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Review

The Impact of Age at Diagnosis and Tumor Location on Overall Survival Rates in Colon Cancer

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Abstract

Objectives: Colorectal cancer (CRC) is one of the most common cancers worldwide, with different survival rates. In this study, we aimed to investigate the impact of age at diagnosis and tumor site among treated and untreated subjects diagnosed with CRC on overall survival rates.

Methods: Data were obtained from open data sources (cBioPortal). Comprising 364 anonymized samples diagnosed with CRC (colon adenocarcinoma), we included patients with available data for the age of diagnosis, treatment regimen, site of tumor, and overall survival. The survival analysis was performed using the Kaplan-Meier method, and the difference in survival was analyzed with a log-rank test.

Results: A total of 364 anonymized samples diagnosed with colorectal cancer (CRC, specifically colon adenocarcinoma) were included in the analysis. The results showed no significant dominance of sex in the study population. According to the site of the tumor, the most common sites for colon cancer were in the sigmoid and rectosigmoid colon, representing 36% of the cases, with a survival rate of 67% and 86% for treated and untreated groups, respectively. The least sites were hepatic flexure & splenic flexure at 12.6% with survival rates of 78% and 86% for treated and untreated groups, respectively. In addition, results showed a better survival rate in the older age group (67-100), representing 54.4% of the cases, with a survival rate of 75% and 80% for treated and untreated groups, respectively. The other age group (0-66), representing 45.6% of cases, had lower survival rates of 60% and 85% for treated and untreated groups, respectively.

Conclusion: The current study showed that right-sided colorectal cancer is more aggressive with lower survival rates compared to left-sided colorectal cancer, and the age of diagnosis in CRC is proportionally related to survival rates. The site of the tumor and age of diagnosis might be important factors in the survival rates of the CRC, which can be supported by other research on different population groups.

1. Introduction

Colorectal cancer (CRC), defined as abnormal growth of cells that begin in a part of the colon and rectum, which in 2020 globally considered the second leading cause of death due to cancer in both genders with 1,000,000 deaths per year. CRC holds third place in new cancer diagnoses worldwide, with more than 1.8 million new cases in 2020 [1,2].

CRC is more common in men than women, and about 3-4 times more among developed than in developing nations [3]. Therefore, colorectal cancer is a major health problem that requires a better understanding and manifestations of both its root causes and possible remedies. A constellation of different factors, including but not limited to age, gender, diet, smoking, family history of CRC or colon polyps, and genetic mutations, is believed to increase the risk for CRC and affect its prognosis [3-5]. Furthermore, the timing of the diagnosis and the site of the tumor in colorectal cancer are exceptionally significant concerns that are well documented in the literature.

Generally, the incidence of CRC increases with the elderly, where more than 40% occur in patients above 70 years old and 44% found in patients 70 years and older [4]. Okamato et al (2002) reported that right-sided colorectal cancer increases with age, specifically adenocarcinoma. Also, the number of concomitant adenomas significantly increases with increasing age, as well as the location of CRC progressively to the right side [5]. Right-sided (cecum to the transverse colon, excluding the appendix) colon cancer is more aggressive than left-sided (splenic flexure to sigmoid, excluding rectum) as a result of unclear causes, but it may be due to biological and environmental factors [6]. Notably, colon cancer patients with comorbidities consulted their general practitioner more frequently with cancer symptoms in the year before their diagnosis compared to non-comorbid patients [7]. For patients under 75 years old, the presence of comorbidities influenced the likelihood of receiving treatment. Furthermore, patients aged 75 and older were less likely to receive treatments such as resection for a cure, adjuvant chemotherapy for Stage III colon cancer, palliative chemotherapy for advanced colorectal cancer, or radiotherapy for rectal cancer, regardless of their comorbidity status [8]. However, a recent study found that hypertension and diabetes were associated with adult-onset CRC who were older than 50 years [9].

The current study aimed to explore the impact of age and the site of the tumor on the overall survival and prognosis of patients who are diagnosed with colorectal cancer. This may help in the development of more effective treatment strategies to improve patient outcomes and overall survival rates.

