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The Effect of Preoperative Waiting Time on Prognosis and Outcome of Colorectal Cancer Patients: Retrospective Cohort Analysis

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ABSTRACT

Background: Colorectal cancer (CRC) was identified as the 3rd most frequent type of malignancy on the globe. The postoperative outcomes as well as prognosis of CRC individuals are influenced by factors such as age, type 2 diabetes mellitus (T2DM) and postoperative complications in addition to tumour stage.

Objective: This study aimed to assess how preoperative waiting time affects CRC individuals' immediate results and prognosis.

Patients and methods: Our research involved 80 individuals with CRC of all grades and stages who underwent major colorectal cancer surgery at Sohag University's Oncology Department in Egypt. Data included age, body mass index (BMI), sex, comorbidities, tumor site, clinical stage, and several tests such as colonoscopies, barium enemas, flexible sigmoidoscopies, abdominal computed tomography scans (CT), X-rays, ultrasounds, and fecal occult blood. Group 1 (n=43) had a waiting time of less than a month, group 2 (n=26) among 1-2 months, and group 3 (n=11) > two months.

Results: The univariate logistic regression analysis identified age, clinical stage, T2DM, BMI, overall complications, as well as serious complications as significant predictors of overall survival. The univariate logistic regression analysis identified clinical stage, age, major complications & overall complications as significant predictors of disease-free survival.

Conclusions: The duration of waiting did not have an influence on the immediate results or prognosis for individuals with CRC. There is a need for a substantial amount of data to evaluate the consequence of preoperative waiting time on the consequences of CRC cases, to enhance the reliability of the findings.

Keywords: Preoperative, Waiting time, Prognosis, Outcome, Colorectal cancer.

INTRODUCTION

Globally, CRC ranks as the third most prevalent tumor. Those below the age of fifty are experiencing an increasing worldwide incidence of CRC. In contrast to older individuals, this population is more prone to have metastatic disease and experiences poorer survival rates [1]. Major fields of research in the recent decades have focused on improving cancer diagnosis and speeding up cancer therapy. Primary surgical removal is the only treatment option for CRC, however even after surgery, recurrence occurs in up to thirty percent of those with potentially curable disease [2]. Nevertheless, problems following CRC surgery continue to affect around one third of people [3].

The postoperative outcomes and prognosis of CRC individuals are influenced by factors such as age, T2DM, tumor stage, as well as postoperative complication [4]. Enhanced recovery programs (ERAS) have been put into action to reduce the duration of hospital stays, lower the occurrence of complications, and decrease post-surgical morbidity [5, 6].

Fast diagnosis and therapy make sense from a pathophysiological and patient-centered standpoint. The growth patterns of many cancers are either linear or exponential [7]. An early diagnosis results in a lower stage of the tumor, which, when followed by quick treatment, is likely to result in a more favorable prognosis. Nevertheless, it is important to recognize the inherent progression of cancer [8].

For the early detection of CRC, it is recommended to use endoscopy, MRI, CT & fecal occult blood test (FOBT). To confirm cases of CRC, the gold standard is the result of a colonoscopic biopsy. The overwhelming burden on the central hospital, medical facility, and the uncertainty experienced by individuals and their families regarding surgery may lead to potential delays in these assessments [9, 10]. Prognosis for individuals with colorectal cancer was not well understood in relation to diagnostic and treatment delays. Population-based methodologies have not thoroughly examined the impact of surgical waiting periods on overall survival [11].

The duration of waiting for surgery is crucial for CRC individuals as surgical removal of the tumor is the primary treatment approach. Nevertheless, certain studies have indicated that extended waiting periods do not pose a risk factor for poorer outcomes for those with CRC. Wait times can be affected by factors linked to the individual and delays within the healthcare system [12, 13]

This research aimed to evaluate the influence of preoperative waiting time on the short-term outcomes and prognosis of individuals with CRC.

METHODS

We conducted a retrospective analysis of data from eighty cases of CRC individuals who performed primary CRC surgery at the Oncology Department of Sohag University, Egypt, from January 2019 to December 2023. After obtaining ethical approval and signed informed consents from all subjects, the research

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was conducted at the First Affiliated Hospital of Sohag University.

