

Effectiveness of adjuvant chemotherapy in patients with Stage II colorectal cancer: A multicenter retrospective study

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Background: Adjuvant chemotherapy (ACT) for patients with Stage II colorectal cancer (CRC) is an area of controversy in oncology. International guidelines recommend the use of ACT in patients with specific high-risk features. This study aimed to investigate the effectiveness of ACT in improving survival in patients with and without high-risk features. **Materials and Methods:** A total of 225 patients with Stage II CRC who underwent primary tumor resection were included in this study. Patients with one or more high-risk features including T4 tumor, poor differentiation, lymphovascular invasion, perineural invasion, bowel obstruction, local perforation, positive resection margins, or suboptimal lymph node sampling (fewer than 12 nodes) were classified as high risk. The survival analysis was performed between patients who only received curative surgery and those received single-agent (5-fluorouracil [5-FU] and leucovorin [LV] or capecitabine) or multiagent ACT (oxaliplatin and 5-FU + LV or oxaliplatin and capecitabine). **Results:** The 5-year overall survival (OS) rate was 88.4%, and the 5-year disease-free survival (DFS) rate was 80.4%. The 5-year OS and DFS rates improved insignificantly with ACT (89.8% vs. 81.2%, $P = 0.59$ and 81.3% vs. 74.6%, $P = 0.41$, respectively); however, multiagent ACT results to inferior 5-year OS and DFS compared to single-agent ACT (82.1 vs. 92.8%, $P = 0.14$ and 70.1% vs. 86%, $P = 0.07$, respectively). ACT was associated with insignificant improved OS and DFS in both high-risk and low-risk groups, but high-risk patients who received multiagent ACT had a significant inferior OS and DFS in comparison with those received single-agent ACT. T4 tumor and obstruction were independent poor prognostic factors affecting OS and DFS. **Conclusion:** In our population, the improvement of OS and DFS with ACT was not statistically significant in high-risk and low-risk patients with Stage II CRC.

Key words: Adjuvant chemotherapy, colorectal neoplasms, survival

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INTRODUCTION

Colorectal cancer (CRC), as the third cause of cancer deaths in the United States, accounts for 8% of cancers in both sexes.^[1] Screening with fecal occult blood testing or colonoscopy can lead to finding the disease at an earlier stage but compliance with CRC screening is fairly low, thereby CRC remains to be identified in symptomatic patients commonly. CRC mortality has been progressively declining; however, it is still remarkable and stays an important health concern.

Growing studies are struggling to develop novel treatments for CRC. Emergent studies investigate the existence and role of cancer stem cells in CRC to introduce innovative therapeutic methods.^[2] Complete surgical resection is currently the mainstay of treatment for patients with locoregional CRC. After a potentially curative surgery, adjuvant chemotherapy (ACT) is administered to eradicate micrometastatic residues and to prevent the formation of distant metastatic disease. Survival benefit from ACT seems to be stage dependent. ACT was reported to improve overall survival (OS) in

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patients with Stage III CRC,^[3-6] and it is acknowledged as the standard of care in patients with Stage III in the international guidelines. However, it is currently unclear whether ACT can be beneficial in patients with Stage II CRC.

The Quick and Simple and Reliable trial on patients with Stages I, II, and III CRC reported a relative risk of death of 0.82 (95% confidence interval [CI], 0.70–0.95) in the patients who underwent ACT as compared with the surgery-alone group. However, *post hoc* analysis showed no significant difference in the survival between ACT and surgery-alone groups in patients with Stage II CRC.^[7] A 2008 Cochrane Review of 33 trials and 17 meta-analyses on patients with Stage II colon cancer showed no significant improvement in OS (relative risk 0.96, 95% CI 0.88–1.05) of patients underwent ACT although the disease-free survival (DFS) was significantly better with the use of ACT (relative risk 0.83, 95% CI 0.75–0.92).^[8] In the absence of strong evidence, clinical guidelines by the National Comprehensive Cancer Network,^[9] the American Society of Clinical Oncology,^[10] and the European Society for Medical Oncology^[11] recommend the use of ACT in Stage II CRC with specific high-risk features. However, the results of studies on the survival improvement with ACT in high-risk Stage II disease are inconclusive.^[12-15]

Given the current controversy in the literature, the present study aimed to evaluate the use of ACT in patients with Stage II CRC and assess the effectiveness of chemotherapy in improving OS and DFS in patients with and without high-risk features.

