Original Article

Clinical Outcomes of Patients with Colorectal Cancer Treated at Vajira Hospital during 2010 to 2014

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Objective: To compare the 3-year disease-free survival (DFS) of stage II and III colorectal cancer (CRC) patients receiving oxaliplatin (Ox)-based and fluoropyrimidine (FP)-based chemotherapy as the adjuvant chemotherapy. The outcomes of patients with rectal cancer and stage IV CRC patients receiving palliative chemotherapy were determined. The sidedness as a prognostic factor of survival in patients with stage III colon cancer was evaluated.

Materials and Methods: A retrospective analysis of CRC patients attending Vajira Hospital between January 1, 2010 and December 31, 2014 was performed.

Results: There were 523 participants. The median follow-up was 68.9 months. One hundred-eighty-one colon cancer patients (both stage II and III) had received adjuvant chemotherapy. Adjuvant Ox-based chemotherapy (n=93, 3-year DFS 66.3%, 95% CI 54.77 to 75.46) was not superior to FP (n=88, 64.2%, 95% CI 51.49 to 74.36), p=0.567. Among patients with rectal cancer, adjuvant post-operative Ox-based regimen was not superior to FP. Adjuvant radiotherapy led to insignificant benefits in terms of DFS and overall survival (OS). Most of the rectal cancer had distant sites of recurrences. Patients with stage III right-sided colon cancer had a trend towards worse OS compared to the left-sided ones.

Conclusion: In the real-world clinical practice, the outcomes of CRC treatment may be inferior to the pivotal clinical trials.

Keywords: Colorectal cancer, Adjuvant, Oxaliplatin

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Colorectal cancer (CRC) is the World's third most common cancer based on the WHO reports in 2012. Around 716,000 men and 614,000 women had been diagnosed and half of them eventually died of the disease[1]. In Thailand, based on the report from the National Cancer Institute's Registry in 2013[2], CRC was the third most common cancer in both men after lung and hepatobiliary cancers and, women after breast and cervical cancers. Therefore, CRC is now one of the most serious health problems in Thailand.

Because recurrence and metastasis are very common among patients with stage III and occasionally with stage II CRC without adjuvant treatment, adjuvant post-operative fluoropyrimidine (FP)-based chemotherapy had been the standard of care since 1990[3-8]. Later, oxaliplatin-based (Ox-based) regimen had demonstrated survival benefits in stage IV CRC[9-11]. MOSAIC trial[12] compared FOLFOX-4 (bolus and infusion 5-fluorouracil (FU), leucovorin, and oxaliplatin) versus 5-FU/leucovorin in patients with stage II and III colon cancer and showed improvement of 3-year disease-free survival (DFS) from 72.9% without oxaliplatin to 78.2% with oxaliplatin. The NSABP C-07 study[13] also revealed better 3-year DFS of FLOX (bolus 5-FU, leucovorin, and oxaliplatin) compared to 5-FU/leucovorin from 71.8% without oxaliplatin to 76.1% with oxaliplatin in patients with stage II and III colon cancer. Both MOSAIC and NSABP C-07 lead to the establishment of Ox-based as the new standard of care. Capecitabine is an oral fluoropyrimidine agent that was demonstrated survival benefit in adjuvant setting when administered concomitantly with oxaliplatin (CapeOx) compared

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to bolus 5-FU/leucovorin according to NO16968 study[14]. Andre et al[15] reported the updated results of MOSAIC trial at median follow-up of 9.5 years and showed consistent overall survival (OS) benefit, especially among patients with stage III colon cancer.

Rectal cancer is the cancer that requires multi-modality treatment including radiotherapy (RT), chemotherapy, and surgery because local recurrence is the concerning failure of treatment and distant metastasis is the most common cause of death. Total meso-rectal excision (TME) is the standard surgical technique, since it had been proven to decrease local recurrence to less than 10% compared to conventional technique[16,17]. When it is combined with either pre- or post-operative RT or concomitant chemo-RT, the chance of local recurrence was shown to be even less common; however, the survival improvement was not obviously demonstrated[18-22]. Post-operative adjuvant treatment with Ox-based regimen has been used ubiquitously, especially among patients with residual tumor after neoadjuvant RT or chemo-RT and patients with pathological stage III without prior neoadjuvant RT or chemo-RT, even though there is no well-designed prospective randomized study demonstrating the benefits. Since 2013, when oxaliplatin had been included in Thailand's National Essential Drug List, the National Health Security Office (NHSO) allowed its use in stage III CRC patients with full re-imbursement[23]. However, the outcomes in a real-world setting among Thai patients has not yet been explored.

