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Original Research

Survival rates analysis on chemotherapy regimens of patient with colorectal cancer (A study at division of hematology and medical oncology Universitas Airlangga teaching hospital)

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Abstract

Background: The 5-year survival rate for patients with colorectal cancer decreases in the presence of metastases. Standard therapy for colorectal cancer includes FOLFOX (5- fluorouracil, leucovorin, and oxaliplatin) and FOLFIRI (5-fluorouracil, leucovorin, and irinotecan) which aims to prolong survival. **Objective:** To analyze the survival rate and hazard ratio (HR) of colorectal cancer patients treated at Universitas Airlangga Teaching Hospital Surabaya with the FOLFOX and FOLFIRI chemotherapy regimens. **Method:** A retrospective cohort approach was used in this study of 39 colorectal cancer patients over the age of 18 who had FOLFOX and FOLFIRI treatment between 2018 and 2022. **Results:** This study involved 27 colorectal cancer patients who got FOLFOX therapy and 12 patients who received FOLFIRI therapy. FOLFOX had a two-year survival rate of 51.9% with a mean time of 18.2 2.01 months, while FOLFIRI had a two-year survival rate of 58.3% with a mean time of 18.8 1.51 months ($p > 0.05$), according to Kaplan- Meier analysis. Patients who had incomplete FOLFOX regimens (<12 cycles) had a 3.8-fold higher probability of mortality than those who received a complete regimen (12 cycles) (HR 3.883; 95% CI 1.195-12.169). **Conclusion:** Patients who take FOLFOX have a lower risk of adverse effects than those who take FOLFIRI, which may influence clinician preferences. The FOLFOX regimen is recommended for colorectal cancer treatment, especially in early and advanced stages, due to potential adverse effects.

Keywords: survival; colorectal cancer; chemotherapy; folfox; folfiri

INTRODUCTION

Colorectal cancer is the cancer that causes the second most mortality in the world, with an estimated 935,173 deaths in 2020 (WHO, 2020). Patients with stage I and II colorectal cancer have a 5-year survival rate of 93%, while it decreases to 60%, 42% and 25% respectively for patients with stages IIIA, IIIB and IIIC. However, the majority of patients with stage IV metastatic colorectal cancer are difficult to cure, with a 5-year survival rate of <10%.[25] Colorectal cancer is caused by tumor mutations due to, among others: sporadic factors (chromosomal instability, microsatellite instability, and cpG island dysfunction) occurring in 94%, 5% comes from inherited mutations, and the remaining 1% from inflammatory bowel disease (IBD).[20]

Tumor mutations occur through APC (Antigen Presenting Cell) activation that deviates from the signaling pathway is one of the early stages of colorectal cancer development. Another important molecular target is EGFR (Epidermal Growth Factor Receptor), because approximately 10% of colorectal tumors and 20-30% of KRAS type tumors depend on the EGFR pathway.[25] Early screening of high-risk individuals and appropriate therapy are associated with risk factors and progression of colorectal cancer. In addition, therapy must be adjusted to the extent of cancer metastases and other causal factors. Therefore, the management of colorectal cancer must be considered carefully by carrying out interprofessional collaboration.[1]

Drug therapy for colorectal cancer patients can be given the FOLFOX, FOLFIRI, FOLFOXIRI and CAPOX regimens. Standard therapy for metastatic colorectal cancer patients includes; FOLFOX (5-fluorouracil, leucovorin, and oxaliplatin) and FOLFIRI (5-fluorouracil, leucovorin, and irinotecan) (NCCN, 2022). FOLFOX and FOLFIRI have been shown to significantly increase response rates, DFS (Disease-Free Survival), and OS (Overall Survival) compared to 5-fluoroauracil single therapy.[13]

The related study compared the mean survival of FOLFOX and FOLFIRI was 21.5 months in 109 patients allocated to FOLFIRI then FOLFOX. Then, about 20.6 months in 111 patients allocated to FOLFOX then FOLFIRI (P 0.99). First-line therapy, FOLFIRI achieved a response rate (RR) of 56% and a median PFS (Progression Free Survival) of 8.5 months, compared to FOLFOX which achieved a 54% RR and median PFS of 8.0 months (P 0.26). Second-line FOLFIRI achieved a 4% RR and 2.5 months median PFS, compared with FOLFOX which achieved