Inclusion criteria: Complete medical records of individuals with all grades as well as stages of CRC, both sexes and age above 18 years old.

Exclusion criteria: Incomplete medical records of participants, atypical histology, inflammatory bowel disease and presence of other types of malignancy.

Data collection

We conducted a retrospective collection of personal history and short-term results utilizing an electronic medical records system. The collected data were on age, BMI, sex & comorbidities as T2DM, hypertension, laparoscopy, family history and smoking. Other information about tumour location, in addition to clinical stage were collected as well as baseline information and information about investigations (colonoscopies, flexible sigmoidoscopies, abdominal CT scans, barium enemas, abdominal X-rays, abdominal ultrasound and fecal occult blood test (FOBT). Also, The time that passed between the suspect's colonoscopy, CT scan, Magnetic resonance imaging (MRI), or FOBT and the CRC procedure was deemed the waiting time [14]. The total wait times (TWTs) were calculated by determining the duration from the initial contact with the healthcare system for symptoms associated with CRC and the date of first treatment, utilizing the dates of healthcare contact [15].

Grouping according to waiting time: Group 1 (n=43): The individuals who participated in the short-waiting group had a wait time of below one month, group 2 (n=26): The intermediate-waiting group, involved the cases with the waiting time among 1-2 months, and group 3 (n=11): long-waiting group, involved individuals with the waiting time over 2 months.

The individual's follow-up records were acquired via the outpatient system and telephone interviews. The immediate results encompassed variables such as surgical duration, number of lymph nodes obtained, length of hospital stay, amount of blood loss, overall problems, and serious complications.

The postoperative complications were categorized utilizing the Clavien-Dindo classification, with complications of grade ≥III being classified as significant complications **[14]**.

The primary outcomes of the research were the participants' overall survival (OS) (that was measured as the duration from the CRC surgery and the last follow-up or death) and the disease-free survival (DFS) that was determined by summing the timestamps of initial tumor recurrence, the last follow-up, or post-surgery death for those with CRC.

Secondary outcomes included the duration of the operation, blood loss, overall complications, length of hospitalization, lymph node retrieval and significant complications.

Ethical Approval: An informed written consent was obtained from the patient. The study was done after approval from the Ethical Committee Oncology Department, Sohag University, Hospital of Sohag University, Egypt, from January 2019 to December 2023 (approval code: Soh-Med-23-03-05PD). The Helsinki Declaration was followed throughout the study's conduct.

Statistical analysis

The statistical analysis was conducted using SPSS version 28 software (IBM Inc., Armonk, NY, USA). The quantitative variables were expressed as the mean ± the standard deviation (SD) and contrasted among the 2 groups applying ANOVA test. For the purpose of evaluating the qualitative variables, which were discussed in terms of percentages and frequencies, the Chi-square test was undertaken. It was determined that a two-tailed P value that was ≤ 0.05 was considered significant. Logistic regression was utilized in order to ascertain the degree of correlation that exists between a dependent variable and either a single independent variable (univariate) or multiple independent variables (multivariate). In this study, the Kaplan-Meier curve was utilized to illustrate both overall and disease-free survival lengths.

RESULTS

Figure (1) showed that a total of 109 CRC individuals who underwent primary CRC surgery at Oncology Department, Sohag University, Egypt from January 2019 to December 2023. 29 individuals were excluded, and 80 eligible CRC cases were enrolled for final analysis.