Materials and Methods

The present study was a retrospective study. The participants were the patients with CRC aged from 18 years old and had stage II to IV according to the AJCC Staging System, Seventh Edition[24], who received medical attention in Vajira Hospital, Navamindradhiraj University between January 1, 2010 and December 31, 2014. The data were retrieved from the hospital's electronic database and written medical records. The patients who had complete official pathological reports and surgical records were eligible for OS outcome evaluation. The participants who also had regular visits were eligible to determine both DFS and OS. Among participants with stage IV CRC, the primary site of tumor, metastatic site(s), and palliative chemotherapy regimens used were recorded. The chemotherapy regimens were categorized into FP-based (5-FU/leucovorin or capecitabine or uracil/tegafur), Ox-based (FOLFOX or CapeOx with or without bevacizumab or anti-epidermal growth factor receptor [EGFR]) and Iri-based (Irinotecan or FOLFIRI with or without bevacizumab or anti-EGFR). Only participants who had confirmed radiological reports subsequently after initiation of a chemotherapy regimen were included in progression-free survival (PFS) and OS analysis, the rest were included only in OS analysis. The survival outcomes were analyzed in intent-to-treat fashion. The data were censored on December 31, 2017. The exact date of death was determined by requesting the Ministry of Interior's Census database. The present study was approved by the Ethics Committee on Medical Research, Navamindradhiraj University.

Definitions of the variables

1) DFS was determined among patients with stage II or III at presentation and calculated as the time from the date of pathological result of CRC diagnosis was revealed as shown on the pathological report until the date of reported documentation of recurrence or metastasis or death from any causes was revealed, no matter what happened first. It was reported in months and inter-quartile range (IQR). 2) 3-year DFS was the ratio between the number of eligible patients who had recurrences or metastases or death from any causes, no matter what happened first, and the number of all eligible patients at the median time of follow-up of three years. It was reported in percent and 95% confidence interval (CI). 3) PFS was determined among patients with stage IV and receiving palliative chemotherapy and calculated as the time from the date of reported documentation of recurrence or metastasis to date of documented significant progression of disease (as assessed by RECIST criteria) or death from any causes, no matter what happened first. It was reported in months and IQR. 4) OS was calculated as the time from the date of pathological results of CRC diagnosis to date of death from any causes. It was reported in months and IQR. 5) 3-year OS was the ratio between the number of eligible patients who died from any causes and the number of all eligible patients at the median time of follow-up of three years. It was reported in percent and 95% CI.

Objectives

The primary objective was to evaluate the 3-year DFS of patients with colon cancer who received adjuvant chemotherapy and to compare between the all patients receiving Ox-based and FP chemotherapy regimens and between such patients stratified as stage II and III. The secondary objectives included 1) 3-year OS of patients with stage II and III colon cancer

receiving adjuvant chemotherapy, 2) PFS and OS of patients with stage IV CRC (divided into de novo metastasis group and recurrent metastasis group) who received palliative chemotherapy, 3) 3-year DFS and 3-year OS of patients with rectal cancer who received adjuvant chemotherapy and to compare between the patients receiving Ox-based and FP chemotherapy regimens, 4) 3-year DFS and 3-year OS of adjuvant RT among patients with sigmoid, recto-sigmoid, upper rectum and rectum who receiving compared with patients not receiving adjuvant RT, and 5) DFS and OS of all patients with right-sided (caecum and ascending colon) compared with left-sided (transverse colon, descending colon, sigmoid colon/recto-sigmoid colon/upper rectum, and rectum) colon and between such patients stratified as stage III and IV.

Statistical analysis

The investigators collected demographic data including age, sex, sites (categorized into ascending, transverse, descending, sigmoid/rectosigmoid/upper rectum, and rectum), TNM staging, tumor differentiation, chemotherapy regimen and history of radiation (pre-operative or post-operative). The descriptive statistics were reported as mean and standard deviation or median and IQR as appropriated. Comparing the demographic data between different groups of interest with either chi-square or independent t-test as appropriated. Kaplan-Meier method was used to estimate the survival outcomes. DFS, PFS and OS were calculated using log rank test and reported as median and 95% CI. Hazard ratio (HR) of DFS, PFS and OS between different groups of interest were calculated using Cox proportional hazard model. All of the statistical data were evaluated using SPSS version 23.0 (IBM Corp., Armonk, NY). The p-value less than 0.05 was considered significant.

Results

There were 523 patients eligible for analyses. With median follow-up time of 68.9 months, the investigators found the following.

