ORIGINAL ARTICLE

Prevalence of hypertension and type 2 diabetes mellitus in patients with colorectal cancer and their median survival time: A cohort study

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Background: Type 2 diabetes mellitus (DM) and hypertension are worldwide epidemic. Association between DM and colon cancer was obtained in previous studies. Prevalence of DM and hypertension in the patients with colorectal cancer (CRC) has not been reported in Iran. The present study was aimed to investigate the prevalence of hypertension and type 2 DM and their effect on median survival time in patients with CRC. **Materials and Methods:** Overall, 2570 individual-year follow-ups were conducted for 1127 patients with CRC. For the diagnosis of type 2 DM, fasting blood sugar test and glycosylated hemoglobin test were used and for hypertension, blood pressure was measured in two turns. The descriptive indices were calculated, and the mean and median survival from CRC diagnosis time was calculated using survival analysis and a comparison among survival times was done through log-rank test. Stata software 12 (Stata Corp. 2011. Stata Statistical Software: Release 12. College Station, TX: Stata Corp LP) was used for data analysis. **Results:** The prevalence of hypertension and type 2 DM in the patients with CRC was respectively 13.38% (95% confidence interval [CI]: 11.1-15.8) and 8.69% (95% CI: 7-10.7). Median survival time in patients with hypertension and DM were 8.52 and 4.9 years. According to log-rank test, no significant difference was observed between the survival time of CRC patients suffering from hypertension and diabetes type 2. **Conclusion:** The obtained findings in this study indicate that survival time in patients with type 2 DM less than hypertension but two metabolic diseases have the same effect on survival rate of the patients with CRC. Understanding the risk factors for CRC may guide the development of strategies targeted toward its prevention.

Key words: Colorectal cancer, diabetes, hypertension, survival time

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INTRODUCTION

Today, cancer is one of the important, fundamental problems in health and treatment worldwide, and its importance is increasing in countries. Colorectal cancer (CRC) is the most prevalent gastrointestinal cancer and the cause of 10% of the cancer mortalities. In Iran, the frequency rate of CRC has been considerably increasing in recent year. Different genetic and environmental factors contribute to the development of this cancer.[1] In addition, lifestyle is an important risk factor for the increased risk of CRC development. Low activity, inappropriate diet, smoking, suffering from metabolic syndrome (obesity, diabetes, hypertension, and dyslipidemia) alongside past medical and family history of cancer development, and polyp are among the risk factors of CRC occurrence.[2] In recent years, survival of CRC patients has enhanced in some regions of the world, and it is not clear which factors have contributed to this. According to the previous literature, body mass index (BMI), inflammatory bowel disease, alcoholism, tumor grade, lymph nodes metastasis, the degree of intestinal wall metastasis, metastasis of other organs, and tumor stage affect the survival of the patients while BMI, type of the first treatment, and metastasis of lymph nodes and other organs contribute to the time of death from CRC and hence it could be said that the effect of risk factors on different sections of colon is different and should be investigated separately.[3] An increasing number of epidemiologic Researches have found that diabetes mellitus (DM) may change the risk of developing a variety of cancers. Higher insulin levels may contribute to increased tumor Growth.[2] In another study, mean survival time of patients with colon cancer was estimated 7.75 ± 1.118 years and that of patients with rectum cancer 3.917 ± 0.26.[3] In a research conducted on female patients with CRC, longer survival was more likely in patients with no history of inflammatory bowel

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disease, distinguished, weak tumor grade, and tumor pathologic with stage one.[4] Type 2 DM and hypertension are a worldwide epidemic. Worldwide, approximately 1 billion people have hypertension, contributing to >7.1 million deaths per year. The increase in the rate of hypertension and type 2 DM could be attributed to the aging of the population, obesity prevalence, salt intake, sedentary life, urbanization, and socioeconomic changes. Patients with diabetes and hypertension are at a higher risk than the general population of developing cancer. There is a growing body of evidence published in recent years that suggest a substantial increase in cancer incidence in diabetic patients. The worldwide prevalence of diabetes was estimated to rise from 171 million in 2000 to 366 million in 2030. About 26.9% of all people over 65 have diabetes, and 60% have cancer. Overall, 8-18% of cancer patients have diabetes.[5-10] In Iran, prevalence of hypertension and type 2 DM in patients with CRC are unknowns. The present study was aimed to investigate the prevalence of hypertension and type 2 DM and their effect on median survival time in patients with CRC.