2. Methodology

This retrospective cohort study utilized open-source clinical data from cBioPortal, comprising 364 anonymized cases of colon adenocarcinoma. Inclusion criteria were the availability of data on age at diagnosis, tumor site, treatment status, and overall survival in months. Cases with missing variables were excluded. Overall survival (OS) was defined as the time from diagnosis to death from any cause or last follow-up, according to the cBioPortal definition.

Patients were stratified by age group (0-66 vs 67-100 years), tumor site (cecum, ascending/transverse/descending colon, hepatic & splenic flexures, sigmoid & rectosigmoid colon), and treatment status (treated vs untreated). Survival analysis was performed using the Kaplan-Meier method, with differences compared via the log-rank test. Statistical significance was set at $p < 0.05$. Survival analysis adopted the time of diagnosis in months for all tested parameters.

3. Result

The current retrospective study included 364 anonymized samples diagnosed with colon cancer (Adenocarcinoma). Tables 1, 2, and 3 summarize the clinicopathological data of the study population in detail, where the median age was 66 years, 198 (54.4%) were aged 67-100 years, and 166 (45.6%) were 0-66 years. There was no significant sex dominance in the study population, where females accounted for 52.2% of the sample. According to the site of the tumor, the sigmoid and rectosigmoid regions were the most frequent tumor sites (36%), while hepatic and splenic flexures were the least common (12.6%), Figure 1. Treatment distribution showed that 72.8% of patients received no treatment, while 27.2% received systemic chemotherapy, platinum-based therapy, or a targeted regimen.

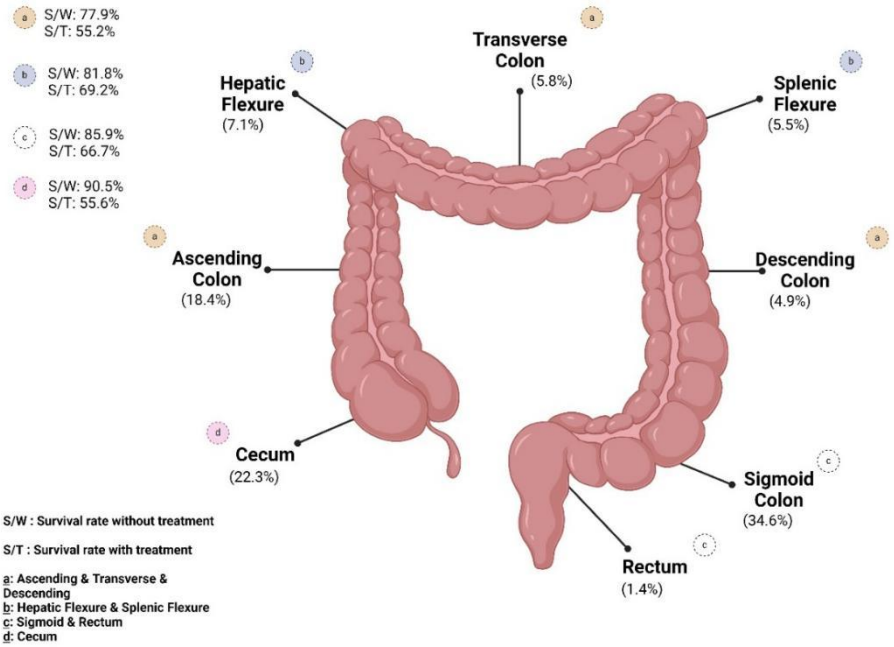

Figure 1. Demonstration of the tumor sites and survival rates of treated and untreated CRC patients.

Table 1. Describes the frequency & percentage of the variables for 364 samples with colon cancer.