3-year DFS of stage II to III colon cancer patients receiving adjuvant chemotherapy

Table 1 shows the baseline demographic data of all participants. There were 181 patients eligible for this analysis. Most of the patients with early stage colon cancer (58%) presented with stage III. Eighty-eight patients received FP and 93 patients received Ox-based adjuvant chemotherapy. Notably, older patients and stage II disease at presentation tended to receive FP, on the other hand the patients with younger and stage III tended to receive Ox-based regimen. No significant difference in 3-year DFS between patients

Table 1. Baseline characteristics of stage II to III colon cancer patients

Baseline characteristics Colon cancer	Ox-based (n=93) n (%)	FP (n=88) n (%)
Age (years)		
Median	59.76	71.23
Range	53.8 to 68.8	61.6 to 77.6
Sex		
Male	44 (47.3)	39 (44.3)
Female	49 (52.7)	49 (55.7)
Disease stage		
II	23 (24.7)	53 (60.2)
III	70 (75.3)	35 (39.8)
Depth of invasion		
T2	5 (5.4)	4 (4.6)
T3	63 (68.5)	57 (65.5)
T4	24 (26.1)	26 (29.9)
Unknown	0 (0.0)	0 (0.0)
No of nodes involved		
N1	33 (47.8)	18 (52.9)
N2	35 (50.7)	16 (47.1)
Unknown	1 (1.5)	0 (0.0)
Histologic appearance		
Well differentiated/ moderate differentiated	74 (80.4)	75 (88.2)
Poorly differentiated	4 (4.4)	0 (0.0)
Unknown	14 (15.2)	10 (11.8)
Patient with stage III disease		
No of nodes involved		
• N1	33 (47.8)	18 (52.9)
• N2	35 (50.7)	16 (47.1)
• Unknown	1 (1.5)	0 (0.0)
Patient with stage II disease		
T2	2 (8.7)	4 (1.9)
T3	15 (65.2)	37 (69.8)
T4	6 (26.1)	15 (28.3)
Histologic appearance		
• Well differentiated/ moderate differentiated	22 (95.7)	49 (92.5)
• Poorly differentiated	0 (0.0)	0 (0.0)
• Unknown	1 (4.3)	4 (7.5)

Ox=oxaliplatin; FP=fluoropyrimidine

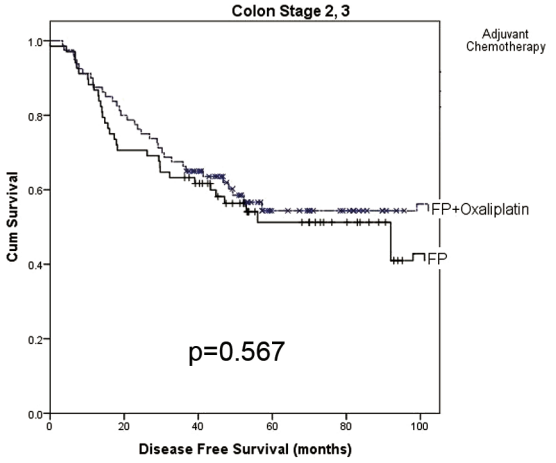


Figure 1. Kaplan-Meier curves comparing DFS of patients with stage II to III colon cancer receiving adjuvant FP vs. Ox-based chemotherapy.

receiving FP [64.2 months (95% CI 51.49 to 74.36)], and patients receiving Ox-based regimen [66.3 months (95% CI 54.77 to 75.46)], p=0.567 (Figure 1). When the present study outcome was stratified according to staging, the difference in 3-year DFS remained insignificant [FP versus Ox-based in stage II, 73.8% (95% CI 57.72 to 84.55) versus 90.5% (95% CI 67 to 97.53), p=0.104, and in stage III, 48% (95% CI 27.81 to 65.64) versus 57.6% (95% CI 44.05 to 69.03), p=0.318] (Figure 2).

3-year OS of stage II to III colon cancer patients receiving adjuvant chemotherapy

When this outcome was stratified according to staging, the difference in 3-year OS was insignificant [FP versus Ox-based in stage II, 79.3% (95% CI 65.66 to 87.93) versus 95.7% (95% CI 72.93 to 99.38), p=0.137; in stage III, 64.7% (95% CI 46.9 to 78.18) versus 72.9% (95% CI 60.81 to 81.74), p=0.214] (Figure 2).