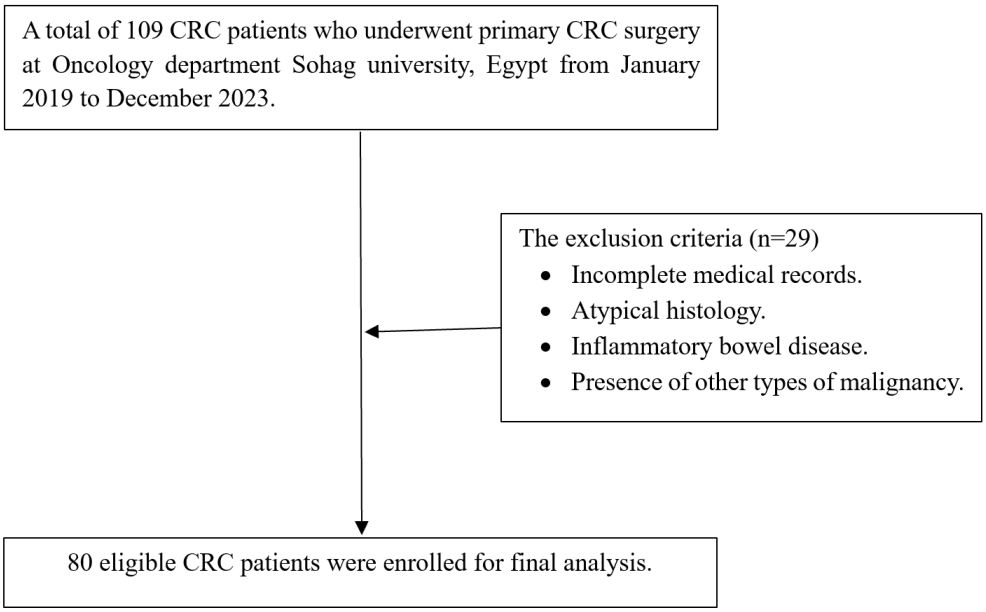

Figure (1): Flowchart of the enrolled patients.

Table (1) showed that 80 eligible CRC cases were enrolled for final analysis. There was insignificant variation among the examined groups concerning the baseline characteristics (age, weight, height, sex & BMI) and the associated comorbidities including hypertension (HTN), T2DM, laparoscopy, smoking and family history of tumor.

Table (1): Baseline characteristics and comorbidities of the studied groups

		Total (n=80)	Group 1 (n=43)	Group 2 (n=26)	Group 3 (n=11)	P value
Age (years)		65.3 ± 7.37	63.98 ± 7.52	66.1 ± 6.4	68.3 ± 8.39	0.176
Sex	**Male**	38 (47.5%)	23 (53.49%)	10 (38.46%)	5 (45.45%)	0.475
	Female	42 (52.5%)	20 (46.51%)	16 (61.54%)	6 (54.55%)	
Weight (Kg)		74.5 ± 9.65	73.5 ± 9.9	75.0 ± 9.17	76.8 ± 10.13	0.567
Height (m)		1.66 ± 0.04	1.65 ± 0.04	1.67 ± 0.04	1.66 ± 0.05	0.252
BMI (Kg/m^2)		27.1 ± 3.9	26.95 ± 4.17	26.9 ± 3.43	28.1 ± 4.03	0.654
Comorbidities						
HTN		31 (38.75%)	16 (37.21%)	11 (42.31%)	4 (36.36%)	0.901
T2DM		21 (26.25%)	11 (25.58%)	6 (23.08%)	4 (36.36%)	0.695
Laparoscopy		64 (80%)	32 (74.42%)	22 (84.62%)	10 (90.91%)	0.368
Smoking		30 (37.5%)	15 (34.88%)	11 (42.31%)	4 (36.36%)	0.823
Family history of tumor		8 (10%)	5 (11.63%)	2 (7.69%)	1 (9.09%)	0.846

Data presented as mean ± SD or frequency (%).

Table (2) showed the site, clinical stage and histology of the tumor, which were insignificantly different among the studied groups.

Table (2): Clinical data of tumor of the examined groups

		Total (n=80)	Group 1 (n=43)	Group 2 (n=26)	Group 3 (n=11)	P value
Site	**Colon**	37 (46.3%)	23 (53.5%)	9 (34.6%)	5 (45.5%)	0.654
	Rectosigmoid	14 (17.5%)	6 (14.0%)	6 (23.1%)	2 (18.2%)	
	Rectum	29 (36.3%)	14 (32.6%)	11 (42.3%)	4 (36.4%)	
Clinical stage	**I**	33 (41.3%)	18 (41.9%)	13 (50%)	2 (18.2%)	0.250
	II	26 (32.5%)	15 (34.9%)	5 (19.2%)	6 (54.5%)	
	III	21 (26.3%)	10 (23.3%)	8 (30.8%)	3 (27.3%)	
Histology	**Differentiated**	56 (70%)	31 (72.1%)	19 (73.1%)	6 (54.5%)	0.482
	Undifferentiated	24 (30%)	12 (27.9%)	7 (26.9%)	5 (45.5%)	

Data presented as frequency (%)

Table (3) showed that the total wait time was significantly longer in group 3 in contrast to group 1 & group 2 and was significantly longer in group 2 contrasted with group 1.