MATERIALS AND METHODS

Study design and participants

All patients with CRC who referred to the oncology clinics of the Shariati, Imam Reza and Arad Hospitals in Tehran, Iran, between April 2001 and September 2015 were identified. Patients with Stage II CRC who underwent primary tumor resection without neoadjuvant therapy were considered to be included in this retrospective study. Patients with a histological diagnosis except adenocarcinoma, those with a prior or synchronous other malignancies, and those who lost to follow-up after the first appointment were excluded from the study. 5-fluorouracil (5-FU)-based regimens were suggested for ACT of patients with Stage II CRC. We categorized the patients into three groups according to ACT: (a) patients who did not receive ACT, (b) patients who received single-agent ACT including those received 5-FU and leucovorin (LV) weekly or monthly and those received oral 5-FU prodrug (capecitabine), (c) patients who received multiagent ACT including those received 5-FU and LV and oxaliplatin (FOLFOX) and those received capecitabine and oxaliplatin (CAPOX). This study was approved by

the Research Ethics Board of the Hematology-Oncology and Stem Cell Transplantation Research Center at Tehran University of Medical Sciences and AJA Cancer Epidemiology Research and Treatment Center at AJA University of Medical Sciences. Informed consent was obtained from all participants included in the study.

Variables' assessment

The following data were obtained from the medical records: demographics (i.e., sex, age); dates of cancer diagnosis and surgery; primary complication (obstruction, perforation, hemorrhage, abdominal pain, and anemia); and tumor characteristics such as tumor location (ascending colon, transverse colon, descending colon, sigmoid, rectosigmoid, and rectum), size, grade (well, moderately, and poorly differentiated) and T classification, mucinous production, number of harvested lymph nodes (LNs), number of involved LNs by tumor, lymphovascular invasion, perineural invasion, positivity of resection margin, details of chemotherapy, and date of recurrence and death.

Stage II CRC includes tumors that are not extended to the LNs and are categorized into Stages IIA (T3N0M0), IIB (T4aN0M0), and IIC (T4bN0M0). A tumor was labeled as T3 when invades through the muscularis propria into pericolorectal tissues, labeled as T4a when penetrates to the surface of the visceral peritoneum and labeled as T4b when directly invades or is adherent to other organs or structures.^[16] Patients with Stage II CRC were classified as high risk if they had any of the following features: T4 tumor, poor differentiation, lymphovascular invasion, perineural invasion, bowel obstruction, local perforation, positive resection margins, or suboptimal LN sampling (fewer than 12 nodes). Patients with no high-risk features were considered as low risk.^[8-10]

Statistical analysis

Categorical and continuous variables are presented as number (%) and mean (standard deviation), respectively. Normality of data was analyzed using the Kolmogorov–Smirnov test. Differences between patients with Stage II CRC based on ACT were assessed using the independent *t*-test for continuous variables and Fisher's exact and Chi-square tests for categorical variables. Size of tumor and number of harvested LNs showed evidence of non-normality in Kolmogorov–Smirnov test ($P < 0.05$); subsequently, Mann–Whitney U test was conducted for evaluating their difference between patient who received ACT and those who did not. Survival (OS and DFS) analyses were estimated by the Kaplan–Meier method and compared by the log-rank test. OS was defined as the time from cancer diagnosis until death from any cause. DFS was defined as the period between the date of cancer diagnosis and the date of disease recurrence. The Cox proportional

hazards regression model was used for computing hazard ratios (HRs) and multivariate survival analysis. Significant factors ($P < 0.2$) from univariate analysis were considered to be entered into the multivariate analysis. The proportional hazards assumption in the Cox proportional hazards model was evaluated by Schoenfeld's global test, and no evidence was found to contradict them ($P = 0.645$). $P < 0.05$ was considered to be statistically significant. SPSS Statistics for Windows (version 21.0; Armonk, NY: IBM Corporation) and R software (version 3.5.1; R Core Team (2016), Vienna, Austria) were employed to conduct statistical analyses.