PFS and OS of patients with stage IV

There were 113 patients with de novo metastatic diseases. Most of them had liver metastasis (n=74, 58.3%), the rest had lung (n=5, 3.9%) and concomitant lung and liver metastases (n=21, 16.5%). Only 43 patients who receiving palliative chemotherapy had radiological confirmation of responses. Eleven patients received FP and 32 patients received Ox-based as the first-line therapy. There was no significant difference in PFS between patients receiving FP [n=11, nine months (IQR 7 to 18)] and Ox-based [n=32, eight months (IQR 1.07 to 11] as the first-line therapy,

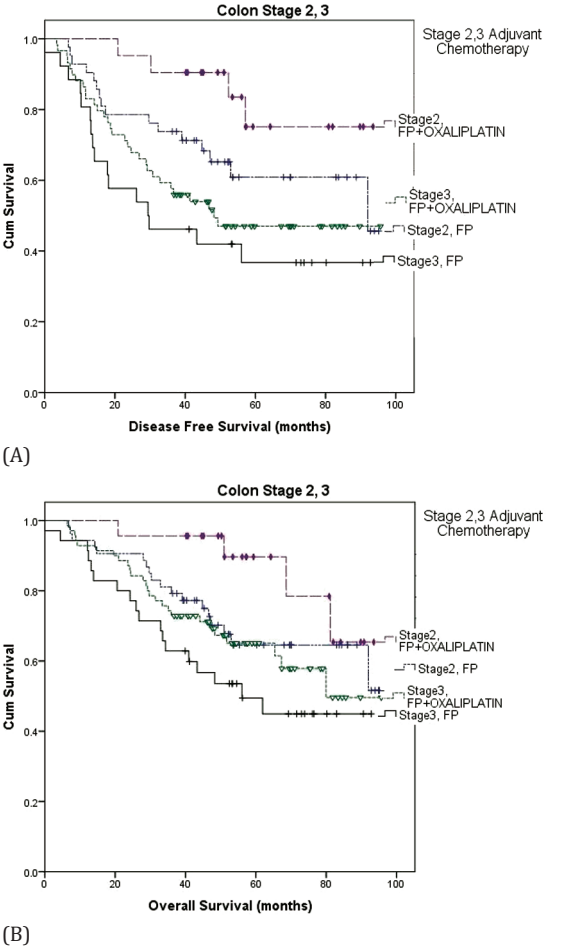


Figure 2. Kaplan-Meier of DFS (A) and OS (B) stage II to III colon cancer patients stratified by stages and types of adjuvant chemotherapy.

p=0.358. There were 83 participants eligible for OS assessment. Twenty-eight patients who received FP as the first line chemotherapy regimen had OS of 12.6 months (IQR 11.54 to 39.31), while 55 patients who received Ox-based chemotherapy had OS of 20.7 months (IQR 7.92 to 20.16). The Ox-based led to significantly better OS (p=0.02). There were 47 patients with subsequent recurrent metastatic diseases, 18 patients (38.3%) had liver metastasis, 12 patients (25.5%) had lung metastasis, one patient (2.1%) had both liver and lung metastases, and 16 patients (34%) had either bone or distant nodal metastases. Only 18 patients who receiving palliative chemotherapy had radiological confirmation of responses. Eight patients received FP and 10 patients received Ox-based as the first-line therapy. There was no significant difference in PFS between patients receiving FP [14 months (IQR 7 to 18)] and Ox-based [10 months (IQR 4 to

Table 2. Baseline characteristics of stage II to III rectal cancer patients receiving adjuvant chemotherapy

Baseline characteristics Rectal cancer	Ox-based (n=57) n (%)	FP (n=74) n (%)
Age (years)		
Median	59.61	61.9
Range	51.84 to 64.6	54.42 to 67.08
Sex		
Male	32 (56.14)	46 (62.16)
Female	25 (43.86)	28 (37.84)
Disease stage		
II	19 (33.33)	33 (44.59)
III	38 (66.67)	41 (55.41)
Depth of invasion		
T2	4 (7.14)	6 (8.22)
T3	38 (67.86)	55 (75.34)
T4	14 (25.00)	12 (16.44)
No of nodes involved		
N1	18 (47.37)	24 (58.54)
N2	20 (52.63)	16 (39.02)
Unknown	0 (0.0)	1 (2.44)
Histologic appearance		
Well differentiated/ moderate differentiated	42 (73.68)	46 (62.16)
Poorly differentiated	1 (1.75)	1 (1.35)
Unknown	14 (24.57)	27 (36.49)

Ox=oxaliplatin; FP=fluoropyrimidine

22)] as the first-line therapy, p=0.579. There were 33 participants eligible for OS assessment. Thirteen patients who received FP as the first line chemotherapy regimen had OS of 48.32 months (IQR 40.95 to 79.97), while 20 patients who received Ox-based chemotherapy had OS of 46.55 months (IQR 27.93 to 67.31). The Ox-based did not lead to significantly better OS (p=0.41), among these patients.