Table (3): Total wait times of the examined groups

	Total (n=80)	**Group 1 (n=43)**	**Group 2 (n=26)**	**Group 3 (n=11)**	**P value**
Total wait time (min)	36.8 ± 27.5	17.2 ± 5.08	45.4 ± 10.3	92.7 ± 17.7	**<0.001***
	P1<0.001*, P2<0.001*, P3<0.001*				

P1: p value among groups 1&2, P2: p value among groups 1&3, P3: p value among groups 2 & 3

Table (4) showed that there was insignificant distinction among the investigated groups concerning the short-term results involving blood loss, hospital stay, operation time, retrieved lymph nodes and the occurrence of overall & major complications.

Table (4): Short term outcomes of the examined groups

	Total (n=80)	**Group 1 (n=43)**	**Group 2 (n=26)**	**Group 3 (n=11)**	**P value**
Operation time (min)	235.6 ± 49.1	237.9 ± 49.1	231.8 ± 50.5	235.9 ± 50.2	0.887
Blood loss (ml)	247.1 ± 78.2	250.9 ± 73.4	247.3 ± 84.4	231.8 ± 86.8	0.774
Retrieved lymph nodes	15.3 ± 3.85	15.3 ± 3.92	14.8 ± 3.7	16.3 ± 4.13	0.595
Hospital stay (days)	11.1 ± 4.9	11.5 ± 5.07	10.5 ± 5	10.8 ± 4.14	0.699
Overall complications	17 (21.3%)	6 (13.95%)	7 (26.92%)	4 (36.36%)	0.185
Major complications	4 (5%)	1 (2.33%)	2 (7.69%)	1 (9.09%)	0.489

Data presented as mean ± SD or frequency (%).

Table (5) showed that the total population showed OS rate 78.8% and DFS rate 66.3%. There was an insignificant variance among the examined groups regarding both OS & DFS.

Table (5): Overall survival and disease-free survival of the studied groups

	Total (n=80)	**Group 1 (n=43)**	**Group 2 (n=26)**	**Group 3 (n=11)**	**P value**
OS	63 (78.8%)	35 (81.4%)	20 (76.92%)	8 (72.73%)	0.790
DFS	53 (66.3%)	31 (72.09%)	16 (61.54%)	6 (54.55%)	0.452

Data presented as frequency (%)

Table (6) showed that significant predictors of overall survival consistent with the univariate logistic regression analysis, were age, BMI, T2DM, clinical stage, and serious comorbidities. The only variables that were found to be significant predictors of overall survival in the multivariate logistic regression analysis were age, clinical stage, BMI, overall complications, and serious complications.

Table (6): Univariate as well as multivariate logistic regression analysis for prediction of the overall survival