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a 15% RR and 4.2 months PFS.[23] Success in chemotherapy and early diagnosis has been proven to reduce the death rate from colorectal cancer in several developed countries.[19] In clinical practice, patients often experience chemotherapy side effects.[14] Another factor studied by Boyke shows that the completeness of the cycle determines the outcome of therapy.[3] Discontinuing chemotherapy will affect survival and may accelerate mortality.[18]

Study related to survival needs to be carried out using the Kaplan-Meier analysis to see the percentage of survival and survival time of colorectal cancer patients in Indonesia, even though the incidence in Indonesia itself is quite small. Apart from the Kaplan-Meier analysis, further analysis with Cox regression also needs to be carried out to identify various factors that influence survival, including: gender, age, stage, metastases, comorbidities and completeness of the chemotherapy cycle to determine the hazard ratio (HR) or factor size. risk to survival of colorectal cancer patients. This study aims to analyze the survival rate, survival time and hazard ratio (HR) factors that influence the survival of colorectal cancer patients after using the FOLFOX and FOLFIRI chemotherapy regimens.

MATERIAL AND METHODS

This study used a retrospective cohort method conducted on 39 colorectal cancer patients aged ≥18 years who were diagnosed for the first time with or without comorbidities/ complications in 2018-2022; who received FOLFOX and FOLFIRI chemotherapy treatment; patients with complete, undamaged, and readable medical records including identity, diagnosis, cytostatic drug therapy, clinical data, laboratory data, radiological examinations. The data collection was carried out between May – July 2023.

ETHICS APPROVAL

This study was approved by the study ethics committee of Universitas Airlangga Hospital (No: 067/KEP/2023).

STATISTICAL ANALYSIS

The sample in this study was all colorectal cancer patients who had undergone chemotherapy since the first chemotherapy administration who met the inclusion criteria using the time limited sampling method. There were 39 patients in this study, consisting of 20 female patients and 19 male patients. Statistical analysis was carried out using SPSS version 26.0. (Chicago, Illinois, USA). Statistical analysis used to determine the correlation between the two variables uses the Pearson statistical test if the data distribution is normal, otherwise, the Spearman test is used. The results of the correlation test were interpreted based on the p value, which was the strength of the correlation and the direction of the correlation.

RESULT

Colorectal cancer patients in this study received FOLFOX and FOLFIRI chemotherapy regimens. Patient characteristics were grouped based on: gender, age, diagnosis, stage, location of metastases, comorbidities, and chemotherapy status as listed in Table 1. This table shows the distribution of samples/patients using FOLFOX and FOLFIRI with certain characteristics. Patient characteristics showed no significant differences between

Tabel 1. Characteristics of Colorectal Cancer Patients (continued)

CHARACTERISTC	**Number of Chemotherapy Patient**		**Total sample**	**%**	***p-value***
	FOLFOX	**FOLFIRI**			
Stage					
Early (I dan II)	1	9	10	26%	0,001
Advanced (III dan IV)	26	3	29	74%	
Metastases*					
There is not	10	11	21	43%	0,002
There is	17	1	18	57%	
Liver	7	1	8	20%	
Lungs	6	0	6	15%	
Lymph gland	3	0	3	8%	
Ovaries	2	0	2	5%	
Bone	2	0	2	5%	
Vagina	1	0	1	2%	
Uterus	1	0	1	2%	
Comorbid*					
There is not	10	7	22	56%	0,216
There is	17	5	17	44%	

Hypertension	8	3	11	32%	
Diabetes mellitus	5	0	4	11%	
GIT disorders	3	0	3	8%	
Cholesterol	1	0	1	3%	
Hepatitis	1	0	1	3%	
Erectile Dysfunction	1	0	1	3%	
Pulmonary TB	1	1	1	3%	
CKD	1	1	1	3%	
Chemotherapy Status					
Complete	21	9	30	77%	1,00
Incomplete	6	3	9	33%	
Total Sample	27	12	39	100%	
Information: *) shows the frequency of metastases and patient comorbidities					

groups, except stage and metastases. The data obtained was then continued with the Kaplan-Meier analysis.