RESULTS

Patients' characteristics

Of 689 patients with CRC that were initially identified, 247 patients had Stage II CRC. We included 225 patients with Stage II CRC that met our inclusion criteria. The median age was 57 years (range 17–88 years), and 135 (60%) patients were male. Seven (3.1%) patients had T4a tumors and 6 (2.7%) patients had T4b tumors categorized, respectively, as Stages IIB and IIC. Fifty-nine (26.2%) patients had no high-risk features and were classified as low risk whereas 166 (73.8%) patients were classified as high risk.

Characteristics of patients stratified by ACT were listed in Table 1. Thirty-six (16%) patients received no ACT and 189 (84%) patients received ACT; 36 (16%) patients received 5-FU + LV weekly, 82 (36.4%) patients received 5-FU + LV monthly, 6 (2.7%) patients received capecitabine, 52 (23.1%) patients received FOLFOX, and 13 (5.8%) patients received CAPOX. Except for the numbers of harvested LNs that were significantly lower in patients who received ACT (9.2 vs. 13.1, $P = 0.004$), there was no significant difference regarding the patients and tumor features between patients who received ACT and those who did not [Table 1].

Survival analysis

The median follow-up time was 45 months (range, 1–174 months) in all patients, 49.5 months (range 1–174 months) in patients without ACT, and 45 months (range 6–173 months) in patients with ACT.

The OS rate at 5 years was 88.4% for all patients [Figure 1]. The 5-year OS rate improved insignificantly from 81.2% to 89.8% with ACT ($P = 0.59$); however, multiagent ACT results to inferior 5-year OS compared to single-agent ACT (82.1 vs. 92.8%, $P = 0.14$). Significant difference of OS was not found between high-risk versus low-risk patients (5-year OS 89.4% vs. 85.9%, $P = 0.87$). In univariate analyses, patients with T4 tumor and obstruction had a significant inferior OS compared with those who did not (HR 4.84, 95% CI 1.41–16.62, $P = 0.01$ and HR 2.47, 95% CI 1.01–6.02, $P = 0.04$, respectively). Multivariate

Table 1: Patient and disease characteristics stratified by adjuvant chemotherapy

	No ACT (n=36)	ACT (n=189)	P
Sex			
Male	20 (55.6)	115 (60.8)	0.55*
Female	16 (44.4)	74 (39.2)	
Age			
Mean	58.9 (11.8)	56.2 (14)	0.27*
<50	8 (22.2)	55 (29.1)	0.69*
50-69	21 (58.3)	99 (52.4)	
≥70	7 (19.4)	35 (18.5)	
Primary complication			
Obstruction	5 (13.9)	39 (20.6)	0.78**
Hemorrhage	7 (19.4)	44 (23.3)	
Other	2 (5.6)	15 (7.9)	
Unknown	22 (61.1)	91 (48.1)	
Tumor location			
Ascending colon	15 (41.7)	66 (34.9)	0.16**
Transverse colon	1 (2.8)	11 (5.8)	
Descending colon and sigmoid	18 (50)	76 (40.2)	
Rectosigmoid and rectum	2 (5.6)	36 (19)	
Type			
Mucinous	2 (5.6)	23 (12.2)	0.42**
Nonmucinous	3 (8.3)	24 (12.7)	
Unknown	31 (86.1)	142 (75.1)	
Tumor grade			
Well	17 (47.2)	83 (43.9)	0.69**
Moderate	14 (38.9)	71 (37.6)	
Poor	1 (2.8)	17 (9)	
Unknown	4 (11.1)	18 (9.5)	
Tumor size			
Mean	6 (3.6)	5.5 (2.5)	0.91##
<5 cm	14 (38.9)	67 (35.4)	0.35*
≥5 cm	13 (36.1)	90 (47.6)	
Unknown	9 (25)	32 (16.9)	
T classification			
T3	36 (92.3)	176 (94.6)	0.23**
T4	0 (0)	13 (6.9)	
Lymphovascular invasion			
Yes	6 (16.7)	31 (16.4)	0.09*
No	18 (50)	124 (65.6)	
Unknown	12 (33.3)	34 (18)	
Perineural invasion			
Yes	6 (16.7)	28 (14.8)	0.12*
No	18 (50)	125 (66.1)	
Unknown	12 (33.3)	36 (19)	
Harvested LN			
Mean	13.1 (6.7)	9.2 (6.4)	0.002**
<12	13 (36.1)	117 (61.9)	0.01*
≥12	14 (38.9)	40 (21.2)	
Unknown	9 (25)	32 (16.9)	
High-risk features			
0	19 (52.8)	40 (21.2)	0.001**
1	9 (25)	77 (40.7)	
2	3 (8.3)	51 (27)	
3	4 (11.1)	17 (9)	
4	1 (2.8)	4 (2.1)	