	Univariate			**Multivariate**		
	OR	**95%CI**	**P**	**OR**	**95%CI**	**P**
Age (years)	0.925	0.861 to 0.994	**0.034***	0.924	0.859 to 0.994	**0.035***
Sex	0.954	0.830 to 1.096	0.509	0.944	0.804 to 1.108	0.482
BMI (Kg/m^2)	0.262	0.077 to 0.893	**0.032***	0.224	0.060 to 0.834	**0.026***
HTN	1.137	0.381 to 3.388	0.817	0.929	0.279 to 3.086	0.905
T2DM	3.418	1.103 to 10.595	**0.033***	2.876	0.877 to 9.434	0.081
Laparoscopy	0.939	0.485 to 1.818	0.852	1.234	0.581 to 2.620	0.583
Smoking	0.633	0.198 to 2.018	0.439	0.641	0.174 to 2.350	0.503
Family history	0.500	0.057 to 4.369	0.531	0.345	0.028 to 4.164	0.403
Site	1.027	0.567 to 1.862	0.927	1.147	0.613 to 2.145	0.667
Clinical stage	0.238	0.072 to 0.787	**0.019***	0.231	0.062 to 0.849	**0.028***
Histology	0.750	0.188 to 2.984	0.683	1.224	0.2731 to 5.490	0.791
Total wait time minute (min)	0.991	0.973 to 1.010	0.375	0.993	0.9790 to 1.007	0.348
Operation time (min)	0.995	0.984 to 1.006	0.415	0.990	0.975 to 1.006	0.239
Blood loss (ml)	0.994	0.986 to 1.001	0.105	0.991	0.982 to 1.001	0.089
Retrieved lymph nodes	0.910	0.784 to 1.056	0.215	0.928	0.770 to 1.118	0.436
Hospital stay (days)	0.902	0.805 to 1.009	0.074	0.976	0.8457 to 1.127	0.748
Overall complications	0.277	0.0911 to 0.847	**0.024***	0.237	0.070 to 0.806	**0.021***
Major complications	10.400	2.944 to 36.729	**<0.001***	26.49	3.780 to 185.61	**0.001***

OR: odds ratio, CI: coefficient interval, *: significant as P value < 0.05

Table (7) showed that in the univariate logistic regression analysis, clinical stage, age, total complications, and severe complications were identified as significant predictors of disease-free survival. The multivariate logistic regression analysis identified only age, clinical stage, severe complications, as well as overall complications as significant predictors of survival free from disease.

Table (7): Univariate and multivariate logistic regression analysis for prediction of the disease-free survival

	Univariate			**Multivariate**		
	OR	**95%CI**	**P**	**OR**	**95%CI**	**P**
Age (years)	0.914	0.858 to 0.975	**0.007***	0.895	0.830 to 0.963	**0.003***
Sex	0.413	0.157 to 1.087	0.073	0.306	0.093 to 0.997	0.052
BMI (Kg/m^2)	0.979	0.869 to 1.104	0.737	0.950	0.816 to 1.105	0.504
HTN	1.134	0.439 to 2.926	0.794	1.191	0.355 to 3.990	0.777
T2DM	2.246	0.805 to 6.260	0.122	1.654	0.468 to 5.832	0.434
Laparoscopy	0.422	0.138 to 1.290	0.130	1.00	0.311 to 3.208	1.00
Smoking	0.914	0.515 to 1.620	0.758	1.300	0.645 to 2.616	0.462
Family history	0.252	0.029 to 2.169	0.209	0.230	0.022 to 2.408	0.220
Site	1.350	0.798 to 2.282	0.262	1.394	0.776 to 2.505	0.265
Clinical stage	0.320	0.111 to 0.919	**0.034***	0.195	0.059 to 0.646	**0.007***
Histology	1.090	0.354 to 3.357	0.879	1.140	0.589 to 2.207	0.696
Total wait time (min)	0.985	0.969 to 1.002	0.096	0.982	0.963 to 1.000	0.056
Operation time (min)	0.992	0.982 to 1.001	0.113	0.991	0.980 to 1.001	0.087
Blood loss (ml)	0.996	0.990 to 1.002	0.208	0.995	0.988 to 1.001	0.147
Retrieved lymph nodes	1.071	0.9486 to 1.209	0.266	1.090	0.953 to 1.245	0.209
Hospital stay (days)	0.927	0.8420 to 1.021	0.128	0.914	0.822 to 1.014	0.092
Overall complications	0.255	0.090 to 0.726	**0.010***	0.200	0.043 to 0.911	**0.038***
Major complications	3.000	1.136 to 7.921	**0.027***	0.208	0.056 to 0.764	**0.018***

OR: odds ratio, CI: coefficient interval, *: significant as P value < 0.05.

Figure (2) showed that the Kaplan-Meier curve analysis revealed an insignificant variation among the examined groups regarding the mean time to both overall survival (Heart rate (HR)=1.00 (95% confidence interval (CI) 0.5773 to 1.7322, 1.00 (95%CI) 0.4639 to 2.1556, P=1.00) & disease-free survival (HR=1.00, (95%CI) 0.5470 to 1.8282, 1.00 (95%CI) 0.4172 to 2.3969, P=1.00).