Data on colorectal cancer patients who are female were 20 and those who are male were 19 patients. Patients aged 18-64 years reached 79% while for patients over 65 years it was 21%. The most common diagnosis experienced by patients was Colonic Ca with a total of 14 patients (35%) followed by Distal 1/3 Rectal Ca with 7 patients (18%). Most of the colorectal cancer patients (74%) who received therapy at Universitas Airlangga Hospital were patients who had advanced stages (IIIA, IIIB, IIIC and IV). Patients who have advanced stages would experience metastases in other organs. The highest location of metastases experienced by patients was in the liver at 20%, followed by the lungs at 15% and lymph nodes at 8%. Meanwhile, for comorbidities, the results of this study showed that hypertension ranks at the top after diabetes mellitus and gastrointestinal disorders. In this study, 77% of patients received complete chemotherapy (12 cycles), while 33% received incomplete chemotherapy (<12 cycles). The completeness of the cycle could influence the patient's therapeutic outcome, because chemotherapy was a therapeutic modality to slow the development of cancer cells. Kaplan Meier analysis was used to see patient survival with the parameters of survival rate and estimated patient survival time.

Colorectal cancer patients who met the inclusion criteria consisted of 27 patients who received the FOLFOX regimen and 12 patients who received the FOLFIRI regimen. The overall survival percentage of patients with the FOLFOX regimen was 44.4% and FOLFIRI 58.3%. Patients who received FOLFOX had the longest survival time reaching 47 months and FOLFIRI reaching 30 months ($p > 0.05$) as stated in Figure 1. From these results, the time period for the study was determined to be 2 years, so that between regimens there was almost the same study period to minimize censored data (data that creates bias). The results of the Kaplan Meier analysis showed that the two-year survival percentage for FOLFOX was 51.9% with a mean survival reaching 16.8 ± 1.51 months and FOLFIRI 58.3% reaching 18.2 ± 2.01 months (p>0, 05) listed in Figure 2.

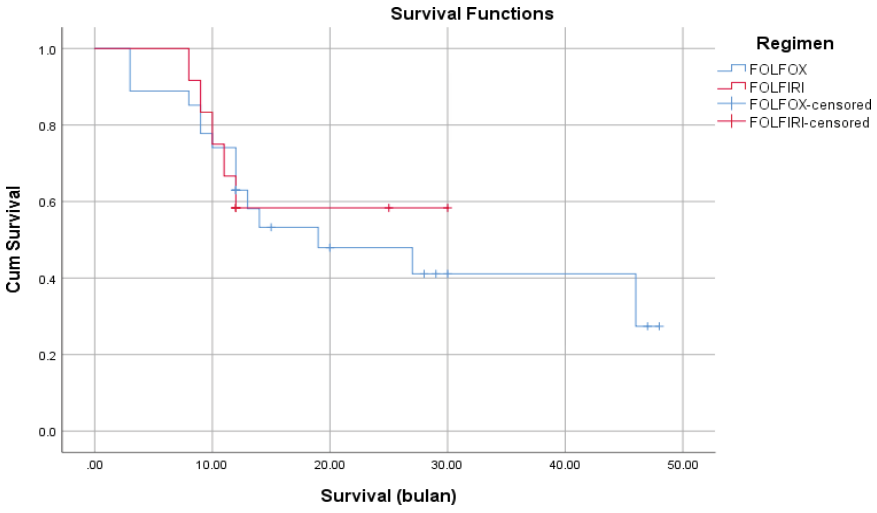

Figure 1. Overall survival graph for colorectal cancer patients (N=39)