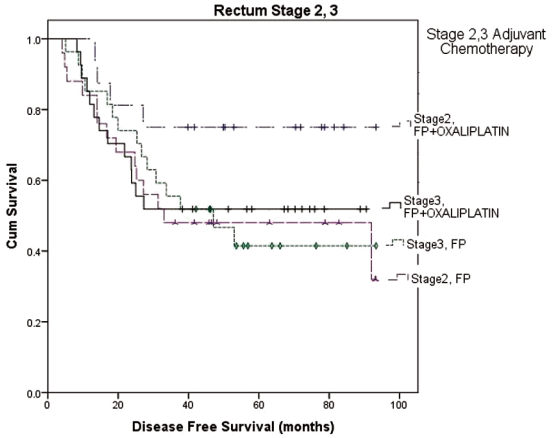
The outcomes of patients with rectal cancer receiving adjuvant chemotherapy

The investigators analyzed only 131 stage II to III cancer participants who had primary site of tumor at mid-to-lower rectum (below the peritoneal reflection). Seventy-four patients received FP and 57 patients received Ox-based as the adjuvant chemotherapy. The investigators did not find any particular differences in baseline characteristics between these two groups of patients (Table 2). Among these groups of patients, 95 patients visited regularly and were eligible for DFS analysis. Fifty-two patients received FP and 43 patients received Ox-based as the adjuvant chemotherapy regimen. No significant difference in 3-year DFS between both groups was seen [FP versus Ox-based, 51.9% (95% CI 37.65 to 64.42) versus 60.5% (95% CI 44.34 to 73.26), p=0.0232]. When this outcome was stratified according to staging, there were 41 patients with stage II, and 54 patients with stage III. Among patients with stage II rectal cancer, 25 patients received FP and had 3-year DFS of 48% (95% CI 27.81 to 65.64) and another 16 patients received Ox-based had 3-year DFS of 75% (95% CI 46.34 to 89.8), which remained statistically insignificant (p=0.084). Among patients with stage III rectal cancer, 27 patients received FP and had 3-year DFS of 55.6% (95% CI 35.22 to 71.81), and another 27 patients received Ox-based had 3-year DFS of 51.9% (95% CI 31.91 to 68.55), which also remained statistically insignificant (p=0.853).

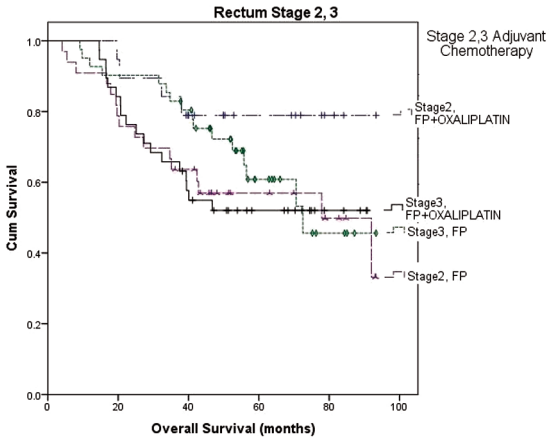
In terms of 3-year OS, there were 74 patients who received FP as the adjuvant chemotherapy regimen and had 3-year OS of 74.3% (95% CI 62.75 to 82.78), and 57 patients who received Ox-based and had 3-year DFS of 71.9% (95% CI 58.33 to 81.76). No significant difference in 3-year OS between both groups was seen (p=0.758). When this outcome was stratified according to staging, there were 52 patients with stage II, 33 patients received FP and had 3-year OS of 63.6% (95% CI 44.95 to 77.46), and 19 patients received Ox-based had 3-year OS of 84.2% (95% CI 58.65 to 94.62); however, there was no statistical difference (p=0.081). Among patients with stage III rectal cancer, there were 79 patients, 41 patients received FP and had 3-year OS of 82.9% (95% CI 67.49 to 91.47) and another 38 patients received Ox-based had 3-year OS of 65.8% (95% CI 48.48 to 78.49); however, there was no statistical difference (p=0.35). In brief, the investigators found no statistically significant evidence of superior survival of Ox-based over FP among patients with rectal cancer (Figure 3).

The effects of adjuvant RT in patients with rectal cancers

Among patients with stage II, the investigators did not find the significant difference in 3-year DFS (p=0.726) between patients receiving adjuvant RT (n=26, 3-year DFS 58.8%, 95% CI 32.54 to 77.82) and patients not receiving RT (n=19, 3-year DFS 53.6%, 95% CI 33.81 to 69.82). Among patients with stage III, the difference in 3-year DFS between patients