Variables		Frequency	Percent %
Gender	Female	190	52.2
	Male	174	47.8
Age	0 - 66	166	45.6
	67 - 100	198	54.4
Tumor Site	Cecum	81	22.3
	Ascending & Transverse & Descending Colon	106	29.1
	Hepatic Flexure & Splenic Flexure	46	12.6
	Sigmoid & Recto sigmoid Colon	131	36.0
Adjuvant Treatment	No Treatment	265	72.8
	Systemic Chemotherapy	40	11.0
	Chemotherapy Incl. Platinum	40	11.0
	Targeted Chemo Mab, Chemotherapy Incl. Platinum	8	2.2
	Chemotherapy Incl. Platinum, Systemic Chemotherapy	3	0.8
	Chemotherapy Nano	5	1.4
	*Other	3	0.8

* Those 3 adjuvant treatments are (Chemotherapy Incl. Platinum, Targeted Chemo Mab, Systemic Chemotherapy, and Radiotherapy & Chemotherapy with Levamisole/Leucovorin/Ledervorin)

Table 2 describes the clinical and pathological data of the CRC patients who are not treated. The data showed no significant difference in the survival rates between age groups, tumor sites, and gender. However, there was a tendency towards better survival in young CRC patients.

Table 3 describes the clinical and pathological data of the CRC patients who are under treatment. The data showed no significant difference in the survival rates between age groups, tumor sites, and gender. Interestingly, the results showed a tendency towards better survival in old CRC patients.

Table 2. Illustrates an analysis of variables in colon cancer cases that didn't receive treatment.

				Censored		
Variables	**Clinicopathological data**	**Total (n)**	**Event (n)**	**n**	**Percent**	***P*-value**
Age of diagnosis	0 - 66	104	11	93	89.4%	0.114
	67 - 100	161	31	130	80.7%	
	Overall	**265**	**42**	**223**	**84.2%**	
Tumor Site	Cecum	63	6	57	90.5%	0.242
	Ascending & Transverse & Descending Colon	77	17	60	77.9%	
	Hepatic Flexure & Splenic Flexure	33	6	27	81.8%	
	Sigmoid & Recto sigmoid Colon	92	13	79	85.9%	
	Overall	**265**	**42**	**223**	**84.2%**	
Gender	Female	144	26	118	81.9%	0.417
	Male	121	16	105	86.8%	
	Overall	**265**	**42**	**223**	**84.2%**	

Table 3. Illustrates analysis of variables with colon cancer cases who received different types of treatment.

				Censored		
Variables	**Clinicopathological data**	**Total (n)**	**Event (n)**	**n**	**Percent**	***P*-value**
Age of diagnosis	0 - 66	62	28	34	54.8%	0.064
	67 - 100	37	10	27	73.0%	
	Overall	**99**	**38**	**61**	**61.6%**	
Site of Tumor	Cecum	18	8	10	55.6%	0.603
	Ascending & Transverse & Descending Colon	29	13	16	55.2%	
	Hepatic Flexure	13	4	9	69.2%	
	Sigmoid & Recto sigmoid Colon	39	13	26	66.7%	
	Overall	**99**	**38**	**61**	**61.6%**	
Gender	Female	46	17	29	63.0%	0.760
	Male	53	21	32	60.4%	
	Overall	**99**	**38**	**61**	**61.6%**	

As observed in Table 4, which summarizes the Log-Rank values for the analyzed variables, the Kaplan–Meier analysis demonstrated that treatment significantly improved overall survival (*P*-value < 0.001; Figure 2). For untreated patients, neither age (*P*-value = 0.114; Figure 3) nor tumor site (*P*-value = 0.242; Figure 4) showed statistically significant differences in overall survival. Among treated patients, survival trends favored older individuals (*P*-value = 0.064; Figure 5) and left-sided tumors (*P*-value = 0.603; Figure 6), though both results lacked statistical significance.

Table 4. Represents the Log-Rank values in this study for the variables that received treatment, the variables that didn't receive treatment, and the comparison between their *P*-values.

Sig (*P*-Value)							
	[a]With Treatment Compared to Without Treatment	**[b]Without Treatment**			**[c]With Treatment**		
		Age of Diagnosis	Site of Tumor	Gender	Age of Diagnosis	Site of Tumor	Gender
Log Rank	**0.001**	0.114	0.242	0.417	0.064	0.603	0.760

(a) In this section is the *P*-value for the sample that received treatment vs the sample that didn't receive treatment so we can see the impact of treatment on overall survival. (b) In this section is the *P*-value for a sample that didn't receive treatment is shown, showing the impact of age of diagnosis, site of tumor, and Gender on overall survival for those who didn't receive treatment. (c) In this section is the *P*-value for a sample that received treatment is shown, showing the impact of age of diagnosis, site of tumor, and gender on overall survival for those who received treatment.