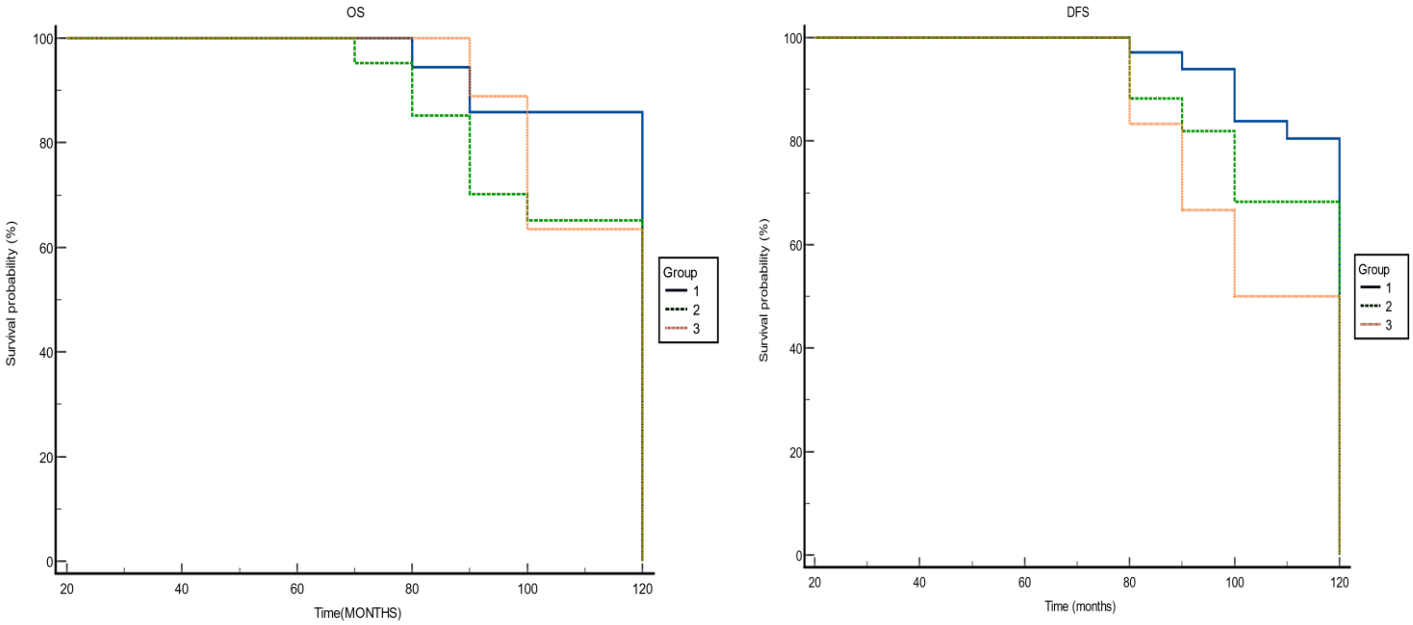

Figure (2): Kaplan- Meier analysis of Overall survival and disease-free survival.

DISCUSSION

There is a lack of research that has specifically investigated the correlation among waiting time and survival in cases with colorectal cancer. There were no significant distinctions identified among the three groups with regard to OS & DFS.

The extended waiting period for surgery specific to malignancy was a source of concern. Evidence has shown that the duration of waiting time before a surgical procedure may impact the outcome of oncological surgery [16]. The variability in waiting time might exacerbate the psychological stress experienced by participants, but it can also allow for more comprehensive preoperative assessment of organic function, particularly in elderly individuals. This variability contributes to the disparities in surgical results among prostate cancer and breast cancer [17, 18].