*Calculated by Chi-square test, **Calculated by Fisher's exact test, #Calculated by independent t-test, ##Calculated by Mann-Whitney U test. Values are presented as n (%) or mean (SD). ACT=Adjuvant chemotherapy; LN=Lymph node; SD=Standard deviation

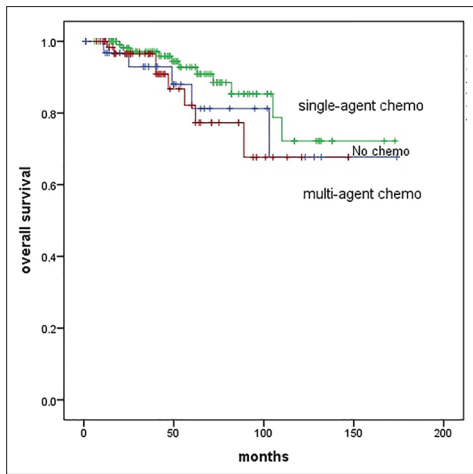


Figure 1: Overall survival curves for patients with no, single-agent, and multiagent adjuvant chemotherapy

analyses including T classification, perineural invasion, and primary complication demonstrated that T4 tumor and obstruction were statistically significant poor prognostic factors affecting OS [Table 2]. In subgroup analysis shown in Table 3, we assess the effects of ACT stratified by risk status groups and found that ACT was associated with insignificant improved OS in both groups, but high-risk patients who received multiagent ACT had a significant worse OS in comparison with those received single-agent ACT (HR 3.3, 95%CI 1.14–9.56, $P = 0.02$).

The DFS rate at 5 years was 80.4% for all patients [Figure 2]. Similar to OS, the 5-year DFS rate improved insignificantly from 74.6% to 81.3% with ACT ($P = 0.41$) and multiagent ACT results to inferior 5-year DFS compared to single-agent ACT (70.1% vs. 86%, $P = 0.07$). The 5-year DFS of

Table 2: Univariate and multivariate analysis of the effects of demographic and clinical characteristics on overall survival and disease-free survival