The impact of treatment on the overall survival rates is shown in Figure 2, which shows how different types of treatment have different impacts on survival rates. By separating them into two categories, one who received treatment and the other who didn't receive any treatment, we calculated the Log-Rank value for the age of diagnosis & site of tumor separately to remove the impact of treatment on our variables.

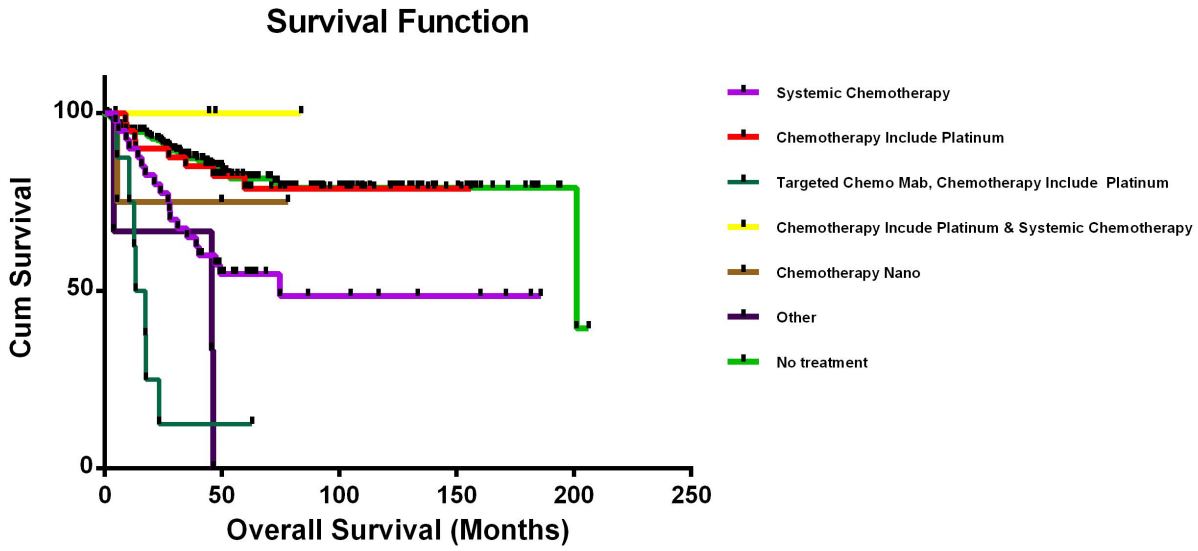

Figure 2. Represents the Kaplan-Meier curve for the impact of different treatments on the survival probability. **(0)** No Treatment (1) Systemic Chemotherapy (2) Chemotherapy Incl. Platinum (3) Targeted Chemo Mab, Chemotherapy Incl. Platinum (4) Chemotherapy Incl. Platinum, Systemic Chemotherapy (5) Chemotherapy Nano (6) Other**: Those 3 adjuvant treatments are (Chemotherapy Incl. Platinum, Targeted Chemo Mab, Systemic Chemotherapy & Radiotherapy & Chemotherapy with Levamisole/Leucovorin/Ledervorin)

The current findings reported a lack of significant impact of age of diagnosis on the overall survival rates in the treated and non-treated groups. In particular, the *P*-value was 0.114 for those who didn't receive any treatment, as shown in Figure 3, which represents the Kaplan-Meier survival analysis according to the age of diagnosis for the sample who didn't receive treatment. On the other hand, the *P*-value for those who received different types of treatment was 0.064, showing a tendency for statistical difference in survival rate as shown in Figure 5, which represents the Kaplan-Meier survival analysis according to the age of diagnosis for samples who received treatment.

Similarly, the *P*-value for the site of the tumor for those who didn't receive any treatment was 0.242, and the survival rate was not statistically different, as shown in Figure 4, which represents the Kaplan-Meier survival analysis according to the site of the tumor for samples that didn't receive treatment. In comparison, the *P*-value for the site of the tumor for those who received different types of treatment was 0.603, and there was no statistical difference in survival rate, as shown in Figure 6, which represents the Kaplan-Meier survival analysis according to the site of the tumor for samples that received treatment.