MATERIALS AND METHODS

In this study we analyzed the data of a prospective, cohort study conducted by Gastroenterology and Liver Disease Research Center affiliated to Shahid Beheshti University of Medical Sciences. The study population was patients with diagnosed CRC from 10 gastrointestinal clinics. Informed, written consent was obtained from all the patients and the design of the study was approved by Shahid Beheshti University Ethics Committee (approval no. 676). The patients were followed-up from definite diagnosis of CRC till death or completion of the study or their censoring once each 6 months. Overall, 2570 individual-year follow-ups were conducted for 1127 patients with CRC. The study was initiated at September 23, 2006, and the patients were followed-up until October 23, 2011. CRC diagnosis was determined according to criteria of International Classification of Pathologies and Diseases, the pathology report, and criteria of American Commission on Cancer. The final outcome in patients was asked through telephone contact. The required data were obtained from 98% of the patients. The test for diagnosing type 2 diabetes and hypertension were done at enrollment of the participants. Diagnosis of the above disease has been made at first stage of cancer. For the diagnosis of type 2 DM, fasting blood sugar test and glycosylated hemoglobin test were used and for that of hypertension, blood pressure (BP) was measured in two turns. BP was measured twice at 5 min interval by a mercury sphygmomanometer. KorotKoff first and fifth phase sounds were recorded as systolic and diastolic BP. The average of these four readings was used for analyses. Hypertension is defined as BP in excess of 140/90 mm Hg. HbA1c was measured using column chromatography method with Nyco card reader II made in Norway. Fetal bovine serum was measured using a spectrophotometer by Erba-XL 300 made in Germany. We estimated and graphed survival curves using the Kaplan-Mier method for CRC patients with DM, hypertension and both of them separately. We also compared survival curves of these groups of patients with log-rank test. To calculated prevalence and data analysis was used stata software (Stata Corp. 2011. Stata Statistical Software: Release 12. College Station, TX: Stata Corp LP). $P > 0.05$ were considered to be significant ($P < 0.05$).

RESULTS

Mean age of the patients at diagnosis was 53.38 (standard deviation [SD]: 14.3) years and the mean tumor size was 53.35 (SD: 31.9) mm. 30.2% of the patients were under 45-year-old, 45.5% between 45 and 65-year-old, and 24.2% over 65-year-old. 61.3% of the patients (*n*: 690) were male. According to the histopathological diagnosis 55.5% of the patients were in grade one, 35.7% in grade two, 8.8% in grade three and four of the disease. Patients' characteristics for demographic variables and mortality rate due to CRC are shown in Table 1. The prevalence of hypertension and type 2 DM in the patients with CRC were respectively 13.38% and 8.69%. The prevalence and confidence interval (CI) of hypertension and type 2 DM are shown in Table 2. Mean and median survival time with CI is shown in Table 3. According to log-rank test, no significant difference was observed between the survival time of CRC patients suffering from hypertension and diabetes type 2 ($P = 0.8188$). Median survival time in patients with hypertension and DM were 8.52 and 4.9 years.

Table 1: Patients' characteristics for demographic variables and mortality rate due to CRC

Variable	Percent	Death	Mortality rate	CI 95% IMR
Gender				
Men	61.3	150	96.9	82.9-113.8
Women	38.7	85	83	67.1-102.7
Marital status				
Married	93	197	85.3	74.2-98.1
Nonmarried	7	24	161	107.9-240.3
Grade				
I	55.5	66	66.1	51.8-84
II	35.7	63	98.6	77-126
III	8.8	20	123.7	79-191
Stage				
First stage	45.2	76	70.6	56.4-88.4
Advanced stage	54.8	124	109.8	92-131
Age groups (year)				
<45	30.2	73	89	70.8-112
45-65	45.5	99	83	68.6-101
>65	24.3	63	111	87-142

CRC = Colorectal cancer; CI = Confidence interval; IMR = Incidence mortality rate; DM = Diabetes mellitus

Table 2: The prevalence (P) of hypertension and type 2 DM in first stage of CRC patients

Disease measure	Total patients			Men			Women		
	Number	Prevalence	95% CI	Number	Prevalence	95% CI	Number	Prevalence	95% CI
Hypertension	116	13.38	11.1-15.8	46	6.6	5.3-7.5	70	16.01	15.2-16.8
DM	77	8.69	7-10.7	28	4.05	3.7-5.2	49	11.21	11-12.2
Both*	26	3.03	1.9-4.3	10	1.44	1.2-2.3	16	3.66	2.8-4.2
With neither* (CRC)	908	0	0	606	0	0	302	0	0

*Hypertension and DM; CRC = Colorectal cancer; CI = Confidence interval; DM = Diabetes mellitus

Table 3: Mean and median survival time with CI in the patients suffering from hypertension and type 2 DM

Medical situation	Survival time				*P* (log-rank test)
	Mean	95% CI	Median	95% CI	
Without hypertension and DM	9.31	7.56-11.06	6.66	5.13-13.1	Reference
Without hypertension and with DM	5.46	4.84-7.07	4.9	3.58-4.91	0.871
With hypertension and without DM	7.69	5.87-10.17	8.52	4.01-8.6	0.638
With hypertension and DM	5.15	3.88-6.42	4.3	3.32-4.85	0.399
Total patients	9.43	7.83-11.02	3.07	6.86-19.53	0.818