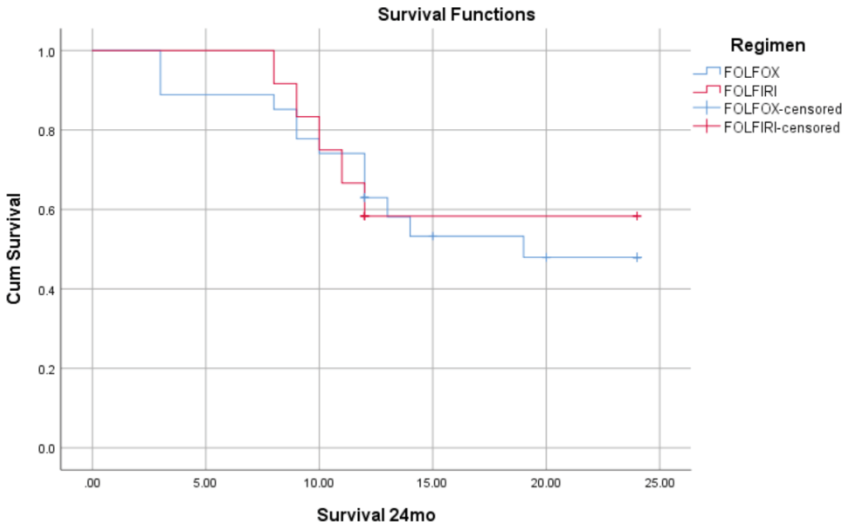

Figure 2. Graph of 2-year Survival of Colorectal Cancer Patients (N=39)

Based on these data, the FOLFIRI regimen had a tendency for a longer survival time than FOLFOX, but this was not statistically significant. The results from the Kaplan Meier data illustrated that the lower the survival percentage, the higher the incidence of patient mortality, which resulted in a lower average patient survival time. The data was then processed with further Cox regression analysis to see the factors that influence the survival of colorectal cancer patients.

Based on Table 1 regarding the characteristics of colorectal cancer patients, the data shows that stage and metastases have a p value <0.05, which indicates that the sample distribution is significantly different. The number of early-stage patients using the FOLFOX regimen was only 1 patient, so it did not qualify for statistical analysis. Therefore, the Kaplan Meier analysis was performed for patients at advanced stages. In Figure 3, analysis of the two-year survival of advanced stage colorectal cancer patients showed that the survival percentage with the FOLFOX regimen was 53.8%, with the survival time reaching 17.35 ± 1.47 months and FOLFIRI 66.7% (p > 0 .05) reached 20.00 ± 3.26 months. The summary results of the survival parameters (survival rate and survival time) described above are listed in Table 2.

After carrying out the Kaplan Meier analysis, the next data processing was Cox regression analysis with the aim of looking at the factors that influence survival parameters. The results of the Cox regression analysis of the influence of these factors on colorectal cancer patients were shown in Table 3. For colorectal cancer patients who received the FOLFOX regimen, the HR (Hazard Ratio) value that showed a significant difference was the chemotherapy status factor (HR 3.883 (CI95% 1.195-12.169)). This means that patients who undergo incomplete chemotherapy cycles (<12 cycles) have a mortality risk of 3,883 times compared to patients who undergo complete chemotherapy cycles (12 cycles). For patients using the FOLFIRI regimen, all of these factors did not show significantly different HR values.

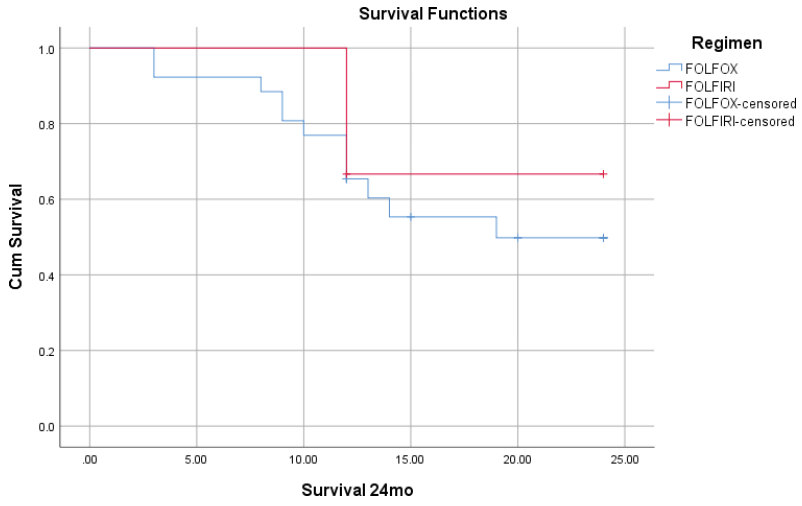

Figure 3. 2-year survival of advanced stage colorectal cancer patients (N=29)

