RESEARCH ARTICLE

Survival of Colorectal Cancer Patients in the Presence of Competing-Risk

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Abstract

Background: Colorectal cancer (CRC) is considered to be a main cause of malignancy-related death in the world, being commonly diagnosed in both men and women. It is the third leading cause of cancer dependent death in the world and there are one million new cases diagnosed per year. In Iran the incidence of colorectal cancer has increased during the last 25 years and it is the fifth cause of cancer in men and the third in women. Materials and Methods: In this article we analyzed the survival of 475 colorectal patients of Taleghani hospital in Tehran with the semi-parametric competing-risks model. Results: There were 55% male cases and at the time of the diagnosis most of the patients were between 48 and 67years old. The probability of a patient death from colorectal cancer with survival of more than 25 years was about 0.4. Body mass index, height, tumour site and gender had no influence. Conclusions: According to these data and by using semi-parametric competing-risks method, we found out that only age at diagnosis has a significant effect on these patient survival time.

Keywords: Survival analysis - competing-risk - colorectal cancer - semi-parametric model

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Introduction

Colorectal cancer (CRC) is a type of cancer in which abnormal cells start dividing and growing without control in the colon or rectum portion of large intestine in the gastrointestinal tract.

Colorectal cancer (CRC) is considered to be a main cause of malignancy-related death in the world (Chen et al., 2013). It is the third leading cause of cancer dependent death in the world and there are one million new cases diagnosed per year (Ranjbar1 et al., 2014). The highest incidence rates of colorectal cancer are located in Europe, North America, and Oceania. In contrast, the lowest rates are observed in Asia, Africa, and South America (Center et al., 2009). In Eastern Asian countries such as China, Japan, South Korea and Singapore have experienced a two to four fold increase in incidence in recent decades (Sung et al., 2005). Also incidence is 20% higher for men than woman (Morrison et al., 2013).

In the recent decade incidence trends of colorectal cancer have differed between populations so that the incidence rate has decreased in USA, slightly increasing or constant in Europe and highly increasing in most Asian countries (Abdifard et al., 2013).

During the last 25 years the incidence of colorectal cancer has increased in Iran (Mousavi et al., 2009). It is the fifth cause of cancer in men and the third in women (Pourhoseingholi and Zali, 2012). Iranian data suggest a younger age distribution for CRC compared to Western reports (Azadeh et al., 2008). Studies show that Kermanshah in Western Iran had the highest risk of colorectal cancer incidence (Abdifard et al., 2013). Also a study in Kerman (a province of Iran) shows that the trend of colorectal cancer is increasing (Roya and Abbas, 2013).

Survival analysis is the modelling of time to event of death to evaluate the effects of treatment on survival time. There are situations in which a studied person can experience one of several different types of events. Occurrence of one event type prevents others from occurring. In this situation the best way to analyse survival time is Competing-risks model (David G Kleinbaum).

In recent years a pilot screening has been performed on individuals at high risk of familial CRC by the Research Institute for Gastroenterology and Liver Disease, Shahid Beheshti University of Medical Science (Safaee et al., 2012). In this article, the survival of colorectal cancer is described using the most recent data available from Taleghani Hospital, Shahid Beheshti University of Medical Sciences.

Survival of a CRC patient means the years between diagnosis of disease and the death because of this cancer. Most researchers would censor a CRC patient who dies of other causes of death just like one who is excluded (Moradi et al., 2009). But this situation is not a type of

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censoring; in censoring the event of interest still happens at later time, but maybe are not able to see when it happens.

The focus of this article is on the deaths due to a colorectal cancer and therefore other causes of death are intended to be competing risks.

Materials and Methods

We analyzed the 475 patients observed and treated at Taleghani hospital Tehran, Iran. These patients were diagnosed during 1985-2012 and followed up to 2013. To obtain information about patients, telephone calls were made. The demographic features were included in the analysis, items such as age at diagnosis, sex, BMI and cancer site. The demographic features which were extracted from hospital documents were included in the analysis as prognostic variables; item, such as age at diagnosis, sex, BMI and tumour site. Among 475 colorectal patients, 29 cases were excluded from the survival study because of their unknown survival time.

In recent follow ups we found that about 11% of colorectal patients died of other causes of death, such as myocardial infarction and stomach cancer so we analyzed the data with competing risks models. In general, a competing-risk situation arises when an individual can experience more than one type of event and the occurrence of one type of event hinders the occurrence of the other types (Pintilie, 2006).

The data were analyzed by STATA version11. As we have competing risks we used competing-risk method. STATA analyzes the competing risks based on Fine and Garry's method. Competing-risk survival regression provides a useful alternative to Cox regression in the presence of one or more competing risks. Unlike censoring, which merely obstructs you from viewing the event, a competing event prevents the event of interest from occurring altogether, and your analysis should adjust accordingly.

In competing-risk setting, a Kaplan-Meier curve is inadequate because it may fail in a situation in which the event of interest would never occur so it is better to use Cumulative Incidence Function's curve (CIFs curve) instead of survival function, therefore we used it (Kim, 2007; Sherif, 2008). Cumulative incidence is defined as the probability that a particular event, such as occurrence of a particular disease, has occurred before a given time (Dodge et al., 2003).

Results

BA total number of 446 patients with colorectal cancer were included in the study. The available telephone numbers were 366, among them 291 telephone numbers were correct and had been answered. The data of 155 patients who did not answer the phone or their number was not available, were included in the study as a right censoring. After recent follow up it is confirmed that 160 cases were alive, 113 cases had died due to colorectal cancer, 18 had died of competing risks and 155 patients were censored. There were 55%male cases and 45% female. We found 1.24:1(male: female) sex ratio for colorectal cancer.