	Univariate analysis				Multivariate analysis			
	OS		DFS		OS*		DFS**	
	HR (95% CI)	P	HR (95% CI)	P	HR (95% CI)	P	HR (95% CI)	P
T classification (T4 versus T3)	4.84 (1.41-16.62)	0.01	5.34 (1.52-18.6)	0.009	5.55 (1.57-19.6)	0.008	5.88 (1.66-20.8)	0.006
Primary complication (obstruction vs. other)	2.47 (1.01-6.02)	0.04	2.54 (0.95-6.78)	0.06	3.05 (1.21-7.7)	0.01	2.75 (1.02-7.41)	0.04
Perineural invasion (yes vs. no)	2.19 (0.72-6.63)	0.16	1.85 (0.52-6.54)	0.33	2.67 (0.85-8.37)	0.09	Not in model	
Harvested LN (<12 vs. ≥12)	1.09 (0.59-2)	0.77	1.07 (0.52-2.2)	0.83	Not in model			
Lymphovascular invasion (yes vs. no)	1.83 (0.6-5.33)	0.28	0.89 (0.2-3.96)	0.88				
Tumor grade (poorly vs. well and moderately differentiated)	0.50 (0.06-3.71)	0.49	0.73 (0.98-5.51)	0.76				
Size (≥5 vs. <5 cm)	1.05 (0.74-1.49)	0.75	1.11 (0.75-1.66)	0.58				
Risk status (high vs. low)	0.93 (0.39-2.19)	0.87	1.07 (0.38-3.01)	0.89				
Sex (male vs. female)	1.34 (0.58-3.08)	0.47	0.9 (0.35-2.29)	0.83				
Age (≥70 vs. <70 years)	1.48 (0.54-3.99)	0.43	1.54 (0.50-4.72)	0.44				

*T classification, perineural invasion and primary complication were included in the multivariable analysis, **T classification and primary complication were included in multivariable analysis. HR=Hazard ratio; CI=Confidence interval; LN=Lymph node; OS=Overall survival; DFS=Disease-free survival

Table 3: Univariate analysis of the effects of adjuvant chemotherapy on overall survival and disease-free survival stratified by risk status

	OS		DFS	
	HR (95% CI)	P	HR (95% CI)	P
All patients				
ACT versus no ACT	0.76 (0.28-2.05)	0.59	0.78 (0.34-1.78)	0.56
Single-agent versus no ACT	0.60 (0.21-1.75)	0.35	0.59 (0.24-1.43)	0.24
Multiagent versus no ACT	1.18 (0.38-3.65)	0.76	1.26 (0.51-3.12)	0.60
Multiagent versus single-agent ACT	1.96 (0.78-4.91)	0.14	2.56 (0.89-7.36)	0.08
High-risk patients				
ACT versus no ACT	0.71 (0.16-3.16)	0.65	0.94 (0.25-4.64)	0.90
Single-agent versus no ACT	0.43 (0.08-2.15)	0.30	0.69 (0.15-3.12)	0.63
Multiagent versus no ACT	1.42 (0.30-6.77)	0.65	2.17 (0.48-9.72)	0.30
Multiagent versus single-agent ACT	3.30 (1.14-9.56)	0.02	3.98 (1.24-12.7)	0.02
Low-risk patients				
ACT versus no ACT	0.76 (0.18-3.22)	0.72	0.61 (0.19-0.195)	0.41
Single-agent versus no ACT	1.01 (0.24-4.27)	0.97	0.76 (0.23-2.50)	0.65
Multiagent versus no ACT	NA	NA	0.29 (0.03-2.48)	0.25
Multiagent versus single-agent ACT	NA	NA	0.37 (0.04-3.11)	0.36

ACT=Adjuvant chemotherapy; HR=Hazard ratio; CI=Confidence interval; NA=Not applicable; OS=Overall survival; DFS=Disease-free survival

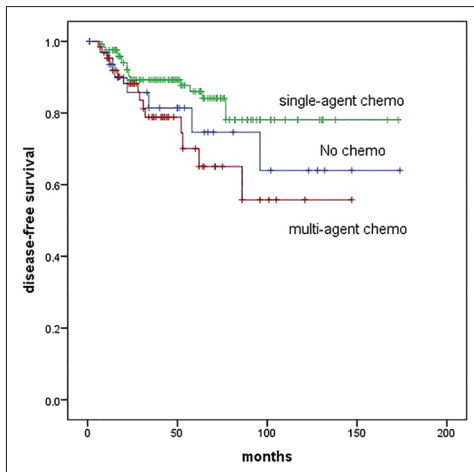


Figure 2: Disease-free survival curves for patients with no, single-agent, and multiagent adjuvant chemotherapy