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Table 2. Survival Rate Results from Kaplan Meier Analysis

Time (year)	*Survival Rate*		*Survival Time*				
	FOLFOX (%)	FOLFIRI (%)	FOLFOX(month)		FOLFIRI (month)		*p-value*
			Mean ± SD	*Median*	*Mean ± SD*	*Median*	
2	51,9	58,3	16,828±1,51	19,00	18,16±2,01	n/a	0,956
Overall	44,4	58,3	26,623±3,77	19,00	21,66±2,85	n/a	0,904
Advanced Stage							
2	53,8	66,7	17,359±1,47	19,00	20,00±3,26	n/a	0,691

Information:
Mean = the average estimated patient survival time; Median = survival time for 50% of patients who died; n/a = *not available*

Table 3. Analysis Table of Factors Influencing Survival

FACTOR	Survival					
		FOLFOX			FOLFIRI	
	p-value	HR	95%CI	*p-value*	HR	95%CI
Sex	0,541	0,672	0,188-2,405	0,968	0,0009	0,00-2,220
Age	0,378	1,852	0,471-7,279	0,798	0,0009	0,00-1,223
Stage	0,146	6,989	0,508-96,129	0,861	0,001	0,00-1,156
Metastases	0,145	2,709	0,708-10,367	0,993	0,087	0,00-5,343
Comorbid	0,198	2,440	0,627-9,488	0,986	0,007	0,00-1,887
Chemotherapy Status	0,024	3,883	1,195-12,619	0,784	0,0009	0,00-3,711

Data of the side effect is shown in Table 4, showing that the frequency of side effects in patients receiving FOLFIRI was higher than in patients receiving FOLFOX. The side effects that often occur, seen from the percentage of consecutive events, were malaise (67%), nausea-vomiting (50%), stomach pain (42%), diarrhea (42%) and decreased appetite (17%) when used. FOLFIRI. The FOLFOX regimen had side effects that often occur, which were malaise (48%), nausea-vomiting (44%), decreased appetite (30%), abdominal pain (22%), diarrhea (11%) and joint pain (15%). The side effects of decreased appetite and joint pain when using FOLFOX showed a higher frequency than FOLFIRI. The FOLFIRI chemotherapy regimen had a mean delay due to side effects of around 10.50 ± 1.71 days and FOLFOX around 9.8 ± 3.83 days. This is related to delaying chemotherapy which can affect the progression of the patient's cancer as well as the patient's acceptance of chemotherapy.

DISCUSSION

The chemotherapy regimen analysis study was conducted on 39 patients who met the inclusion criteria for colorectal cancer who received their first chemotherapy regimen. The study was conducted on patients at the Integrated Oncology Installation (IOT) at Universitas Airlangga Hospital, Surabaya. The group of patients who received FOLFOX totaled 27 patients and 12 patients in the FOLFIRI group. The sample distribution for comorbid colorectal cancer patients did not show any differences between regimens ($p > 0.05$). Meanwhile, stage and metastases showed significant differences between regimens. This was because most of the patients in the FOLFOX group were at an advanced stage and those in the FOLFIRI group were at an early stage. The sample distribution in this study did not meet the number of samples/patients for further statistical analysis in the early stages, so survival analysis was determined only for patients in the advanced stage group. According to the National Formulary (FORNAS) policy, there were restrictions on oxaliplatin (FOLFOX) and irinotecan (FOLFIRI) regarding the administration of colorectal cancer chemotherapy. Oxaliplatin administration could be accepted by patients with stage III metastases with 12 administrations while irinotecan was given to colorectal cancer patients (Ministry of Health, 2021). The administration of irinotecan did not explain the limitations of the patient's stage so that irinotecan could be given to colorectal cancer patients without metastases. Colorectal cancer patients who received the FOLFOX regimen were mostly given to advanced stage patients and the FOLFIRI regimen to early-stage patients. These factors were limitations of study on colorectal cancer patients at Universitas Airlangga Hospital.