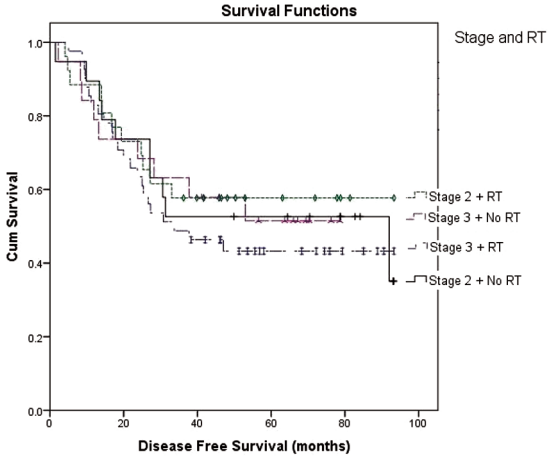


(A) Stage II p=0.084; Stage III p=0.853

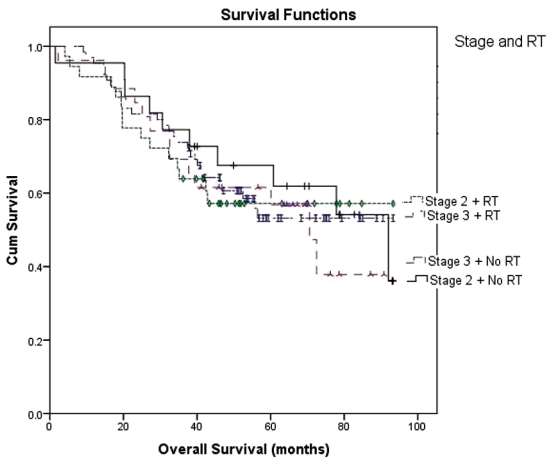


(B) Stage II p=0.081; Stage III p=0.35

Figure 3. Kaplan-Meier curves comparing (A) DFS and (B) OS of stage II, III rectal cancer patients receiving adjuvant FP vs. Ox-based chemotherapy.



(A) Stage II p=0.726; Stage III p=0.554



(B) Stage II p=0.684; Stage III p=0.762

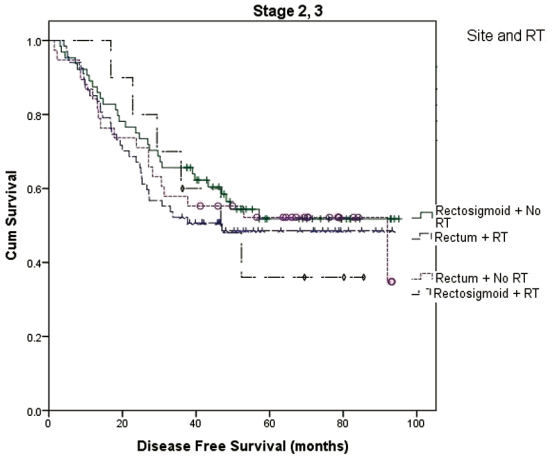
Figure 4. Kaplan-Meier curves comparing (A) DFS and (B) OS of stage II to III rectal cancer patients receiving vs. not receiving adjuvant radiotherapy.

receiving adjuvant RT (n=41, 3-year DFS 50%, 95% CI 32.94 to 64.88) and patients not receiving RT (n=19, 3-year DFS 58.3%, 95% CI 36.45 to 74.99), remained insignificant (p=0.554). In terms of 3-year OS, the investigators again did not find significant difference, both among patients with stage II [receiving RT versus not; n=36, 3-year OS 68% (95% CI 46.09 to 82.53) versus n=22, 69.7% (95% CI 51.01 to 82.4); p=0.684], and stage III [receiving RT versus not; n=65, 3-year OS 72.7% (95% CI 58.9 to 82.57) versus n=26, 72.2% (95% CI 54.53 to 83.98); p=0.762] (Figure 4). In brief, RT did not contribute to survival benefits.

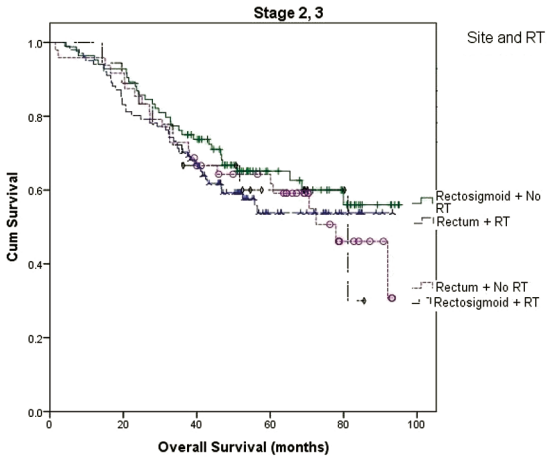
The investigators also found that some of patients with sigmoid, recto-sigmoid and upper rectal cancers receiving adjuvant RT. Ten of 74 eligible patients (those who attended regular visits) received adjuvant RT. No significant difference in terms of 3-year DFS [receiving RT versus not, 62.5% (95% CI 22.93 to 86.07) versus 61.4% (95% CI 50.37 to 70.63), p=0.599]. In terms of 3-year OS, there were 102 evaluable patients, 18 patients received RT and 84 patients did not receive. No significant difference was noted [receiving RT versus not, 68.75% (95% CI 40.46 to 85.63) versus 50% (95% CI 42.45 to 57.08), p=0.631]. When compared to patients with rectal cancer, there was no 3-year OS difference (p=0.36) (Figure 5).