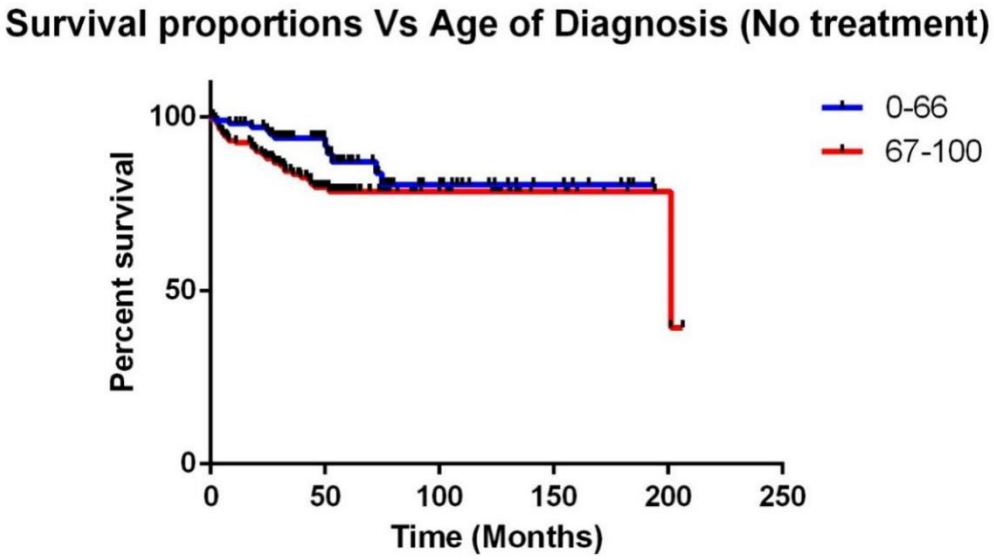

Figure 3. Represents the Kaplan-Meier curve for the impact of age at diagnosis on the survival probability for samples that didn't receive treatment. (1) 0-66 Years (2) 67-100 years with a *P*-value = 0.114.

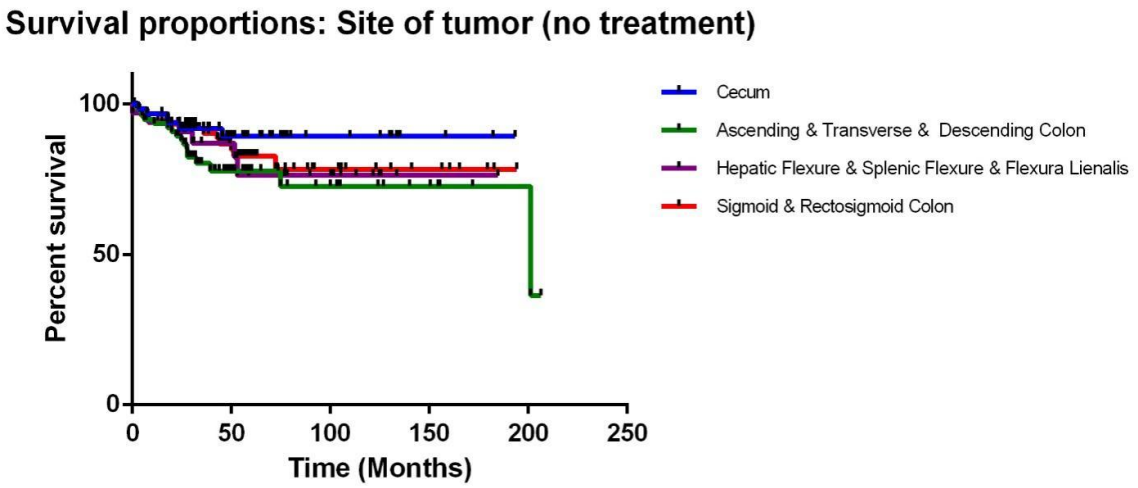

Figure 4. Represents the Kaplan-Meier curve for the impact of the site of the tumor on the survival probability for samples that didn't receive treatment. (1) Cecum (2) Ascending & Transverse & Descending Colon (3) Hepatic Flexure & Splenic Flexure (4) Sigmoid & Rectosigmoid Colon with a *P*-value = 0.242.