Based on the Kaplan Meier analysis (shown in Table 2), the percentage of two-year survival in colorectal cancer patients with the FOLFOX regimen was 51.9% and the average survival time was 16.8 ± 1.51 months. Meanwhile, patients who received the FOLFIRI regimen had a survival percentage of 58.3% with a mean survival time of 18.2 ± 2.01 months ($p > 0.05$). Based on these data, it shows that FOLFIRI had a tendency for a longer survival time than FOLFOX, but this was not statistically significant. Due to sample limitations in FOLFIRI, Kaplan Meier analysis in early-stage patients could not be performed, so a follow-up two-year survival analysis was performed in advanced-stage colorectal cancer patients (listed

Table 4. Incidence of Side Effects of Chemotherapy while Colorectal Cancer Patients Live

Side Effect	Chemotherapy		Information
	FOLFOX	FOLFIRI	Average Delay Time
Malaise	48%	67%	
Nausea-Vomiting	44%	50%	**FOLFOX** Mean 9.80 days ± 1.71 Range 7-14 days **FOLFIRI** Mean 10,50 days ± 3,83 Range 7-14 days
Diarrhea	11%	42%	
Stomach Pain	22%	42%	
Anemia	21%	33%	
Neutropenia	21%	25%	
Decreased Appetite	30%	17%	
Joint pain	15%	8%	

in Table 5.2 and Figure 5.4). The survival percentage results for patients with advanced colorectal cancer on the FOLFOX regimen were 53.8% and FOLFIRI 66.7% (p > 0.05). Meanwhile, the average two-year survival time in advanced stage patients on the FOLFOX regimen reached 17.35 ± 1.47 months and FOLFIRI reached 20.00 ± 3.26 months. The results of the analysis regarding survival illustrate that if the percentage of survival was lower, the average survival time was also lower, followed by a high incidence of patient mortality. Survival analysis showed a median of 50% of patients who received FOLFOX died at month 19. In the group of patients who received FOLFIRI, 50% of patients were still alive, so the median value could not be assessed. The results of statistical analysis regarding the survival of patients who received FOLFOX and FOLFIRI in this study did not show significantly different results, in accordance with the study reported by Ikoma et al which concluded that the effectiveness of the FOLFOX and FOLFIRI regimens was equally effective as first-line colorectal cancer therapy.[6] In the 2005-2014 study, the survival of patients receiving FOLFOX was comparable to that of FOLFIRI, with a mean overall survival of 19.1 months versus 20.5 months (p > 0.05).[16] In the GERCOR (Oncology Multidisciplinary Study Group) study, 230 patients with advanced colorectal cancer were compared. The results of the analysis showed no significant difference between the FOLFIRI-first-line and FOLFOX-first-line groups with median overall survival (21.5 vs. 20.6 months, p=0.99).[24] Hence, the results of this study have shown the same results as studies that have been conducted previously.

After the Kaplan Meier analysis, a Cox regression analysis was carried out to determine the factors that influence the survival of colorectal cancer patients. The results of the analysis between the factors that influence the survival of those receiving FOLFOX (listed in Table 5.3) showed that there was a significant influence (p<0.05) on chemotherapy status (HR 3.883 (CI95% 1.195-12.169)). This means that patients who undergone incomplete chemotherapy cycles (<12 cycles) have a mortality risk of 3,883 times compared to patients who undergone complete chemotherapy (12 cycles). The average number of patients who received incomplete chemotherapy cycles was 5.26 times. The results of analysis of other factors that influence survival in the FOLFOX group did not show any influence (p > 0.05), including: gender, age, stage, metastases and comorbidities. The results of the analysis of factors that influence FOLFIRI also did not show significant results for any factor (p > 0.05). The results of this study show the same results as other study. According to Tsai et al's study, chemotherapy status showed the completeness of the number of cycles the patient has undergone. The number of cycles a patient undergone had a significant effect on survival of the patient (p <0.050) because it was a significant prognostic factor in stage III colon cancer patients. FOLFOX requires at least 8 cycles to have an effect on overall survival.[24]