high-risk patients did not differ significantly with low-risk patients (81.4% vs. 77.9%, $P = 0.8$). Univariate analysis showed that T4 classification was the only tumor-associated significant factor that affects DFS (HR 6.54, 95% CI 1.69–25.3, $P = 0.007$). Multivariate analyses containing T classification and primary complication showed that T4 tumor and obstruction were significant poor prognostic factors affecting DFS [Table 2]. In both high-risk and low-risk groups, ACT was related to insignificant better DFS [Table 3]. High-risk patients who received multiagent ACT had a significant inferior DFS compared with those received single-agent ACT (HR 3.98, 95% CI 1.24–12.7, $P = 0.02$).

DISCUSSION

Since the introduction of 5-FU-based regimens in 1980s, ACT has been considered as the standard approach for patients with CRC.^[17] The 2004 MOSAIC (Multicenter International Study of oxaliplatin/5-FU/LV in the Adjuvant Treatment of Colon Cancer) trial demonstrated that adding oxaliplatin to 5-FU-based regimens results in survival improvement in CRC patients.^[3] After Food and Drug Administration approval of oxaliplatin in 2004, FOLFOX became a popular regimen for ACT in CRC patients. However, studies on the benefits from FOLFOX as well as 5-FU + LV alone for Stage II CRC patients were inconclusive.^[5-8] Despite unsatisfying evidence, the consideration of ACT was recommended for CRC patients with specific features. As a result, the decision of using ACT in the clinical care of patients with Stage II CRC varies among physicians and institutions worldwide.

In the present study, among the suggested high-risk features for recurrence by practical guidelines, the T4 tumor and obstruction were found to be independent poor prognostic factors for OS and DFS. We found that ACT was a favorable insignificant factor affecting OS and DFS in both high-risk

and low-risk patients. Interestingly, this effect was only seen when single-agent ACT was employed. Contradictory, multiagent ACT was found to be a poor prognostic factor leading to inferior OS and DFS.

Our results are comparable with previous relevant studies. Booth *et al.*^[18] in a retrospective analysis of Canadian patients with Stage II colon cancer reported that ACT is not associated with improved OS (HR 1.16, 95% CI 0.94–1.42) among patients with Stage II colon cancer including those with high-risk disease (HR 1.02, 95% CI 0.79–1.31). O'Connor *et al.*^[12] in an analysis of 24,847 patients with Stage II colon cancer from the Surveillance, Epidemiology, and End Results (SEER)-Medicare database reported that no OS benefit was observed for patients with no poor prognostic features (HR, 1.02; 95% CI, 0.84–1.25) or patients with any poor prognostic features (HR, 1.03; 95% CI, 0.94–1.13). Glimelius *et al.*^[19] in a study of Nordic patients reported that there was no statistically significant benefit seen in comparison of surgery-alone group with surgery and ACT groups in Stage II colon cancer (5-year OS: 79% vs. 79%, $P = 0.81$) and in Stage II rectum cancer (5-year DFS 73% vs. 81%, $P = 0.09$).

On the other hand, several studies showed significant improvement in survival with ACT in patients with Stage II CRC. Artac *et al.*^[14] in a study of Turkish patients with Stage II colon cancer reported the age above 60 years and T4 tumor as independent poor prognostic factors and ACT as independent favorable prognostic factor for DFS. In a study on Korean patients with Stage II colon cancer, age ≥ 60 years, vascular invasion, and obstruction were found to be independent risk factors affecting the OS. In both high-risk and low-risk patients, ACT resulted in significantly better OS and DFS rates.^[20] Casadaban *et al.*^[21] retrospectively analyzed the 153,110 patients with Stage II colon cancer in the National Cancer Data Base and demonstrated that improved OS was associated with the receipt of ACT in all the patient subgroups regardless of high-risk tumor pathologic features, age, or chemotherapy regimen. A systematic review of 12 randomized controlled trials demonstrated that ACT is associated with improved 5-year OS, 5-year DFS, and reduction in risk of recurrence in patients with Stage II CRC.^[22]