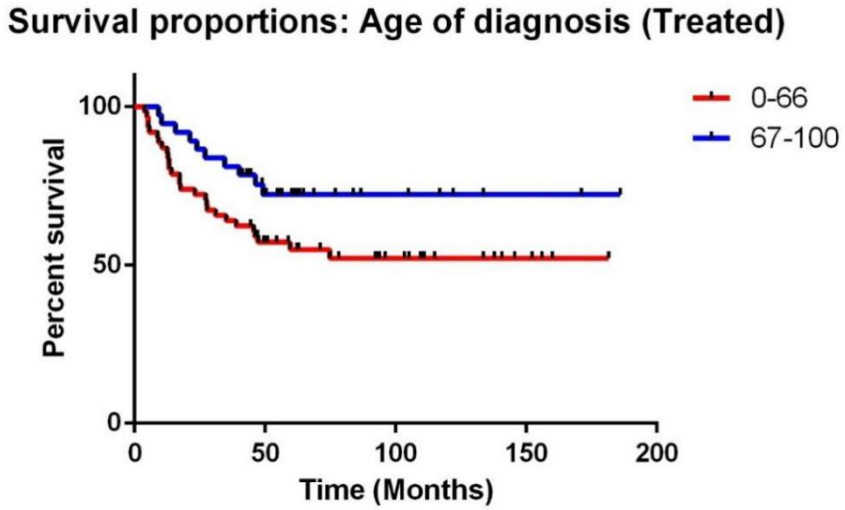

Figure 5. Represents the Kaplan-Meier curve for the impact of age at diagnosis on the survival probability for samples that received treatment. (1) 0-66 Years (2) 67-100 years with a *P*-value = 0.064.

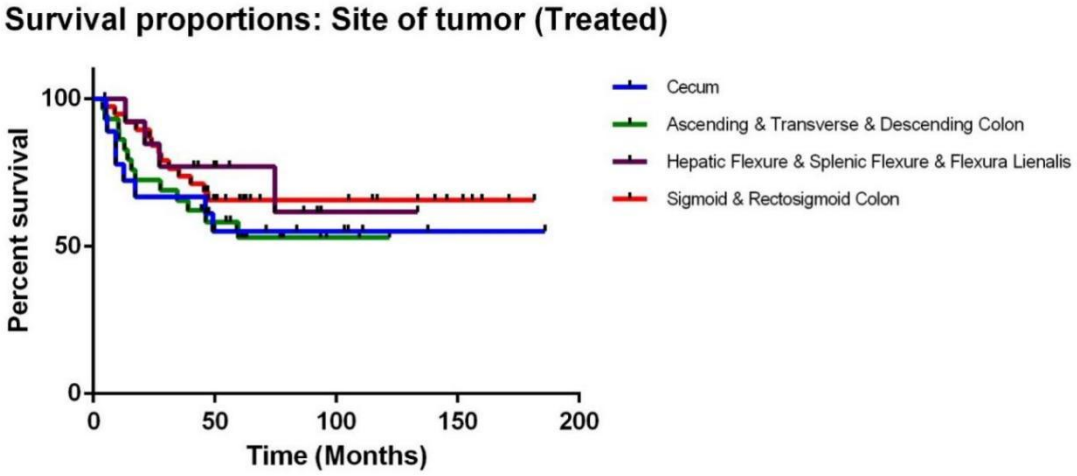

Figure 6. Represents the Kaplan-Meier curve for the impact of the site of the tumor on the survival probability for samples that received treatment. (1) Cecum (2) Ascending & Transverse & Descending Colon (3) Hepatic Flexure & Splenic Flexure (4) Sigmoid & Rectosigmoid Colon with a *P*-value = 0.603.

