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Does ethnicity affect survival following colorectal cancer? A prospective, cohort study using Iranian cancer registry

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Abstract

Background: The present study compared the differences between survivals of patients with colorectal cancer according to their ethnicity adjusted for other predictors of survival.

Methods: In this prospective cohort study patients were followed up from definite diagnosis of colorectal cancer to death. Totally, 2431 person-year follow-ups were undertaken for 1127 colorectal cancer patients once every six months. The data were analyzed by stata software using bivariate analysis, multivariate analysis, and Cox regression.

Results: The age at diagnosis was significantly different between men and women ($p<0.03$). 61.2% were male and the rest were female. Most patients were Fars (51.2%), followed by Turciks (21.5%), Kurds (8.2%), and 7.5% Lurs. Of the patients, 75% had a survival of more than 2.72 years, 50% a survival of 5.83 years, and 25% longer than 13.1 years after diagnosis. Risk ratio was significantly different among ethnics ($p<0.05$). The variables of ethnicity, being non married, tumor grade, family history of cancer, and smoking were considered as determinants of the patients' survival in Cox regression model. The median survival time in Fars, Kurds, Lurs, Turks and other ethnics was 5.83, 2.44, 5.49, and 8.52 years, respectively.

Conclusion: Ethnicity and access to healthcare are predictors of survival of patients with colorectal cancer which may define priorities in controlling cancer and implementing interventional and prevention plans.

Keywords: Colorectal cancer, Disparity, Ethnicity, Mortality, Survival time.

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Introduction

Colorectal cancer (CRC) is one of the most important reasons for death worldwide. It is the third leading cancer resulting in death in western countries (1). Racial-ethnic disparities are well known for influencing CRC outcomes. The global burden of cancers is increasing. The survival of the sufferers in developing countries is less compared to developed countries. In developing countries, cancer is diagnosed at late stages and access to standard diagnostic and therapeutic services is limited (2). CRC is the third prevalent cancer among men and the second prevalent cancer among women. In 2008, more than 1.2 million new cases of CRC and 608700 deaths due to CRC were reported (1-3). CRC is also the second cancer leading to death in the United States. Although CRC-associated deaths are declining in the United States, racial and ethnic disparities exist in its outcomes. One of the reasons is that ethnic minorities are less willing to undergo CRC screening (4). Low socioeconomic status is also inversely associated with increase in the risk of CRC occurrence. The risk of CRC in low socioeconomic classes is 30% higher compared to high socioeconomic classes (5). The increase in CRC prevalence is rap-

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idly growing in the countries with western culture (6). CRC occurrence is mainly observed in the population above 55 years old. The occurrence is different among different populations and is decreasing in the United States (7,8). There is some hidden or constant increase in CRC in Europe. CRC is also on increase in Asian countries (9). Ethnic and/or racial disparities appear to influence CRC occurrence in many countries including the United States, New Zealand, and Australia (between natives and non-natives, and blacks and whites) (8,10-13). Iran is also a multi-ethnic country. Different access rate to diagnostic and therapeutic services play the most important role in ethnic CRC disparities (10,14). Regarding lack of report on survival time for CRC in Iranian societies we conducted the present study to compare the survival rate in the patients with CRC according to their ethnicity. The present study compares the differences of survival of patients with colorectal cancer according to their ethnicity adjusted for other predictors of survival in these patients.

Methods

The present study was a prospective, cohort one. Data were obtained from Cancer Registry Center of the Research Institute of Gastroenterology and Liver Disease (RIGLD) affiliated to Shaheed Beheshti University of Medical Sciences, Tehran, Iran. The time period of the study was specified from 2008 to 2012. The patients from public and private collaborative hospitals were treated and referred to the cancer registry. This study was based on the data derived from cancer registry forms including demographic variables, family history, and diagnosis. All patients with CRC diagnosis based on the pathology report of cancer registry were eligible for this study. Each participant was interviewed by a physician who performed a physical examination and obtained a detailed medical history. The data were recorded meticulously. The outcome in question was survival time of the patients from the time of diagnosis. The main exposure in question was the patients' ethnic which was measured by questionnaire and categorized into five categories (Fars, Turks, Kurds, Lurs, and others). To evaluate other prognostic factors of survival we also entered the following variables in the model: tumor stage according to tumor, node, metastases (TNM) index (advanced stage versus early stage), tumor grade (grade III to IV, grade II versus grade I), marital status (married versus non married), gender (female versus male), education (university degree, high school, primary school versus illiterate), age group (>65years, 45-65 years, versus<45 years), family history of cancer (yes versus no), and current smoking situation (smoking versus nonsmoking). CRC diagnosis was done according to the criteria of International Classification of Diseases and Pathologies and US Commission on Cancer's Report of Pathology and Criteria.

This study held Shaheed Beheshti University of Medical Sciences Ethics Committee's approval no. 676. All the patients signed an informed consent before taking part in the study. All the patients were followed up from the time of diagnosis until death or completion of study time. Final outcome was asked by telephone call during each 6 months through follow-up. Response rate was very good and 98% of patients were followed up. Descriptive indices, occurrence rate were calculated and univariate analyses were performed. Cox regression model was used to assess the effect of ethnicity on survival adjusted for other prognostic variables. Proportional hazards assumption was evaluated by measuring Schoenfeld residuals for the variables entered into the model. P value less than 0.05 was considered as the level of significance. All the analyses were performed using Stata software version 12.