The results of analysis of other factors on FOLFOX did not show any influence on survival (p > 0.05), including: gender, age, stage, metastases and comorbidities. Analysis of factors influencing survival on FOLFIRI also did not show significant results for any factor (p > 0.05). This study shows that gender does not affect patient survival in accordance with existing study. The results of this study are in accordance with studies regarding the relationship between gender and the survival of colorectal cancer patients which states that the survival of women and men has the same results.[28]

The results of the next influencing factors that does not affect survival were age and disease. In this study, the disease suffered by the patient was only recorded in the anamnesis in the medical record, so it was not known about the relevant routine examinations carried out by the patient. This is one of the reasons that comorbidity was a factor that did not have a significant effect in this study. This is not in accordance with Van Eghen's study which showed that age and disease were important factors that influence the survival of colon cancer patients. However, this study also stated that in rectal cancer patients, age and comorbidities did not significantly influence survival (p > 0.05).[26] According to Jeo and Subrata, the survival rate for colorectal cancer patients aged ≥45 years reached 50% at 20 months of observation (95% CI 44.03-57.32). Based on the analysis, patients aged <45 years showed better five-year survival (47.4% vs 41.3%).[8] Based on comparisons with other studies, prospective study was recommended so that comorbid factors had a clearer influence on survival.

Apart from age and comorbidities, the results of this study indicated that stage and metastases were not factors that influence survival due to the limited number of study samples/

patients. The results of this study were not in accordance with previous studies which explained that metastases are related to patient survival.[25,27] According to Van Cutsem et al, patients with stage I and II colorectal cancer had the 5-year survival rate reached 93%, whereas it decreased to 60%, 42% and 25% for patients with stages IIIA, IIIB and IIIC, respectively. In the majority of patients with stage IV metastatic colorectal cancer the survival rate decreased to <10%.25 According to Wang et al, metastases in the liver and lungs showed a better survival rate than metastases that occured in the brain and bones because metastases in the brain affect the nervous system and metastases in the bones would accelerate the decline in bone mineral density (BMD) which could affect the quality of the patient survival (HR 0.82, 95%CI 0.71-0.94).[27]

Beside the factors above, the occurrence of side effects is an important factor that influences the survival of colorectal cancer patients. The limited number of samples in this study was the reason that further statistical analysis could not be carried out, so the data was only processed descriptively to see the average and range of days of delay in chemotherapy for colorectal cancer patients who received FOLFOX and FOLFIRI chemotherapy. The most frequent side effects seen from the percentage of incidence (listed in Table 2) were malaise (67%) after using the FOLFIRI regimen followed by: nausea-vomiting (50%), stomach cramps (42%), diarrhea (42%) and decreased appetite (17%). When using the FOLFOX regimen, side effects are almost the same as the FOLFIRI regimen, respectively: malaise (48%), nausea-vomiting (44%), decreased appetite (30%), abdominal discomfort (22%), diarrhea (11 %) and joint pain (15%). The results of this study showed that patients using FOLFOX experienced a better risk of side effects than using FOLFIRI. These factors will influence clinician preferences regarding the selection and administration of therapy. The highest frequency of FOLFIRI side effects was malaise, this result is in accordance with existing studies, which was a cross-sectional study regarding the side effects of colorectal cancer chemotherapy conducted at Margono Soekarjo Hospital, Purwokerto, Central Java. The results of Wiratama et al's study concluded that of 32 colorectal cancer patients (30-60 years) who underwent at least 3 cycles experienced similar side effects, the results of statistical analysis showed that FOLFIRI caused malaise more often than FOLFOX ($p<0.05$). In fact, in general, both regimens often cause gastrointestinal side effects including nausea, decreased appetite and stomach ache.[7] However, the results of other studies reported that neuropathy side effects often occurred when using FOLFOX (oxaliplatin), while neutropenia and diarrhea occurred when using FOLFIRI (irinotekan).[5] Post-chemotherapy side effects were one of the factors in delaying or stopping chemotherapy received by patients which would have an impact on disease progression.

