

Survival Rate and its Predictors in Colorectal Cancer Patients, Southern Iran

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Abstract: Because of some progress in treatment, survival rate of colorectal cancer has been increasing in recent decades. The purposes of this study were to investigate the colorectal cancer survival rate and its determining factors among a group of Iranian patients. In a retrospective cohort, data from 243 patients diagnosed with colorectal cancer during years 2003 to 2008 were entered into our study. Kaplan-Meier method, log-rank test and Cox regression model were used to analyze the data. All analyses were done by SPSS statistical software, version 16. The mean of follow-up time was 35.4 ± 37.49 months and 1, 3 and 5-year survival rates of colorectal cancer were 93.9, 50.3 and 27.2% respectively. Multiple Cox regression model revealed that the primary diagnosis method, income status, history of alcohol use, primary treatment method and history of metastasis have significant relationship with survival rate. In spite of advancement in treatment, the 5-year survival rate of the colorectal cancer in Iran is lower than that in developed countries.

Key words: Colorectal Cancer % Survival Rate % Risk Factors % Cox Regression Model

INTRODUCTION

Despite the progress in control and prevention of infectious diseases, the morbidity and mortality of chronic diseases have seen an increasing trend in recent decades [1]. In this between, in most of the countries and especially the developed ones, cancers have become the second major cause of mortality after the cardiovascular diseases [2, 3] and it is now one of the most important public health challenges in our societies [4-6]. However, next to cardiovascular diseases and accidents, cancers are the third major cause of mortality in Iran [7-9].

Almost one million new cases of colorectal cancer are diagnosed each year globally from whom approximately 50 percent die within the first five years of disease onset [10]. Next to lung and prostate cancers, colorectal cancer is the third most prevalent cancer in world and among men, afflicting 663600 people. After breast cancer, it is also the second most prevalent cancer amongst women having 570100 cases afflicted [11, 12]. In addition, after lung, liver and gastric cancers, colorectal cancer are the fourth mortality reason among men with 320600 mortality cases.

It is also the third reason of mortality among women with 288100 mortality cases after the breast and lung cancers [11, 12]. In a report in 2009, the colorectal cancer was also identified as the third common reason of mortality and also the third reason of cancer-induced mortalities among men and women [13]. The standardized incidence of this cancer in Iranian male and female is 8.2 and 7 cases in one hundred thousand people, respectively [14]. In Fars province, this rate is estimated to be 3.4 and 2.6 cases in one hundred thousand people for men and women respectively [15].

The survival rate of colorectal cancer has had an increasing trend during the past years [16, 17]. Its 5-year survival rate in England has reached to more than 50 percent [17, 18] and it is also reported as 56.3 percent in France [19]. In Sweden, this rate is 57.2 and 57.6 percent for colon and rectal cancers respectively [20].

Although Fars province is a colorectal cancer referral center in southern Iran, no study is done on colorectal cancer survival rate in this part of Iran. Thus, we aimed to investigate this matter in the present study and revealed the factors that influence colorectal cancer survival rate.

MATERIALS AND METHODS

In a retrospective cohort study, 243 patients diagnosed with colorectal cancer in Shiraz (Southern Iran) during years 2003 to 2008, were followed up. In this study, the time of diagnosis was considered as the "initial event" and the time of death (due to colorectal cancer) was considered as the "end point event". In cases where the end point event did not occur, whether due to completion of study, follow-up interruption or the patient's death due to the reasons except for colorectal cancer, the gathered data was treated as censored data.

The investigated variables in present study were as follows; demographics, diagnosis and treatment and history of being exposed to risk factors.

The Kaplan-Meier method was used to calculate the survival probabilities. Comparisons between survival curves were made through log-rank test. Predictors modeling (control for confounders in revealing survival rate influential factors), estimation of hazard ratio (HR) and its 95% of confidence interval (CI) all were done using Cox Regression Model and variable selection was done using Forward Stepwise Method. The assumption of HR proportionality (as one of the Cox model assumptions) was also studied through plotting Log (-log (t)) scatter diagram on log (t), on which the parallelism of curves indicated the approval of the HR proportionality assumption.

In present study qualitative variables were described in numbers and percentages and quantitative variables in means and standard deviations. All data analyses were done by SPSS software (version 16) and a *P*-value lower than 0.05 was considered as significance level.

RESULTS

Our findings showed that almost 60 percent of patients were male, most of them were urban dwellers (84.0%), married (90.1%), with a normal BMI (50.0%) and between 45-60 years old (32.1%). The mean of age in women and men were 58.65 ± 13.58 and 52.37 ± 15.04 years respectively; and the mean of BMI in men and women were 24.15 ± 5.05 and 22.6 ± 6.8 kg/m² respectively.