Overall, older patients (67-100 years) exhibited a slightly better overall survival rate (73%) compared to younger patients (55%) in the treated cohort, possibly due to differences in treatment response or disease biology. Tumor laterality reveals the expected pattern that right-sided tumors had lower survival, but without statistical significance. These findings reveal that treatment is the strongest determinant of overall survival in this dataset.

4. Discussion

Several studies have evaluated survival in patients with colorectal cancer, with conflicting findings concerning the impact that age at diagnosis has on survival [10]. In this study, we compared individuals who were diagnosed with CRC at ages between 0-66 and 67-100, in which both groups were divided into two subgroups according to whether they received anti-cancer treatment versus the untreated group.

Our results showed that the overall survival rate for both age groups of the untreated group was not statistically different, and the survival rate was 85% for 50 months for the 0-66 years old age group, while the 67-100 age group had a survival rate of 80% at the same period. On the other hand, the results of the treated group showed a better overall survival rate for older-treated individuals (67-100 years) (75% at 50 months) compared to the younger-treated individuals (0-66 years) (60% at 50 months). Our results are consistent with previous reports that revealed an association between the age of diagnosis of treated patients and survival rates [11,12]. However, Onyoh EF et al found that the mortality rate was higher in elderly patients [13], which is also found in other reports [14]. Otherwise, Wan Ibrahim et al found that there was no association between the survival rate and the age of CRC patients [15]. However, there is an increased incidence of CRC at young ages, especially among patients less than 50 years [16,17]. This led us to increase screening for those patients with a high risk of developing CRC [17]. The contradictory findings can be attributed to the type of anti-tumor treatment, ethnic origin, race differences, genetic predispositions, and environmental factors. Therefore, a comprehensive analysis of the age impact on the survival rates in CRC patients can offer a clear answer, for instance, meta-analyses studies would be a very helpful tool.

Moreover, according to our findings, the tumor site is another factor that showed a difference in the patient's survival. The current results support previous studies that revealed that the most common site of the tumor in colorectal cancer is the sigmoid & rectosigmoid colon, followed by ascending & transverse & descending colon, cecum, and the least common hepatic flexure & splenic flexure [18,19]. The results of this study showed that the overall survival rate, according to the tumor site in the treated individuals, was not statistically significant, though trends were observed. In particular, the hepatic flexure & splenic flexure sites showed better survival rates (78% at 50 months), followed by the sigmoid & rectosigmoid colon (67% at 50 months), cecum (60% at 50 months), and the lowest was for the ascending & transverse & descending colon (59% at 50 months). These findings support the results of a previous study in Japan that testified to lower survival rates of right-sided tumors compared to left-sided tumors in individuals older than 40 years individuals [20].

On the other hand, interestingly, the untreated group showed an inverse relationship in the survival rates according to the site of the tumor. The cecum site showed the best survival rate (90% at 50 months), followed by the sigmoid & rectosigmoid colon and hepatic flexure & splenic flexure (~ 86% at 50 months), and the lowest rate of survival was in ascending & transverse & descending colon tumors (78% at 50 months). Consistently, patients with a right-sided primary have more negative prognostic factors and have inferior outcomes compared with those with left-sided tumors, regardless of the CRC stage [21-24]. Also, Loupakis F et al found that metastatic left-sided CRC had significantly higher overall survival (OS) and progression-free survival (PFS) than metastatic right-sided CRC [25] with a mean of survival of 34 and 15.5 months in left and right-sided CRC patients, respectively [26]. Nevertheless, a meta-analysis that included 1,437,846 colon cancer patients found that left-sided tumor was significantly associated with a lower mortality rate compared to right-sided locations [27]. For instance, in 2019, the researchers concluded that patients with RCC (right colorectal cancer) had a significantly worse 1-year relative survival of 40% compared with more than 50% for patients with LCC (left colorectal cancer) and rectal [21]. Although Odeny TA et al found that overall survival was 77.3% and 64.4% in patients with LCC and RCC, respectively, this was not statistically significant [28]. Also, this was consistent with Snyder et al findings with no significant correlation between site and OS [29]. Accordingly, this can make some differences in the first-line treatment of CRC according to the tumor's right or left location [29-31]. For example, using anti-EGFR monoclonal antibody (MAB) therapy was found to improve significantly OS and PFS for left-sided CRC tumors, but not significantly for right-sided CRC [32].