The delaying which was due to side effects, occurred in this study. The FOLFOX regimen had a shorter delay time due to side effects, namely 9.80 ± 1.71 days compared to the FOLFIRI regimen, namely a mean delay time of around 10.50 ± 3.83 days. According to study conducted by Kogan, 43% of patients experienced at least one unplanned delay before completing 6 cycles. Delaying chemotherapy could reduce chemotherapy dose intensity, increase hospital visits and increase costs incurred by patients.[11] Delaying chemotherapy will also reduce patient survival.[24] The results of this study showed that FOLFOX had a lower incidence of side effects with a shorter average delay than FOLFIRI but both regimens still give the same side effects to patients, so monitoring and vigilance by pharmacists was needed regarding this ESO event.

In relation to drug problems, oxaliplatin is a platinum group cytostatic which can cause impaired sense of taste, decreased appetite and malnutrition which ultimately will affect the patient's quality of life because it is associated with impaired regulation of T1R2 expression in experimental animal studies.[17] For joint pain, oxaliplatin triggers the accumulation of platinum compounds in dorsal root ganglia cells, causing mitochondrial atrophy and dysfunction.[2] Oxaliplatin also triggers neurotoxicity in patients due to disruption of ion channel activity and increased sensitivity of TRP channels in sensory neurons.[9]

Meanwhile, for the side effects of neutropenia and diarrhea, the irinotecan contained in FOLFIRI had a working mechanism of stimulating the formation of the active metabolite SN-38 through the action of hydrolysis by carboxylesterase. In addition, this activity is triggered by UDP-glucanosyltransferases which inactivate SN-38 into the SN-38G form[12,4] (; Shao et al., 2016). Irinotecan causes severe colonic damage due to increased apoptosis, hypoplasia, colonic dilation and excessive mucus secretion due to chemotherapy. Increased cell apoptosis along with histopathological changes in the jejunum and colon, changes in the number of goblet cells can cause changes in absorption rates and trigger diarrhea.[21] Results from several studies showed that FOLFOX had a lower incidence of side effects than the FOLFIRI regimen so that this regimen was more recommended in colorectal cancer therapy.

Study regarding the effectiveness between FOLFOX and FOLFIRI regimens was discussed by several studies. According to Neugut, both combination therapy regimens provided similar survival times and quality of life, but FOLFOX provided a much lower cost per life year for colorectal cancer patients.[16] Study on pharmacokinetics/pharmacodynamics (PK/PD) in the treatment of colorectal cancer patients using oxaliplatin and irinotecan concluded that patient responses were similar between oxaliplatin and irinotecan therapy with regard to survival (HR = 1.05, 95%CI [0.97;1 .15]) and objective response rate (OR = 1.15, 95%CI [1.00;1.32]).[30] Based on comparisons with several studies, the use of FOLFOX and FOLFIRI had similar effectiveness, but FOLFOX had lower costs and a better incidence of side effects than FOLFIRI.

CONCLUSION

The results of study analyzing chemotherapy regimens on the survival rate of colorectal cancer patients can be concluded that the percentage of two-year survival in colorectal cancer patients with the FOLFOX regimen was 51.9% with a mean survival time of 16.8 ± 1.51 months and FOLFIRI regimen 58.3% and 18.2 ± 2.01 months. Colorectal cancer patients who received an incomplete regimen of FOLFOX (<12 cycles) had a

3.8-fold risk of mortality compared to patients who received a complete cycle (12 cycles). Patients who take FOLFOX have a lower risk of adverse effects than those who take FOLFIRI, which may influence clinician preferences. The FOLFOX regimen is recommended for colorectal cancer treatment, especially in early and advanced stages, due to potential adverse effects.

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