In present study, 86 cases (35.4%) were dead and 157 cases (64.6%) were alive till end of follow up time and considered as censored data. The mean of follow-up time was 35.4 ± 37.49 months. Also, the median of patient's survival time was 36.06 ± 2.98 months.

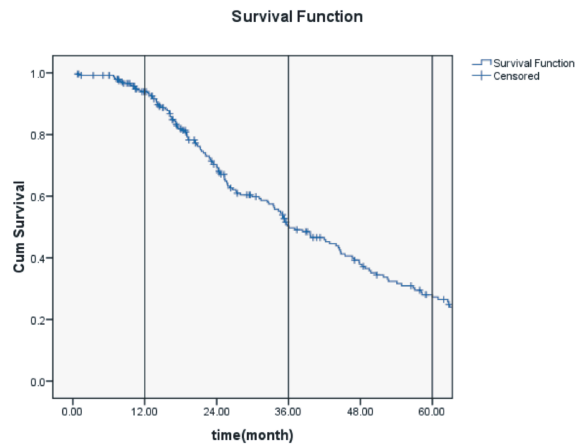


Fig. 1: Survival curves of colorectal cancer in southern Iran, (n=243)

As it is shown in figure 1, the 1, 3 and 5-year survival rates of studied patients were about 93.9, 50.3 and 27.2 percent, respectively.

Distribution of cases based on studied variables and also the relationship between these variables and survival rates were illustrated in table 1. Using univariate analysis method, it was revealed that variables of primary diagnosis method (*P*=0.001), history of alcohol use (*P*=0.001) and the primary treatment method (*P*=0.001) had a significant relationship with the survival rate.

Using the Cox regression model, multi-variable analysis was also conducted. In this method, the variables with a *P*-value lower than 0.2 in the univariate analysis were entered into the model. As it is shown in table 2, after controlling for confounders, income status, primary diagnosis method, history of alcohol use, primary treatment method and history of metastasis had a significant relationship with survival rate.

DISCUSSION

The five-year survival rate of the colorectal cancer in this study was about 27.2 percent. The Cox regression model showed that the income status, primary diagnosis method, history of alcohol use, primary treatment method and the history of metastasis had a significant relationship with survival rate.

Our findings showed that 1, 3 and 5-year survival rates in studied colorectal cancer patients were about 93.9, 50.3 and 27.2 percent respectively. Nasiri *et al.* [21] reported survival rates of 72, 54 and 47 percent for 1, 3 and 5 years respectively. On the contrary, in comparison with

Table 1: Median of survival time and frequency of variables entered into Kaplan-Meier and log-rank univariate analysis

	Variable	Frequency (%)	Median survival time (month)	p-value ^a
Gender	Male	147 (60.5)	39.6	0.32
	Female	96 (39.5)	35.6	
Place of residence	Urban	204 (84)	35.6	0.82
	Rural	39 (16)	44.6	
Marital status	Single	6 (2.5)	27.2	0.9
	Married	219 (90.1)	35.6	
	Other	18 (7.4)	44.3	
Income status	Low	71 (29.5)	45.4	0.06
	Middle	140 (58.1)	32.4	
	High	30 (12.4)	58.2	
Blood group	A	62 (25.7)	35.7	0.47
	B	59 (24.5)	46.6	
	AB	21 (8.7)	42.2	
	O	99 (41.1)	53.3	
Diagnosis method	C.T. Scan	17 (7.1)	18.8	0.001*
	Histologic	53 (22.1)	47.8	
	Colonoscopy	26 (10.8)	21.4	
	Other	144 (60)	41.9	
Cancer in far relatives	Yes	29 (11.9)	48.2	0.26
	No	214 (88.1)	35.7	
Cancer in close relatives	Yes	63 (25.9)	44.3	0.41
	No	180 (74.1)	35.6	
Hospital type	University-affiliated	235 (97.9)	37.03	0.06
	Private	5 (2.1)	16.5	
Alcohol use	No	223 (96.1)	39.6	0.001*
	Casual	9 (3.9)	22.7	
Smoking	No (cigarette)	157 (66.2)	34.6	0.55
	Yes (cigarette)	29 (12.2)	37.03	
	Casual (cigarette)	15 (6.3)	42.2	
	Water pipe (Hookah)	26 (11)	44.7	
	Morphine and Heroin	10 (4.2)	75.5	
Metastasis history	Yes	45 (18.5)	39.63	0.1
	No	198 (81.5)	35.6	
Primary treatment	Surgery	142 (58.4)	35	.001*
	Chemotherapy	9 (3.7)	74.03	
	Surgery and Radiotherapy	5 (2.1)	70.2	
	Surgery and chemotherapy	47 (19.3)	34.3	
	Surgery, Chemotherapy and Radiotherapy	38 (15.6)	47.8	
	None	2 (0.8)	10.4	
Cancerous region	Anorectal and Rectosigmoid	109 (44.9)	45.5	0.74
	Colon	143 (55.1)	35.2	
BMI	Under 18.5	18 (8.3)	42.2	0.74
	18.5-24.9	109 (50.5)	35.4	
	25-29.9	70 (32.4)	33.6	
	30 and over	19 (8.8)	33.6	
Age	Under 45	64 (26.3)	35.03	0.64
	45-60	78 (32.1)	33.66	
	60-75	76 (31.3)	45.4	
	Over 75	25 (10.3)	24.3	

*p values using log-rank test.

