

## RESEARCH ARTICLE

# Social Determinants of Health and 5-year Survival of Colorectal Cancer

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### Abstract

**Background:** Early in the 21st century, cancers are the second cause of death worldwide. Colon cancer is third most common cancer and one of the few amenable to early diagnosis and treatment. Evaluation of factors affecting this cancer is important to increase survival time. Some of these factors affecting all diseases including cancer are social determinants of health. According to the importance of this disease and relation with these factors, this study was conducted to assess the relationship between social determinants of health and colon cancer survival. **Materials and Methods:** This was a cross-sectional, descriptive study for patients with colon cancer registered in the Cancer Research Center of Shahid Beheshti University of Medical Science, from April 2005 to November 2006, performed using questionnaires filled by telephone interview with patients (if patients had died, with family members). Data was analyzed with SPSS software (version 19) for descriptive analysis and STATA software for survival analysis including log rank test and three step Cox Proportional Hazard regression. **Results:** Five hundred fifty nine patients with ages ranging from 23 to 88 years with mean  $\pm$  standard deviation of  $63 \pm 11.8$  years were included in the study. The five year survival was 68.3% (387 patients were alive and 172 patients were dead by the end of the study). The Cox proportional hazard regression showed 5-year survival was related to age (HR=0.53,  $p=0.042$  for  $>50$  years versus  $<50$  years old) in first step, gender (HR=0.60,  $p=0.006$  for female versus male) in second step, job (HR=1.7,  $p=0.001$  for manual versus non manual jobs), region of residency (HR=3.49,  $p=0.018$  for west versus south regions), parents in childhood (HR=2.87,  $p=0.012$  for having both parents versus not having), anatomical cancer location (HR=2.16,  $p<0.033$  for colon versus rectal cancer) and complete treatment (HR=5.96,  $p<0.001$  for incomplete versus complete treatment). **Conclusions:** Social determinants of health such as job, city region residency and having parents during childhood have significant effects in 5-year survival of colon cancer and it may be better to consider these factors in addition to developing cancer treatment and to focus on these determinants of health in long-time planning.

**Keywords:** Social determinant of health - colorectal cancer - survival - Iran

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### Introduction

Early in 21<sup>st</sup> century, cancers are the second cause of death and have the highest burden of diseases (Boyle et al., 2008). According to the WHO world health statistics report 2012, the estimated annual cancer deaths will increase from 7.6 million in 2008 to 13 million in 2030 (World Health Statistics Report, 2012). In EMRO (Eastern Mediterranean Office Region) and Iran, cancers are third cause of death (Mathers et al., 2001). Among cancers, colon cancer is third cause of death after lung and stomach cancer (WHO, 2009) and in Iran, is third and fourth cause of death among men and women, respectively (Sadjadi et al., 2005). Population studies in Iran show increasing average age of population, so it suggests that cancers will increase in future (Jemal et al., 2011). According to increasing burden and prevalence of cancers with time, it is

necessary to focus on key factors in addition to developing diagnostic and treatment modalities and considering causes of diseases. Social determinants of health are the important factors affecting diseases which include: early life, social gradient, workplace, unemployment, diet, transportation, addiction, social isolation and support (Marmot et al., 2006).

Based on evidence, poor countries have more inadequate health consequences than rich countries (Wagstaff, 2002). Compared to high socioeconomic status, people living in low socioeconomic status, have poorer health and shorter life (Niu et al., 2010). Social determinants of health, especially socioeconomic status of cancer patients, have an important role; although there are sophisticated diagnostic and treatment modalities. These factors play an important role in prevalence, screening, morbidity, mortality and survival of cancers (Jemal et al.,