Sidedness as a prognostic factor

Among 92 eligible patients with stage III colon cancer, 31 patients had right-sided tumor and 61 patients had left-sided one, the investigators found no DFS and 3-year DFS differences (p=0.302) between

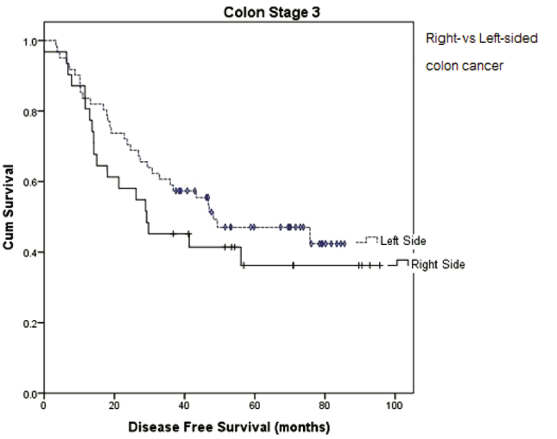


(A) Rectosigmoid colon p=0.599; Rectum p=0.772

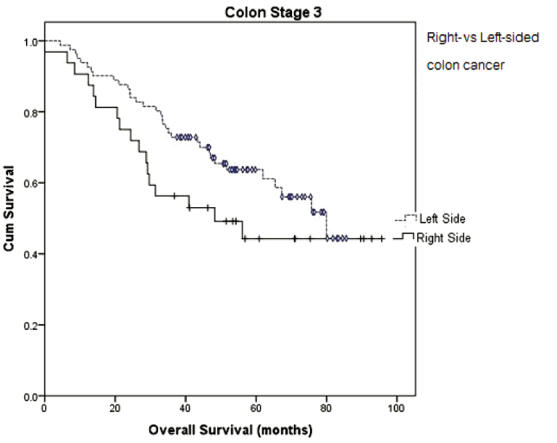


(B) Rectosigmoid colon p=0.631; Rectum p=0.936

Figure 5. Kaplan-Meier curves comparing (A) DFS and (B) OS of patients with stage II to III rectal vs. rectosigmoid cancer receiving vs. not receiving adjuvant radiotherapy.



(A) p=0.302



(B) p=0.151

Figure 6. Kaplan-Meier curves comparing (A) DFS and (B) OS of patients with right-sided vs. left-sided stage III colon cancers.

patients with right-sided [47.7 months (SD 6.944) and 45.2%] and left-sided [52.38 months (SD 4.206) and 59%] tumors. However, there was a trend (p=0.151) towards worse OS in patients with right-sided [n=32, OS 56.61 months (SD 6.609)] compared with left-sided [n=81, OS 62.34 months (p=0.151)] (Figure 6).

Discussion

Before 2013, when oxaliplatin had not yet included in the National Essential Drug List, the Ox-based chemotherapy was given under the discretion of physicians. During that period, the survival benefit in stage II colon cancer had still been under evaluation. Patients with younger ages and those who fully reimbursed from the Thailand's Comptroller General's Department tended to receive Ox-based regimen both in adjuvant and palliative settings. Therefore, there were both patients with stage II and III who received either FP or Ox-based regimen in adjuvant setting as well as patients with stage IV. The investigators used 3-year DFS as the primary endpoint because the 3-year DFS was demonstrated to transfer to 5-year OS and able to be a validated surrogate marker of the OS[25]. The investigators found that the outcomes in patients treated in Vajira Hospital seemed to be inferior to the landmark MOSAIC trial. The 3-year DFS of participants receiving FP versus Ox-based regimen as the adjuvant treatment were 64.2% versus 66.3%; on the other hand, the 3-year DFS of patients enrolled in MOSAIC trial were 72.9% versus 78.2%[12]. The explanation was possibly in part as a result of incorrect staging at diagnosis. Most of the

patients who underwent emergency operation due to gut obstruction did not obtain full scans of chest and abdomen compared to those who underwent elective operation. The investigators demonstrated that Ox-based regimen was not superior to FP when the survival analysis was stratified by staging at diagnosis (II and III). Racial and genetic background would be the explanation of differential response, but the small-sized study with retrospective fashion was impossible to prove such hypothesis. The investigators suggested the collaboration between centers in Thailand to analyze the pooled data.