Peng *et al.* [19] revealed that The extended preoperative waiting period for individuals with gastric cancer resulted in a reduced length of stay in the hospital after surgery. However, the increased waiting time did not have any effect on OS. Regarding CRC, certain research has indicated that there is no correlation among the duration of waiting time before surgery and the subsequent outcomes and survival rates [20, 21]. However, **Pita-Fernandez *et al.*** [22] reported the opposite conclusion that a shorter waiting period was related to increased mortality among individuals with rectal cancer. The goal of the trail was to analyse the impact of waiting time on individuals who have colorectal cancer (CRC).

Yun *et al.* [23] in their large-scale cohort research that examined 66,825 individuals who received surgery as their initial definitive treatment. However, they did not account for the stage of cancer in their analysis. The authors concluded that a preoperative wait time over 31 days did not correlate with decreased survival rates in individuals diagnosed with gastric cancer.

Di Girolamo *et al.* [24] indicated a population-based analysis in the UK to examine the relationship among cancer waiting time targets in addition to survival rates. The study focused on 3542 individuals with CRC who were between the ages of 15 and 44. The researchers examined three different time intervals for delays: The period from when an individual is referred to a specialist consultation, the time from when a treatment decision is made till treatment is started, and the duration from referral to treatment. Longer intervals were not related to survival. **Kim *et al.*** [25] conducted a study that analyzed data from 693 individuals with CRC who were 45 years old or younger, focusing on a single medical center. Their findings indicated that a time period of more than three months among the appearance of symptoms and the diagnosis was linked to a more severe carotid sinus syndrome (CSS) compared to a time period of less than 1 month (adjusted hazard ratio, 2.57 [95% confidence range, 1.34-4.94]).

Ramos *et al.* [26, 27] conducted two systematic reviews of older people with CRC to examine delay, stage & survival. Four of twenty-six studies found that longer delay periods enhanced survival, while two found the opposite. Thus, this literature indicates longer intervals do not clearly affect participants' outcomes. Similarly, **Liu *et al.*** [13] showed that among the three time waiting groups, there was no statistically significant variation in OS or DFS. Results for CRC individuals' short-term results and prognoses were unaffected by the amount of time they had to wait before surgery. When looking at the immediate results, they found no statistically significant disparity among the groups.

There is a strong correlation between the postoperative state and the short-term results. In cases with colorectal cancer, some research has shown no correlation between a delayed diagnosis and worse short-term prognosis [28]. **Liu *et al.*** [13] found that there was no correlation between waiting time and short-term consequences. The primary factor influencing outcomes was tumor stage [29] . Due to the slow progression of colorectal cancer, there was no statistically significant negative impact of increased waiting time on outcomes [15, 30].

In our multivariate research, we discovered that older age, overall problems, advanced clinical stage, and significant complications were identified as independent factors affecting OS and DFS. This is in accordance with the results of **Liu *et al.*** [13] who revealed that age, underlying diseases, tumor stage, and postoperative complications are some of the variables that impact OS and DFS in CRC individuals according to previous research. These results are consistent with what we predicted. Previous researches have shown no association among waiting time and survival rates. Their results indicated that the amount of time patients had to wait before surgery was not a significant predictor of overall survival or disease-free survival in cases with CRC [27, 28, 31- 33].

Evaluating wait times is a complicated task, but it can be accomplished utilizing administrative databases. Administrative databases provide accurate and easily available data for estimating surgical wait times [34].

Limitations: This study examined the effect of CRC individuals' preoperative waiting time on their outcomes using a small dataset. There was a possibility of selection bias because it was retrospective research performed at just one center. In addition, the median follow-up period was rather short. Furthermore, there was a deficiency in the information pertaining to neoadjuvant therapy and postoperative therapy. Nevertheless, the available data were constrained by their retroactive character and further compounded by coding errors and the absence of crucial information, such as exploratory tests. Consequently, we were incapable of computing the waiting durations for all individuals. We were also unable to determine those individuals who were diagnosed with CRC by screening.

CONCLUSION

Prognosis and short-term outcomes in individuals with CRC were unaffected by the waiting time. There was a gab in knowledge regarding the effect of waiting time on CRC. So, we need the most data possible to determine the impact of preoperative waiting time on CRC individuals so that we can trust the results. Independent predictors of overall survival and disease-free survival included age, clinical stage, and severe sequelae.

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