Results

Totally, 2431 person-year follow-ups were performed for 1127 patients with CRC. Of 1127 patients with CRC, 690

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Table 1. Demographic and clinical characteristics of population under study and 3/5 year mortality rate in demographic and clinical subgroups of patients

Characteristic		No. (%)	Death (No.)	IRM * (per 1000)	IRM (95% CI)
Ethnicity	Fars	52	120	94.5	79 – 113.1
	Kurd	8.2	15	103.7	62.4 – 171.9
	Lur	7.5	16	88.7	54.3 – 144.8
	Turcik	21.5	38	70.8	51.5 – 97.3
	Others **	10.8	46	153	114.6– 204.2
Age Group	< 45	30.2	73	89	70.8 – 112
	45-65	45.5	99	83	68.6 – 101
	> 65	24.3	63	111	87 - 142
Sex	Male	61.3	150	96.9	82.9 – 113.8
	female	38.7	85	83	67.1 – 102.7
Marital status	Married	93	197	85.3	74.2 – 98.1
	non married	7	24	161	107.9 –240.3
Education	illiterate	26.5	56	113	86.9 – 146.8
	primary school	32.2	49	79.8	60.3 – 105.5
	high school	24.5	35	76.2	54.7 – 106.1
	university	16.8	31	80	56.3 – 113.9
Tumor grade	grade I	55.5	66	66.1	51.8 – 84
	grade II	35.7	63	98.6	77 – 126
	grades III to IV	8.8	20	123.7	79 - 191
Stage	early stage	45.2	76	70.6	56.4 – 88.4
	advanced stage	54.8	124	109.8	92 - 131
Family history of cancer	No	63.2	145	99	84 – 116
	Yes	36.8	79	78	62 - 97
Smoking	No	73.5	150	86.8	64-101.9
	Yes	26.5	65	101.5	79.6-129.5

* Incidence rate of mortality, ** Others: Balouch, Gilaki, Mazani, Arab, and Afghan.

(61.2%) were male and 437 were female. Their age range was 14-94 years old. Mean (SD) of age at the time of CRC diagnosis was 53.5 (14) years. Of the patients, 30.2% were under 45 years old, 45.5% were 45-65 years old, and 24.3% were older than 65 years old. Most patients (45.5 %) were at 45-65 years age group. The mean age at diagnosis was 54.3 years for men and 52.4 years for women. The difference was statistically, but not practically, significant ($p< 0.03$). Most patients were Fars (51.2%), followed by Turciks (21.5%), Kurds (8.2%), Lurs (7.5%), and other ethnics (consisting of Balouch, Gilaki, Mazani, Arab, and Afghan (10.8%)).

Table 1 shows the demographic characteristics of the population under study and also the basic statistics about the outcome in different subgroups of demographic characteristics and clinical stages of the patients. Of the patients, 75% had survival of more than 13.1 years, 50% survival of 5.84 years, and 25% survival of longer than 13 years after diagnosis. Among the ethnics, Kurds had the highest incidence rate of mortality (IRM) (103.7) and Turks the lowest (70.8). Hazard ratio was significantly different among different ethnics ($p< 0.05$). The variables of ethnicity, being non married, cancer grade, family history of cancer, and smoking were considered as determinants of the patients' survival in Cox regression model. The median survival time in Fars, Kurds, Lurs, Turks, other ethnics, and all of the patients was respectively 5.83, 2.44, 5.49, 8.52, and 3.72 years.

Results of univariate and multivariate Cox regression analysis for estimating the hazard of ethnicity adjusted for demographic and clinical characteristics on mortality of CRC patients are presented in Table 2.

Discussion

Conventionally, a group of people with similar or common ancestral and familial characteristics is called ethnicity. Ethnic groups hold cultural, lingual, behavioral, and religious commonalities which may go back to their ancestors and/or could emerge for other reasons. Therefore, an ethnic group could be a cultural community as

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Table 2. Results of univariate and multivariate cox regression analysis for estimating the hazard of ethnicity adjusted for demographic and clinical characteristics on mortality of CRC patients