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2004; Robbins et al., 2012). Some cancers have genetic origin (Burke et al., 1997), whereas, others were seen in some especial races (Ghafoor et al., 2003). Differences in prevalence and mortality of cancers in difference ethnic/race groups are related to differences in social factors rather than genetic and cultural factors nowadays (Glanz et al., 2003). One study showed that participation in screening programs is higher in high socioeconomic people (Wardle et al., 2004). In low socioeconomic status, there is higher number of diagnoses in later stages and lower survival rate which is correlated to lower access of vulnerable individuals to health care systems (Groome et al., 2008; Chau et al., 2013). Colon cancer is the only common cancer which is relatively curable by early diagnosis and treatment. Therefore, determining the role of these factors in colon cancer can be effective in increasing survival. Considering importance of cancer and correlation of prevalence, morbidity, mortality and survival of cancer with social factors such as socioeconomic status, it seems that study to understand correlation of social determinant of health and survival time of colon cancer is necessary. The aim of the study was to determine the correlation of social determinants of health and survival time of colon cancer.

## Materials and Methods

This was a cross-sectional, descriptive study for patients with colon cancer registered in Cancer Research Center of Shahid Beheshti University of Medical Science, since April 2005 to November 2006. Inclusion criteria were residency in Tehran in mentioned period, so patients living out of Tehran were excluded. Study sample was calculated by use of survival sample size formula. The least sample size with 5%  $\alpha$  and 20%  $\beta$  with complete 5-year survival is 380.

The questionnaire of social determinants of health was designed including social factors: city region residency, education level, occupation; economic level: income, average living area; behavioral risks: smoking, addiction; early life status: living site in childhood, parents in childhood; individual factors: age, gender, family history of colon cancer, cancer location; health care access: health insurance status, treatment type, complete course of treatment and follow up.

To classify Tehran city regions into 5 regions, Urban HEART Study (Fereshtehnejad et al., 2010) was used which classified regions as follows: North: 1, 2, 3, 6, East: 4, 7, 8, 13, West: 5, 21, 22, Center: 9, 10, 11, 12, South: 14, 15, 16, 17, 18, 19, 20, 21, 22.

Education was categorized into three levels: less than high school (< 8 years), high school (8-12 years) and academic (>12 years). Elias (1997), occupational classification was performed using ISCO88 international classification which has 10 major groups and 390 classes of jobs. In this study, some groups were merged because they were too small.

Income was categorized into three levels: first level (less than 500,000), second level (500,000 - 1,000,000) and third level (>1,000,000) Tomans.

Also economic status was assessed by average living

area in square meters per person ( $m^2/p$ ). Average living area or home size was categorized into three levels: less than 30, 30-60, equal or more than 60 square meters per person.

Method for collecting data was telephone connection and interview with patients, after gathering primary information from Cancer Research Center of SBUMS. Five hundred eighty connections were successful and interview with patients (if dead, with family and relatives) were performed. In telephone interview, first question was about present status of patient. Three hundred eighty nine patients were alive and interview was done with patient him/herself. One hundred ninety one patients had been died during the 5-year period and interview was done with his/her family. Interviewers were two college-educated people who were informed about interview and questioning pattern.

### Statistical analysis

Several social factors are known to predict long-term survival of cancer patients and they include age, gender, childhood status, inheritance, education, home size, job class, employment, city region residency, cancer location, insurance, treatment type, complete treatment, complete follow up, smoking and addiction status.

Prognostic factors of cancer were identified by using nonparametric survival methods such as Kaplan-Meier and Cox Proportional Hazard (PH) in many studies. This study used Kaplan-Meier method to determine risk factors which have effect on survival time of patients. The results of Kaplan-Meier are shown in Table 1.

Cox Proportional Hazard regression model was used to assess association between social determinants, which were meaningful in Kaplan-Meier, and survival time of patients diagnosed with cancer. Survival time was defined as a period between the diagnosis of disease and death or the end of 5<sup>th</sup> year.

A binary censoring variable was used to indicate whether a patient died of the cancer.

The Cox PH model is usually written in terms of the hazard model formula. This model gives an expression for the hazard at time  $t$  for an individual with a given specification of a set of explanatory variables. Results of the regression analysis are reported in the form of the hazard ratio (HR). In general, a hazard ratio is defined as the hazard for one individual divided by the hazard for a different individual. The Cox PH model assumes that the hazard ratio comparing any two specifications of predictors is constant over time. Equivalently, this means that the hazard for one individual is proportional to the hazard for any other individual, where the proportionality constant is independent of time.