Chemotherapy showed a dramatic enhancement of the quality of Life (QOL) compared to a placebo or patients with observation without chemotherapy [33]. Furthermore, chemotherapy can increase CRC patients' overall survival (OS) and disease-free survival (DFS), especially in patients with stage two and all types of stage three CRC [34]. Moreover, systemic chemotherapy can increase OS and QOL in patients with stage four CRC who have metastasis [35]. Otherwise, not having chemotherapy was considered a negative prognostic factor in patients with CRC [24]. Nevertheless, according to the data of the studied population, the survival rates showed intriguing variations of survival rates between the untreated and different treatment regimens. For instance, the best survival rate reported in the chemotherapy arm included platinum (like oxaliplatin) and systemic chemotherapy. While the lowest survival was reported in the targeted chemo Mab and chemotherapy, which included the platinum arm. In addition, the untreated group shared the same survival rate as chemotherapy, including the platinum arm, where

both showed better survival than the systemic chemotherapy arm.

In a Croatian study that included 483 patients with stages II and III CRC, the survival over 5 years was better among stage III patients and younger patients. However, there was no difference in survival according to the tumor location, whether having chemotherapy and without chemotherapy [34]. Moreover, treatment with systemic chemotherapy "leucovorin (LV)/5-Fluorouracil (5FU)" can improve survival, decrease recurrence, and metastasis in both CRC stages II and III [34]. Also, Hotta T. et. al. found that LV/5FU can improve the DFS in stage three patients, but no difference in the OS among patients treated with chemotherapy and not [36]. Although systemic chemotherapy was considered the backbone in the treatment of CRC patients [37]. The usage of biological (Mab) chemo combined with systemic chemotherapy proved to improve OS, QoL, and response in CRC patients [38]. Accordingly, Bevacizumab in addition to triple chemotherapy (LV, 5FU, oxaliplatin, and irinotecan "FOLFOXIRI"), was found to improve OS and DFS compared to Bevacizumab with double chemotherapy (LV, 5FU, and irinotecan "FOLFIRI" or LV, 5FU, and oxaliplatin "FOLFOX") in patients with metastatic CRC [39]. However, the introduction of immunotherapy started to change the pattern of CRC treatment [40]. Consequently, immunotherapy and targeted therapy were found to have the most advantageous role in improving the QOL in CRC patients in comparison to chemotherapy and targeted therapy or patients without treatment [33]. These continuous developments in lines of CRC treatments and guidelines make it hard for physicians to decide the appropriate treatment for CRC patients [40].

The limitations for this study include the retrospective nature of the dataset we used, small subgroup sizes, especially for certain tumor locations, lack of detailed treatment data like dosage & timing, and absence of molecular profiles. Future research should categorize colorectal cancer survival by other variables like therapeutic strategies and genomic markers, to better understand these interactions.

5. Conclusion

This study identified that despite treatment, significant improvement in overall survival, but neither tumor site nor age at diagnosis independently reached statistical significance as predictors of overall survival. Trends indicated slightly better survival among older treated patients and among those with left-sided tumors. These findings reveal the multifactorial nature of colorectal cancer prognosis and focus attention on the need for large-scale studies including molecular and therapeutic data to refine survival prediction and optimize treatment planning.

Authors Contribution

MAZ: Conceptualization, drafting, editing, data analysis, supervision, and approval of the final version. **QUS**: Conceptualization, drafting, editing, data analysis. **NAD**: Conceptualization, data modification, methodology section. **SAR**: Result, discussion, conclusion section. **ZAY**: Introduction, discussion, conclusion section. **AYA**: Abstract, discussion, conclusion section. **MAR**: Literature review. **SM**: editing, drafting, Literature review. **NEE**: Literature review. **AK**: Editing, Drafting, Literature review, data modification, discussion, and conclusion sections. **RMZ**: Conceptualization, drafting, editing, data analysis, supervision, and approval of the final version.

Conflict of Interest

All authors declared there is no conflict of interest in this work.

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