The age ranges were from 18 to 83 years at the time of diagnosis. The mean of these patients's age at the time of diagnosis is 53±14. Most of the patients at the time of the diagnosis were between 48 and 67years old (Table 1). Tumour location was classified into six groups and the term "not specified" belongs to the patients whose tumour location was not registered (Table 1).

The body mass index "BMI" is defined as the individual's body mass divided by the square of their height (kg/m^2). The World Health Organisation "WHO", use the BMI to help decide whether people are too fat or too thin. Our aim is to see whether it has statistically significant effect on colorectal patient's survival time or not? The mean of these patients's BMI is 25±4.2.

We also interested to see whether patient's height has statistically significant effect on colorectal patient's survival time or not? Among these patients the minimum height was 144 centimetres and the maximum was 195 centimetres.

The prognostic variables included in the model are age at diagnosis, tumour site, BMI, gender and height. The effect of age at diagnosis is statistically significant on survival time, but the others do not have any statistically significant effect on the colorectal patient's survival time. (Table 2)

The Cumulative Incidence Function's (CIF) curve for these patients separated by gender is shown in figure 1.

Table 1. Age and Tumour site Distribution of the 446 Cases of Colorectal Cancer

Age	Frequency	%	Tumour site	Frequency	%
18-27	23	5	Cecum	20	4.5
28-37	38	9	Right Colon	24	5.4
38-47	81	18	Transverse Colon	29	6.5
48-57	133	30	Left Colon	16	3.6
58-67	104	23	Sigmoid Colon	31	7
68-77	54	12	Rectum	134	30
78-83	13	3	Not specified	192	43

Table 2. Competing Risk Regression of 446 Cases of Colorectal Cancer

Variables	Coefficient	sd	p value
BMI	-0.012	0.028	0.666
Age At Diagnosis	0.022	0.008	0.009
Tumour Site	0.081	0.058	0.165
Gender	-0.322	0.227	0.158
Height	-0.013	0.014	0.359

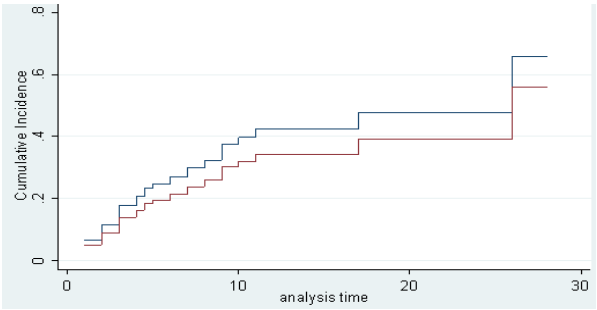

Figure 1. Competing-Risks Regression. Red line belongs to women and blue line belongs to men

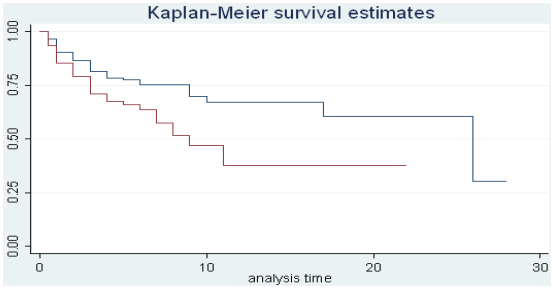

Figure 2. Survival Functions Separated by Age. The red line belongs to patients whose cancer diagnosis is after 53 years old

The probability of a patient's death from colorectal cancer with survival more than 25 years is about 0.4.

Figure 2 shows the survival function of patients whose age at diagnosis is before 53 years against those whose cancer diagnosis is after the age 53.

Discussion

Colorectal cancer is one of the important public health problems and it is expected to become a major health problem globally as a result of high and increasing incidence and survival rate (Moradi et al., 2009). In these data there are five different failures; dying of CRC cancer, dying due to myocardial infarction, dying by stomach cancer or kidney and lung disease. Surly in other researches the death of all patients were not do to colorectal cancer, so we suggest the best way to analyse the patient's survival time is competing-risk method. By using this method our results shows slightly different results compared to previous researches (Azadeh et al., 2008; Mousavi et al., 2009).

This study suggests that age at diagnosis of the cancer has significant effects on these patient's survival time which is in line with the Li's study (Li et al., 2013). Also Morrison's study indicated only age was significant determinant of both colon and rectum cancer (Morrison et al., 2013). The sex ratio 1.24:1(male: female) for colorectal cancer is approximately equal to the results of Safaee's research (Safaee et al., 2012). Although the CIF curve shows higher survival rates for men than women, the difference is not significant; so gender does not have statistically significant effect on survival time which is in line with the li's study as well (Li et al., 2013).

These results are in contrary with Heidarnia's study in which age and gender have statistically significant effect on colorectal patient's survival time (Heidarnia et al., 2013).The effect of height did not have statistically significant effect on survival time of colorectal patients while Batty et al (2010) study in Asian Pacific shows that it has significant effect on diagnosis of the cancer.

Age at diagnosis of the cancer has significant effects on patient's survival time. One can conclude a patient whose disease has diagnosed before the age of 53 has a longer life in comparison to one whose disease has diagnosed after the age of 53. This study shows that the Iranian data still suggest a younger age distribution compared to Western report for CRC. Appropriate screening strategies especially in relatives of the patient should be considered (Pourhoseingholi and Zali, 2012).

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