidine, was demonstrated to be equivalent to bolus 5-FU/LV in patients with Stage III colon cancer in the X-ACT trial ($P = 0.07$ for OS) (18). The 3-year DFS of 76.5% shown in the older group ($\geq$65 years) of our study also compares favorably with the 3-year DFS of 64.2% in the capecitabine arm in the X-ACT trial (18, 19). We have previously reported a tailored dosing adjuvant capecitabine study in older patients ($\geq$70 years) performed at the same institution, and 3-year DFS was 56.2% in older patients with Stage III colon cancer patients treated with adjuvant capecitabine (20). Although different patient populations and study settings limit meaningful comparisons, these comparisons suggest favorable outcomes of FOLFOX4 in older patients with Stage III colon cancer over capecitabine.

The limitations of our study include the small sample size and short follow-up duration, which could decrease the power to detect a small difference in DFS and OS. The retrospective nature of our study also precludes detailed descriptions of toxicities. The most critical limitation was the age criterion of 65 years of age delineating the older population, which is too low according to current standards. When we used the cut-off value of 70 year old, the estimated 3-year DFS and OS did not differ significantly between younger and older patients (estimated 3-year DFS: 79.2 versus 80.6%, $P = 0.75$; estimated 3-year OS: 92.3 versus 93.5% $P = 0.44$) (Supplementary data, Fig. S1). In toxicity profile, more patients older than 70 years of age suffered Grade 3/4 neutropenia and diarrhea (61.3 versus 51.5% in Grade 3/4 neutropenia, $P = 0.02$; 12.9 versus 4.0% in Grade 3/4 diarrhea, $P = 0.03$) (Supplementary data, Table S4). More common early treatment withdrawal rates were observed in patients over 70 years of age (12.9 versus 5.0%; $P < 0.01$) (Supplementary data, Table S3).

Despite these limitations, our study described a real-world outcome of FOLFOX4 adjuvant chemotherapy in a homogenous population of Korean patients with Stage III colon cancer and confirmed the value of FOLFOX4 chemotherapy in older patients with Stage III colon cancer. Our older patients were mostly youngest olds (median age 68), with most (97.7%) patients having an ECOG performance score of 0–1 and 65.5% of patients starting chemotherapy within 4 weeks of surgery. For such older patients, our results support the use of FOLFOX4 chemotherapy in Stage III colon cancer.

Conclusion

In conclusion, adjuvant chemotherapy with FOLFOX4 resulted in similar efficacy and toxicities in patients aged 65 years and older to younger patients. For colon cancer patients aged $\geq$65, FOLFOX4 chemotherapy can be recommended as safe and effective adjuvant chemotherapy after curative surgery in Asia.

Supplementary data

Supplementary data are available at http://www.jjco.oxfordjournals.org.

Conflict of interest statement

None declared.

References

1. Altekruse S, Kosary C, Krapcho M, et al. *SEER Cancer Statistics Review, 1975–2007*. Bethesda, MD: National Cancer Institute 2010;7.
2. Laurie JA, Moertel CG, Fleming TR, et al. Surgical adjuvant therapy of large-bowel carcinoma: an evaluation of levamisole and the combination of levamisole and fluorouracil. The North Central Cancer Treatment Group and the Mayo Clinic. *J Clin Oncol* 1989;7:1447–56.
3. Moertel CG, Fleming TR, Macdonald JS, et al. Levamisole and fluorouracil for adjuvant therapy of resected colon carcinoma. *N Engl J Med* 1990;322:352–8.
4. O'Connell MJ, Laurie JA, Kahn M, et al. Prospectively randomized trial of postoperative adjuvant chemotherapy in patients with high-risk colon cancer. *J Clin Oncol* 1998;16:295–300.
5. Sargent DJ, Goldberg RM, Jacobson SD, et al. A pooled analysis of adjuvant chemotherapy for resected colon cancer in elderly patients. *N Engl J Med* 2001;345:1091–7.
6. Jessup JM, Stewart A, Greene FL, Minsky BD. Adjuvant chemotherapy for stage III colon cancer: implications of race/ethnicity, age, and differentiation. *J Am Med Assoc* 2005;294:2703–11.
7. Andre T, Boni C, Mounedji-Boudiaf L, et al. Oxaliplatin, fluorouracil, and leucovorin as adjuvant treatment for colon cancer. *N Engl J Med* 2004;350:2343–51.
8. Goldberg RM, Tabah-Fisch I, Bleiberg H, et al. Pooled analysis of safety and efficacy of oxaliplatin plus fluorouracil/leucovorin administered bimonthly in elderly patients with colorectal cancer. *J Clin Oncol* 2006;24:4085–91.
9. Jackson McCleary NA, Meyerhardt J, Green E, et al. Impact of older age on the efficacy of newer adjuvant therapies in >12500 patients (pts) with stage II/III colon cancer: Findings from the ACCENT Database. *J Clin Oncol* 2009;27(Suppl.):15s. (abstr 4010).
10. Greene FL. *American Joint Committee on Cancer, American Cancer Society. AJCC Cancer Staging Manual*. New York: Springer 2002.
11. National Cancer Institute (U.S.). *Common Terminology Criteria for Adverse Events (CTCAE)*. Bethesda, MD: U.S. Department of Health and Human Services, National Institutes of Health, National Cancer Institute 2009.
12. Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chronic Dis* 1987;40:373–83.
13. Ouellette JR, Small DG, Termuhlen PM. Evaluation of Charlson-Age Comorbidity Index as predictor of morbidity and mortality in patients with colorectal carcinoma. *J Gastrointest Surg* 2004;8:1061–7.
14. Freyer G, Geay JF, Touzet S, et al. Comprehensive geriatric assessment predicts tolerance to chemotherapy and survival in elderly patients with advanced ovarian carcinoma: a GINECO study. *Ann Oncol* 2005;16:1795–800.
15. Lee PH, Park YS, Ji JF, et al. Safety and tolerability of FOLFOX4 in the adjuvant treatment of colon cancer in Asian patients: the MASCOT study. *Asia-Pacific J Clin Oncol* 2009;5:101–10.
16. Sugihara K, Ohtsu A, Shimada Y, et al. Safety analysis of FOLFOX4 treatment in colorectal cancer patients: a comparison between two Asian studies and four Western studies. *Clin Colorectal Cancer* 2012;11:127–37.
17. Kahn KL, Adams JL, Weeks JC, et al. Adjuvant chemotherapy use and adverse events among older patients with stage III colon cancer. *J Am Med Assoc* 2010;303:1037–45.
18. Twelves C, Wong A, Nowacki MP, et al. Capecitabine as adjuvant treatment for stage III colon cancer. *N Engl J Med* 2005;352:2696–704.
19. Twelves C, Scheithauer W, McKendrick J, et al. Capecitabine versus 5-fluorouracil/folinic acid as adjuvant therapy for stage III colon cancer: final results from the X-ACT trial with analysis by age and preliminary evidence of a pharmacodynamic marker of efficacy. *Ann Oncol* 2012;23:1190–7.
20. Chang HJ, Lee KW, Kim JH, et al. Adjuvant capecitabine chemotherapy using a tailored-dose strategy in elderly patients with colon cancer. *Ann Oncol* 2012;23:911–8.