In this study, Cox PH regression predicts the hazard ratio of cancer patients in terms of the demographic, socioeconomic, and health care access variables.

The models were derived in sequence based on the time-order of each group of variables, where demographic factors affect socioeconomic factors, which subsequently influence medical care access and hence, survival time. Therefore, Model 1 contains only demographic factors; Model 2 shows socioeconomic factors adjusted for

**Table 1. Case Summary and Overall Comparisons by Kaplan-Meier Method in 5-year Survival of Colon Cancer Patients in Cancer Research Center of Shahid Beheshti University of Medical Science**

Variable		Total No.	No. of Event	p value*
Age	<50 years	61	11	0.016*
	>50 years	504	162	
Gender	Female	265	64	0.002*
	Male	299	108	
Cancer Location	Colon	461	157	0.000*
	Rectum	105	16	
Parents	Both parents	536	153	0.000*
	Others	31	20	
Inheritance	Yes	124	50	0.009*
	No	438	123	
Education	<High school	303	99	0.396
	Diploma	157	47	
	Academic	101	27	
Income(Toman)	<500,000	362	112	0.549
	500,000-1000,000	172	61	
	>1000,000	42	14	
Home Size (m <sup>2</sup> /p)	<30	292	93	0.308
	30-60	186	56	
	>60	82	18	
Job Class	Manual	57	32	0.000**
	Non-manual	493	140	
District	North	231	60	0.012**
	East	84	38	
	West	33	12	
	Center	70	20	
	South	148	43	
Complete Treatment	Yes	499	111	0.000**
	No	63	61	
Complete Follow up	Yes	468	101	0.000**
	No	92	71	
Treatment Type	Surgery	495	142	0.061**
	Multiple treatment	64	27	
Smoking Status	Yes	85	23	0.486
	No	481	150	
Insurance	Yes	528	159	0.645
	No	35	11	
Childhood Residence	Rural	144	48	0.495
	Urban	422	125	

\*Log-rank test of equality of survival distributions for the different levels of variables; \*\*Columns labeled show statistically significant at p<0.05

demographic factors; and Model 3 consists of the full model, showing the effects of health care access factors controlling for all other factors in the model.

## Results

Study was performed on 580 colon cancer patients, 23-88 years old. Mean age was 63 years old (SD=11.8) and median age was 64 years old. After 5 years from diagnosing cancer, 387 patients (68.3%) were alive and 172 patients (30.3%) were dead.

Using log rank test, there were significant differences between different levels of KM survival distributions of variables age, gender, job, city region residency, parents in childhood (having Father and Mother), cancer location, family history of cancer and complete treatment and follow up (p<0.05) and there were no statistical significant differences in different levels of KM survival distributions of variables income, home size, education, insurance, treatment type, living location in childhood, smoking and addiction status (p>0.05).

Cox regression models, labeled Models 1, 2, and 3 in Table 2, were estimated to reflect the social determinants of survival time for patients diagnosed with cancer. The data showed that the hazard of dying due to cancer throughout five years is about half for younger patients to older ones. Holding all other demographic variables in the model constant, the hazard of patient under 50 years is 0.53 times of hazard for patients age 50 years and older (HR=0.53, p=0.042). Likewise, the hazard ratio of female to male is 0.59 (HR=0.59, p=0.001). There is also greater

**Table 2. Hazard Ratios of Death because of Colon Cancer by Cox PH Model of Patients in Cancer Research Center of Shahid Beheshti University of Medical Science**