Table 2: Modeling of the influential predictors on colorectal cancer survival using the Cox regression model

	Variable	p-value	Adjusted Hazard Ratio	95% confidence interval
Income status	Low	0.017	2.11	1.14-3.91
	Middle	0.001	2.92	1.61-5.31
	High	-	1	-
Diagnosis method	C.T. Scan	0.006	2.8	1.35-6
	Histologic	0.4	0.83	0.53-1.3
	Colonoscopy	0.002	3.13	1.53-6.3
	Other	-	1	-
Alcohol use	No	0.001	0.213	0.09-0.5
	occasional	-	1	-
Metastasis history	Yes	0.013	2.07	1.16-3.69
	No	-	1	-
Primary treatment	Surgery	0.59	1.15	0.68-1.93
	Chemotherapy	0.25	0.54	0.18-1.5
	Surgery and Radiotherapy	0.06	0.14	0.019-1.12
	Surgery and chemotherapy	0.6	1.17	0.64-2.14
	Surgery, Chemotherapy and Radiotherapy	-	1	-
	None	0.002	11.3	2.37-54.7

*mentioned, whether they were adjusted with each other?

Tehran's study, the present study had a lower five-year survival rate. This rate has been over 50 percent in most of studies conducted in European countries [16-20]. It shows that comparing to European countries Iranian patients suffer from lower survival rates.

Controlling for confounders, our findings showed no significant relationship between the survival rate and demographic variables including age, gender, BMI, place of residence and blood group. Similar to our study, age has not shown a significant relationship with survival rate in most of other studies [22, 23]. However, quite the contrary in the study conducted by Nasiri *et al.* [21], the under 65-years old patients had a higher mean of survival in comparison with over 65-years old patients. Also, Akhoond *et al.* [23] and Birgisson *et al.* [20] showed that gender has a significant relationship with survival rate. Finally in line with Akhoond *et al.* [23] study, our study could not approve a significant relationship between survival rate and marital status.

In our study, smoking history was of variables which did not show a significant relationship with survival rate of colorectal cancer. This finding is in line with other studies [22]. However, against these findings smoking is still known as a factor that increases the risk of mortality in colorectal cancer patients [24, 25]. On the other hand, alcohol use showed a significant relationship with survival rate so that the survival rate among the non-alcoholic group was significantly higher than the rate in patients who had history of alcohol use. This finding is in contrast with the result of Phips *et al.* [24].

The present study showed that individuals with low or middle-income have a lower survival rate than high-income persons. Similar finding is reported in San Francisco study [26]; however, no such a relationship between income and survival rate was found among Toronto dwellers in that study [26]. Moller *et al.* [18] also found such a relationship between low-income and lower survival rate, whereas Kelsall *et al.* [27] and Nur *et al.* [28] did not report a significant relationship between socioeconomic status and colorectal cancer survival rate.

Treatment of patients with metastasis history is one of the most important healthcare problems faced today and thanks to new methods of treatment such as chemotherapy, survival rate of this group has also improved to a great extent recently [29]. In our study, this variable (metastasis history) demonstrated a significant relationship with survival rate. Akhoond *et al.* [23] also found such a significant relationship between metastasis history and mortality rate of colon cancer.

During the recent years, surgery for colon cancers and compound method (surgery, chemotherapy and radiotherapy) for rectal cancers has been the most common methods of treatment [30]. And surgery also was the most regular method of treatment in present study. This might lead to relatively higher survival rates in our study. Indeed, as it is reported in the majority of studies, the survival rate of colorectal cancer has been increasing in recent years [10]. This can be due to two major reasons: firstly, existence of more exact diagnosis methods;

this has helped in diagnosis of cancer in early stages and thus better response to treatment. And secondly, introduction of new treatment methods and effective combination of the current methods; these has resulted in remarkable increase of survival rate of the patients. However, there can be some other initiatives that would increase survival rate effectively if performed correctly; development of screening programs along with establishment of cancer registry programs. These programs are not a routine care in most of countries; Iran included and should be of primary importance in future public health agendas.

The findings of present study showed that one-year survival rate in our sample is higher than the rate found in other centers of the country, whereas in longer survival times, our sample had a lower rates relatively. However, in comparison with European countries it seems that Iranian patients had lower survival rates altogether. The income status, history of alcohol use, metastasis history, primary diagnosis and treatment method are the predictors for survival rate.

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