Characteristic		Univariate Analysis: HR (95% CI)	Multivariate Cox model			
			Hazard Ratio	SE	P-Value	95% CI
Ethnicity	Fars	-	-	-	-	-
	Kurd	1.1 : 0.6-1.8	1.95	0.65	0.046	1.01 – 3.76
	Lur	0.9 : 0.5 – 1.6	0.44	0.19	0.071	0.18 – 1.07
	Turcik	0.7 : 0.5 – 1.1	0.59	0.17	0.071	0.33 – 1.04
	Others *	1.6 : 1.1 -2.3	1.44	0.45	0.234	0.78 – 2.67
Marital status	Married	-	-	-	-	-
	non married	1.8 : 1.2 – 2.8	2.14	0.63	0.010	1.19 – 3.84
Education	Illiterate	1.4: 0.9 -2.1	1.54	0.43	0.12	0.89 – 2.68
	Primary school	0.9 : 0.6 -1.5	0.93	0.26	0.806	0.53 – 1.63
	High school	0.9 : 0.5 -1.5	0.94	0.99	0.849	0.51 – 1.72
	University	-	-	-	-	-
Tumor grade	grade I	-	-	-	-	-
	grade II	1.4 : 1.1 -2.1	1.21	0.26	0.372	0.79 – 1.86
	grades III to IV	1.8 : 1.1-3.1	2.11	0.61	0.010	1.19 – 3.75
Age of Diagnosis		1.2 : 0.9 – 1.7	1.004	0.07	0.611	0.98 – 1.01
Family history	No	-	-	-	-	-
	Yes	0.7 : 0.6 – 1.1	0.58	0.12	0.014	0.38 – 0.89
Smoking	No	-	-	-	-	-
	Yes	1.1 : 0.8 – 1.5	1.55	0.32	0.036	1.03 – 2.34

* Others: Balouch, Gilaki, Mazani, Arab, and Afghan.

well. In slavery and feudal societies, ethnicity is referred to a kind of commonality among people with blood ties, shared land, language, and culture; however, this commonality is not firm enough and, in national scale, the economic commonalities are not still complete. Iran's nation consists of different ethnics including Fars (53%), Azarbaijanis (16%), Kurds (10%), Gilakis and Mazanis (7%), Lurs (6%), Balouch (2%), Arabs (2%), Turkmens and Qashqais (2%), and others (2%). Ethnicity is used as an important underlying variable in examining health and equality of accessing healthcare and treatment services (25-27). Ethnicity could represent a genetic factor, environmental exposure, and nutritional habits of a particular ethnic group in a region. Study of diseases in different ethnics could help in identifying genetic and environmental reasons for disease, the difference in diseases' burden, and the interventions undertaken for reducing this difference in society (27). In the present study, a disparity was observed in CRC-associated risk ratio among Iranian ethnics. In Iran diagnostic, healthcare, and therapeutic services for CRC have been concentrated in Tehran and other major cities, which is different from smaller cities and settlements of ethnic minorities.

This research is the first conducted on the role of ethnicity in survival after colorectal carcinomas in Iranian population. Comparison among Iranian ethnics indicated that Kurds had the minimum survival and Turks had the maximum survival following colorectal carcinoma. In Cox regression model, risk ratio despite other variables and controlling for confounding factors was obtained as 1.95 for Kurds, which was significant (p=0.046). It was obtained as 0.44 for Lurs, which was the lowest in the model. The third grade of cancer, family history of cancer occurrence, and smoking were significant variables ($p<0.05$) in Cox regression model. Our results are consistent with those of studies that reported disparities in occurrence rate of cancer in Hispanic whites and non-Hispanic populations in the United States (1,8). In the present study, CRC and its associated mortalities were strongly and inversely associated with the level of education and literacy. CRC Survival in illiterate patients was lower compared to the literate. This is also consistent with studies conducted in other countries (5,11). Therefore, the illiterate people should be given priority in interventions, control, and prevention plans developed for

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CRC. The stage or grade of CRC at diagnosis was an important and significant variable in the model, which is consistent with another study (12). CRC-associated mortalities were higher in above 65-year-old patients compared to the other age groups. There was no significant difference in survival between the two genders. However, the age at diagnosis was two years lower for women compared to men. This finding probably is in agreement with other studies reporting that women follow healthcare more and have higher rate of participation in screening plans compared to men (15-19). In the present study, smoking increased the risk of death in the patients, which is consistent with a study in the United States that reported smoking increased mortality risk after CRC diagnosis (20). In this study, positive family history was not a significant risk factor for increase in death and decrease in survival. In several studies, positive family history has been offered as a factor for screening CRC. However, a study conducted in Germany reported that smoking and being male are more effective on CRC compared to family history, (21) that is consistent with our study. The median of survival time after CRC treatment was 4-13 months in the present study and 15.4 months in a study conducted in the United States (22). In our study, survival of the married was higher than that of non-married, which is in agreement with similar studies (23,24). In the present study, the demographic determinants of the patients' survival are consistent with similar studies. Risk ratio for CRC death has been reported in terms of ethnicity.

Conclusion

Therefore, through determining the above-mentioned variables, policy makers and planners of health system could pay more attention to access to and quality of the diagnostic and therapeutic services in Iranian ethnics and promotion of these services in the ethnics with shorter survival time, and hence decrease the disparity in the patients' survival in different ethnics. Relevant studies in national scale are recommended to determine genetic or environmental reasons for the disease including nutritional regime and cultural and behavioral habits in different ethnics to establish the reasons for the difference in CRC survival among the ethnics. Socioeconomic status, ethnicity, and access to health care may explain major ethnic disparities in CRC patients. Addressing priorities in controlling cancer and implementing interventional and prevention plans is recommended.

Conflict of interest

The authors of the present work declare no conflict of interest.

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