Regarding the efficacy of palliative chemotherapy, the clinical trials revealed that either Ox-based or Iri-based (irinotecan) would lead to equal PFS (8 to 8.5 months) and OS (20.6 to 21.5 months), no matter which one was used first in palliative setting[26]. The investigators did not observe the PFS difference, no matter Ox-based or FP was used first in metastatic setting. However, patients who received Ox-based as the first-line regimen had significant longer OS (20.7 months in Ox-based versus 12.6 months in FP, p=0.02). The investigators postulated that most of the patients who received Ox-based as the first-line treatment would receive more subsequent lines. The reimbursement policy was the main factor attributable to such finding.

Among participants with rectal cancer, the investigators analyzed the outcomes of the patients with primary site of tumor specifically at middle to lower rectum. Because middle rectum and lower rectum are assumed to locate below the peritoneal reflection and vulnerable to local recurrences, therefore it was the part that would gain most benefits from adjuvant RT. RT with or without chemotherapy is strongly indicated in such patients with locally advanced (stage II and III) diseases at this site. The investigators could not demonstrate the DFS and OS differences among patients receiving RT versus not, both in the whole populations and when stratified by staging at diagnosis. The effect of RT is mainly to decrease local recurrences, therefore relapse-free survival (RFS) is the more appropriate outcome to be explored. However, the present study collected the data retrospectively and interval scans were not routinely obtained in the real-life practices. The investigators found that around two-thirds of rectal cancer patients succumbed to distant metastasis and most of the patients with local recurrences had concomitant or subsequent metastasis. It would explain why adjuvant RT would not lead to survival benefits. A systemic review by Breugom et al[27] revealed that adjuvant FP was beneficial in improvement of disease-free and distant-free survivals compared to no adjuvant chemotherapy only among patients with tumors located above 10 centimeters from anal verge. The investigators could not show the DFS and OS differences between patients receiving adjuvant Ox-based versus FP, both in the whole populations and when stratified by staging at diagnosis. Adjuvant Ox-based regimen in rectal cancer is still a controversial issue. Due to the a small-sized study and analyzed in a retrospective fashion, the true benefit of adjuvant Ox-based regimen would be impossible to be determined.

The tumor sideness is the increasingly concerning issue in clinical trials. Pooled retrospective analysis by Hoch et al[28] demonstrated the survival difference among patients who received an anti-EGFR (cetuximab or panitumumab) combination therapy as the first-line treatment in metastatic setting when tumor sideness was the comparable factor. Those with the primary tumor at right-sided location had significantly shorter survival when they received an anti-EGFR combination therapy compared to anti-vascular endothelial growth factor (VEGF) (bevacizumab) combination therapy. Moreover, those with primary tumor at right-sided location had independently and significantly shorter survival compared to those at left-sided one. The investigators could not demonstrate the survival differences among patients with stage IV diseases due to the small number of patients. However, the investigators showed the trend towards worse survival outcome among stage III patients with primary site at right-sided colon. This notion corresponds to the report by Cascinu et al[24].

Limitation

The present study was a retrospective study. No randomization would lead to biases. Many crucial information was missed and would result in the unreliable outcomes.

Strength

The present study explored the data in a real-world practice. The investigators' findings would be a reference for the stakeholders and policy makers.

Conclusion

The survival of Thai patients with colon cancer was shorter than the patients in the pivotal trials. No survival differences in terms of both 3-year DFS and OS was found among patients with stage II, stage III and both stage II and III who receiving either Ox-based or FP chemotherapy as the adjuvant

treatment. Regarding the efficacy in palliative setting, the investigators found no difference in terms of PFS between those who received Ox-based and FP as the first-line treatment. However, the OS among patients who received Ox-based first was significantly longer. However, such patients tended to receive more subsequent lines of treatment. Most of the patients with rectal cancer failed at distant site rather than the local one. Effective systemic treatment is encouraged to be investigated in randomized trials. Patients with stage III colon cancer with primary location on the right side had shorter survival compared to the left one. Further pooled analysis among Thai patients is suggested to confirm the hypothesis.

What is already known on this topic?

Most of CRC present with stage III disease; however, the number of patients with de novo metastatic disease at presentation is substantial. Distant failure is still the most common site of relapse and leads to fatality.

What this study adds?

Ox-based regimen may not be superior to FP-based in the real-world practice, at least in an adjuvant setting. In metastatic setting, the chances of receiving multiple lines of treatments likely determine the superior outcomes.

Conflicts of interest

The authors declare no conflict of interest.

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