Variable	Model 1			Model 2			Model 3			
	p value	HR	95%CI	p value	HR	95%CI	p value	HR	95%CI	
<b>Demographic</b>										
Age	<50 years	0.042*	0.53	(0.29,0.98)	0.060	0.55	(0.29,1.03)	0.162	0.57	(0.26,1.25)
	>50 years (ref.)		1.00			1.00		1.00		
Gender	Female	0.001*	0.59	(0.43,0.80)	0.006*	0.60	(0.42,0.86)	0.218	0.72	(0.43,1.21)
	Male (ref.)		1.00			1.00		1.00		
Cancer Location	Colon	0.000*	2.61	(1.55,4.39)	0.000*	2.65	(1.56,4.52)	0.033*	2.16	(1.06,4.37)
	Rectum (ref.)		1.00			1.00		1.00		
Parents	Both parents (ref.)		1.00			1.00		1.00		
	Others	0.002*	2.11	(1.31,3.40)	0.006*	2.03	(1.22,3.37)	0.012*	2.87	(1.26,6.54)
Inheritance	Yes (ref.)		1.00			1.00		1.00		
	No	0.250	0.82	(0.58,1.15)	0.068	0.71	(0.49,1.02)	0.809	0.93	(0.54,1.62)
<b>Socioeconomic</b>										
Education	< High school				0.434	1.23	(0.75,1.96)	0.788	0.91	(0.45,1.82)
	High School				0.470	1.21	(0.72,2.02)	0.936	0.97	(0.48,1.96)
	Academic (ref.)					1.00		1.00		
Home Size (m <sup>2</sup> /p)	<30				0.192	1.44	(0.83,2.51)	0.543	1.29	(0.57,2.90)
	30-60				0.294	1.33	(0.78,2.3)	0.397	1.38	(0.65,2.91)
	>60 (ref.)					1.00		1.00		
Job Class	Manual				0.000*	2.31	(1.45,3.66)	0.001	1.70	(0.90,3.21)
	Non manual (ref.)					1.00		1.00		
District	North				0.663	1.10	(0.70,1.73)	0.604	1.16	(0.65,2.08)
	East				0.008*	1.93	(1.19,3.13)	0.350	0.70	(0.34,1.47)
	West				0.186	1.57	(0.80,3.09)	0.018*	3.49	(1.24,9.81)
	Center				0.479	0.82	(0.47,1.43)	0.370	0.67	(0.28,1.61)
	South (ref)					1.00		1.00		
<b>Health Care Access</b>										
Treatment	Yes (ref.)							1.00		
	No							0.000*	5.96	(2.89,12.3)
Follow up	Yes (ref.)							1.00		
	No							0.273	1.48	(0.73,2.99)

\*Columns labeled show statistically significant at p<0.05

hazard associated with cancer location of colon rather than rectum (HR=2.61,  $p<0.001$ ). In addition, hazard of death for patients who were not raised by their parents in childhood is two times of the group who was raised by both parents (HR=2.11,  $p=0.002$ ). However the hazard for patients with risk of inheritance in their family was more than those without inheritance, this difference was not statistically significant ( $p>0.1$ ).

Socioeconomic factors are added to the analysis in Model 2. Despite being non-significant in Kaplan-Meier regression, "Education" and 'Home Size' were kept in the model because they are important in epidemiological research. The results of Cox model showed that education and home size did not have significant effects on survival time of patients ( $p>0.1$ ). However, the job class was meaningful; hazard of patients with manual job is almost two times of hazard of those with non-manual job (HR=2.31,  $p<0.001$ ).

Comparison of hazards of residents of North, west and East to hazard of South was only significant for East; the hazard of dying because of cancer within 5 years is almost two times for residents of East rather than South (HR=1.93,  $p=0.008$ ).

Model 3 shows the results of adding health care access to the analysis. Controlling for other variables in the model, findings showed that the hazard of patients who did not complete their treatment was about 6 times more than those who did (HR=5.96,  $p<0.001$ ); completing the follow up also decrease the hazards of patients' death but the change was not significant ( $p>0.1$ ).

## Discussion

This research is performed to assess the relationship between social factors affecting health and colon cancer survival in patients registered in Cancer Research Center of Shahid Beheshti University of Medical Science. According to the results, using three-step Cox regression models, 5-year survival was related to job, city region residency, parents in childhood, cancer location and complete treatment.