CI = Confidence interval; DM = Diabetes mellitus

DISCUSSION

Colorectal cancer is ranked as the fourth cause of death from cancers with 320,600 mortalities in men after lung cancer, liver cancer, and gastric cancer and as the third cause of death with 288,100 mortalities in women after lung cancer and breast cancer in the world.[11,12] In Iran, this cancer has been reported to occur in seven per 100,000 individuals.[12,13] It seems that rapid growth of CRC in our society could be derived from the contribution of environmental factors including particular nutritional habits such as increase in carbohydrates and fat consumption and decrease in fiber intake especially among youth, change of lifestyle, lack of sufficient activity and obesity, large numbers of youth in society, and possibly involvement of genetic issues.[14] The rate of CRC survival in Iran is low compared with advanced countries. Income status, alcohol consumption history, metastasis, and the approach to diagnosis and treatment are among the factors effective on survival rate.[15] Diabetes and hypertension are among risk factors for CRC, in this regard, there are theories stating that the individuals with diabetes are at a higher risk of developing CRC compared with healthy individuals and it occurs in men more frequently compared with women. In addition decreased short-term survival rates were noted among diabetics undergoing surgical resection of CRC. The association between glucose-level and cancer was approximately linear across full range of fasting glucose-levels. An increase in 1 mmol/L of fasting plasma glucose-levels was associated with risk ratio (RR) 1.05 (95% CI; 1.01-1.10) and 1.11 (1.05-1.16) for incidental cancer in men and women, respectively. RR was 1.37 (1.14-1.64, for trend = 0.002) for all-site cancer incidence in men (excluding prostate cancer) and 1.42 (1.18-1.74, *P* for trend <0.001) in women.[15-19] Several case-control studies have also confirmed the positive association of diabetes with CRC occurrence in male patients, which is not the case for women. Most recent meta-analysis comprising 24 studies (8 case control and 16 cohorts) linked diabetes with modest increase in risk of CRC, the most common cancer of digestive tract in western societies, with RRs 1.26 (95% CI; 1.20-1.31).[20-28] Some mechanisms are suggested for the increased CRC occurrence in the patients with diabetes in comparison to healthy individuals. Diabetes cause slow transmission of substance throughout bowel which results in retention of intraintestinal toxic substances. Diabetes causes production of carcinogenic, biliary acids, the increase in blood insulin level causes an increase in tumor growth, and delayed transmission of carcinogenic substance exacerbates the damage to DNA and other cells.[24] A study of diabetic and nondiabetic individuals reported that substance transmission in intestine of diabetic individuals is 70-80% longer compared with nondiabetic.[25] In other studies, the symptoms of constipation in the patients with diabetes were more prevalent compared with nondiabetic individuals.[26,28] In a study conducted on women with diabetes, these women were found to have a higher risk of developing CRC; but the survival of the patients with CRC was not affected by diabetes, in a way that a same survival of CRC has been found for diabetic and nondiabetic individuals.[28] This study is consistent with the findings of the present study because diabetes had no effect on survival of CRC patients. In some studies the effect of hypertension on CRC has been measured, showing that the foods causing decline in BP, if consumed daily, contribute greatly to decrease in CRC occurrence.[29-31] In many studies, the patients with CRC and hypertension treated with bevacizumab had a higher likelihood of survival compared with the group not suffering from hypertension.[32-38] In the present study, hypertension had no effect on the survival of the patients with CRC and the prevalence of hypertension and diabetes type 2 in population under study was estimated 13.38% and 8.69%, respectively, while in a study in Malaysia on

138 patients with CRC, the prevalence of diabetes type 2 and hypertension was obtained 13% and 34.8%, respectively, reporting that these two metabolic diseases were associated with CRC.[30,31] The researchers found that among patients with early stage disease, patients with diabetes or high BP had a significantly greater risk of cancer recurrence rate and death after treatment. For example, 47.7% of patients who did not have diabetes were still alive 5 years after diagnosis compared to only 41.3% of patients with diabetes. When the researchers looked more closely, they also found that cancer recurrence rates at 5 years were approximately 8% higher in patients with diabetes or hypertension.

CONCLUSION

Diabetes and hypertension is a high-risk state for several diseases, such as CRC. The obtained findings in this study indicate that survival time in patients with type 2 DM less than Hypertension, but two metabolic diseases (type 2 DM and hypertension) have no effect on survival rate of the patients with CRC and the survival of these patients may be dependent on other factors including the site of cancer, the stage when the disease is diagnosed to treatment commencement, type of treatment, nutrition status, etc.

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AUTHOR'S CONTRIBUTION

All authors contributed in design of the research. AA and SSH analyzed the data. MM, ZM and AB wrote the manuscript. SSH, MM, AA and AB edited the paper. All authors read and approved the paper.

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