In the 2009 MOSAIC study, ACT with FOLFOX regimen resulted in improved DFS in Stage II CRC cases with T4 tumors, bowel obstruction, poor differentiation, vascular invasion, or with the number of dissected LNs < 10 .^[5] Sato *et al.*^[23] in a retrospective analysis of patients with Stage II CRC found that the number of dissected LNs < 12 , male sex, age > 50 years, emergency operation, and venous invasion were independently associated with poor OS. ACT was a favorable prognostic factor in patients with extensive

venous invasion, those with fewer than 13 dissected LNs, male patients, and patients >50 years of age.

The 5-year OS of patients receiving ACT in our study (89.8%) is similar to Korean (90.1%) study^[20] which is higher than OS reported by most other studies done in Western countries such as 81.2% in patients in NCBD database^[21] and 75.3% in patients in SEER-Medicare database.^[13] These diversities between the outcomes of the ACT that were observed in different studies and trials could be explained by considering the biological differences between races that result in dissimilar response to chemotherapy agents. Supporting this, studies show a significant effect of race on the ability of patients to tolerate 5-FU.^[24]

In our study, similar to most other studies, patients with the recommended high-risk features by the International Guidelines had no significant inferior survival than patients without any of those features. In the absence of consensus regarding poor prognostic pathological variable, various molecular biomarkers were introduced to risk stratify colon cancer patients. Microsatellite instability (MSI) is one of the most well-known examples of these biomarkers. Based on this marker, colorectal tumors are classified into MSI-high (MSI-H), MSI-low (MSI-L), and microsatellite stable (MSS). Ribic *et al.*^[25] reported that among patients with Stages II and III cancer and those with MSI-H tumors had greater 5-year survival as compared to MSI-L/MSS tumors colon cancer. They reported that patients with MSI-H tumors contrary to those with MSI-L/MSS tumors did not benefit from adjuvant 5-FU therapy. Nazemalhosseini Mojarad *et al.*^[26] found that in CRC patients with Stage II cancer, MSI-L cases showed significantly poorer survival as compared with patients who had MSI-H or MSS tumors. Other prognostic factors that are currently under investigation include 18q loss of heterozygosity^[27] and mutation of KRAS and BRAF genes.^[28]

In the present study, we showed that benefit from ACT only was seen with single-agent therapy whereas multiagent therapies by FOLFOX or CAPOX act as a poor prognostic factor on OS and DFS. In an analysis of the MOSAIC data, no benefit in OS (HR 1 95% CI 0.7–1.41) or DFS (HR 0.84 with 95% CI 0.62–1.14) was seen with adding oxaliplatin to 5-FU + LV. This effect was observed in both high-risk and low-risk patients.^[29] Analysis of the NSABP C-07 showed no significant benefit from ACT with 5-FU + LV, and oxaliplatin compared with 5-FU + LV alone was observed in OS and DFS for patients with Stage II colon cancer.^[30] In our study, six patients (9.2%) suffered from devastating peripheral neuropathy. Toxic reactions including neurotoxicity of oxaliplatin in the lack of significant benefit proposed a very limited role for oxaliplatin in the management of Stage II CRC patients.

The retrospective nature of our study is the main limitation. Analysis of performance status and molecular biomarkers was not performed due to the unavailability of the data. Furthermore, the number of patients who received ACT was not similar to those who did not receive ACT. However, our results are valuable because of no prior investigation regarding the effectiveness of ACT in Iranian patients with Stage II CRC.

CONCLUSION

Our results indicate that the improvement of OS and DFS with ACT was not statistically significant in high-risk and low-risk patients with Stage II CRC. We report the unfavorable effect of the oxaliplatin as multiagent therapy in this group of patients. Further studies with larger sample size need to be done to investigate the role of chemotherapy regimen in the treatment of Stage II CRC.

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Conflicts of interest

There are no conflicts of interest.

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