Results of this study are discussable on many points. First, 5-year survival differences between female and male colon cancer patients which were statistically significant in log rank test and Cox regression first step but in second step of regression, were because of socioeconomic factors affecting health, so it was not statistically significant. One possible explanation is that 5-year survival differences between female and male individuals are due to socioeconomic factors and by considering these factors, it seems that there is no difference in survival between female and male individuals. In other studies, Aarts and Moller showed the higher survival for female than male individuals (Aarts et al., 2010; Møller et al., 2011). The relationship between age and survival was significant and hazard ratio for under 50 years old individuals were half of individuals above 50 years old. In other studies, it has been shown that there is strong correlation between age and 5-year survival of cancer (Wrigley et al., 2005; Li et al., 2013). For older patients risk and benefit balancing, drug toxicity and co morbidities may be made more

complex in treatment decision making (Jorgensen et al., 2013). There is correlation between job and 5-year survival of colon cancer. Hazard ratio of patients in manual works was 2.3 times higher than patients in other jobs. In Eloranta study, also there was correlation between job and 5-year survival of colon cancer (Eloranta et al., 2010). Egeberg showed that unemployment and non-permanent income decrease the survival of colon cancer (Egeberg et al., 2008). Since job type determines the income and is a marker of social level, it has effective role in socioeconomic status and it's correlation with survival reflects the importance of socioeconomic status in 5-year survival of colon cancer. According to its level of significance ( $p=0.0001$ ) in Cox regression, job type is the most important factor determining survival rate after treatment. In this study, there was correlation between city region residency and 5-year survival. Although the reasons for difference between various regions are not characterized, it is clear that this difference is due to different socioeconomic factors in various city regions. Blais et.al obtained similar results in their study (Blais et al., 2006); the differences were attributed to social factors and different access to health care services. Dejardin showed that there is correlation between 5-year survival with city region residency because of distance to a cancer treatment center (Dejardin et al., 2006).

In this study, there was a correlation between complete treatment and increasing 5-year survival.

Other studies showed the strong relationship between increasing poor survival and decreasing quality of treatment (Kong et al., 2010; Rashid et al., 2009)

Although there was not statistically significant correlation between education and 5-year survival, hazard ratio 1.23 for college-educated to less than 8 year educated reflects the different survival rate between different educations that is noticeable. High average age (63 years old) and high percent of low educated individuals in this study may be the reasons for this non-significant correlation. There are different results in other studies in this regard. Dalton and Hussain showed direct correlation between education and survival of colon cancer (Dalton et al., 2008; Hussain et al., 2008). But in study by Menvielle in France, there was no correlation between education and colon cancer mortality (Menvielle et al., 2005). Although there was not significant correlation between home size and 5-year survival in this study, hazard ratio 1.599 for home size fewer than 30 to above 60 (square meters/person) reflects lower survival rate in lower home size; though it is not statistically significant, it is still noticeable. In Egeberg study, it has shown that decreasing survival is directly correlated to lower home size and renting (Egeberg et al., 2008).

There was no significant correlation between income and survival in the study. The studies of Shaw and Gorey showed that there is direct correlation between income and survival (Shaw et al., 2006; Gorey et al., 2011) which are different from our results. Although there was not significant correlation between income and survival, correlation between job type (which reflects income) and survival shows the effect of economic status on 5-year survival.

In this study, there was significant correlation between cancer location (colon vs. rectum) and 5-year survival. This result has been supported by other studies. Wray showed that in diagnosis, rectum cancer has lower stage due to lower mortality, compared to colon cancer (Wray et al., 2009). Meguid showed that survival of left colon cancer (which includes rectum) is higher than survival of right colon cancer (Meguid et al., 2008).

Although having parents in childhood associated to 5 year survival of colon cancer, this issue has not been addressed in other studies and more studies are needed to improve it.

In conclusion, this study showed the effects of social determinants of health especially job, city region residency and childhood condition on colon cancer survival. Further studies are recommended to assess socioeconomic status effect in details in cancers survival. Additionally, it is better to focus on these factors in addition to develop treatment modalities and to consider these determinants of health in long-time planning and policy making.

There were some limitations in the study. For dead patients, information obtained from family and relatives may not be accurate. Also, it may be recall bias in interviewing about the information referred to last 5 years of patients' life.

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