

Time of Occurrence and Age Distribution of Digestive Tract Cancers in Northern Iran

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(Received 24 May 2007; accepted 7 Jan 2008)

Abstract

Background: Previous studies indicate a high incidence of digestive cancers along southern parts of Caspian Sea including Mazandaran Province. The present study was conducted to further investigate time to occurrence, age distribution and possible risks associated with the incidence time of digestive cancers in the above regions.

Methods: For this purpose the data of digestive cancer incidence of 3723 cases during a five-year period of 2001 to 2005 collected from Babol Cancer Registry Center in Iran. Almost all cancer cases residence of Mazandaran Province is included in this study and so the results could be considered a population-based conclusion. In order to modify the mortality due to other causes before digestive cancers, and to adjust the effect of digestive cancers correlations, a competing risks model was used. The Cox regression model was used for study of risk factors on cancer incidence.

Results: Although incidence of colorectal cancer was relatively low, however, unfortunately the age of onset was at the age category of 15-19, much sooner than occurrence of stomach cancer which was at 20-24 yr ($P < 0.0001$), and esophageal cancer at age category of 30-34 yr ($P < 0.0001$).

Conclusion: Life tables of all digestive cancer, esophageal cancer, stomach and colorectal cancers were presented in this paper. Risks related to these cancers are significantly higher in men and residences of urban areas than their baseline counterparts. ($P < 0.0001$) More studies needed to identify risk factors and high risk cases for screening and prevention programs.

Keywords: Competing risks model, Digestive cancers, Survival analysis, UN west life table model, Iran

Introduction

The global burden of diseases has changed during the last century. The decreasing importance of infectious disease is not limited to developed countries; developing countries have experienced such changes too (1). Cancer is a serious health problem worldwide, imposing a large economical and psychological burden as well as loss of life and productivity (2). According to recent statistics issued by the Ministry of Health of Iran cancer is the third most common known cause of death in country, after cardiovascular diseases and accidents (3). For more than 40 yr, several groups have tried to map out cancer incidence rates in different area of Iran (4- 10). Among these, only the Caspian Cancer Registry located in the city of Babol which was established in 1969 by joint

collaboration of the Institute of Public Health Research of Tehran University and the IARC, has provided a reliable source of data on cancer incidence in the Caspian littoral of Iran (11). However, these efforts were discontinued due to the sociopolitical events of the 1980s in Iran. Babol cancer registration resumed its regular activities again in year 1990 as a local cancer registry.

We selected Mazandaran Province for two main reasons. Firstly, Mazandaran was reported to have a high incidence of gastric cancer in Iran. In this region, 38.8% of all cancer occurrences in females and 58.1% of all cancer occurrences in males was related to digestive system in 2003 (10). Secondly, the cancer registry data of this region was readily available to us and more reliable for data analyses. We aimed to obtain time to selected digestive can-

cers (all sites, esophageal, stomach, and colorectal) occurrence from the whole province, to select the target population for future screening and control trials and hot spots for future field studies. Multiple decrement tables are not only a useful way of summarizing mortality data of a given population subject to different risks of dying, but also a powerful analytical tool for studying decrement data in general. The concept of multiple decrements originated in investigations of components cause of death; however, it has many applications in other research areas. In this study, we considered two forces (hazard) of decrement, namely death and occurrence of digestive cancers. The multiple decrement tables are directly related to the theory of competing risks (12). The theory has been developed to evaluate the hazard of competing risks under investigation. According to this theory, there are two types of failure probability with respect to one or several risks: The crude probability (the probability of failure from a specific cause in presence of competition of other risks acting in a population), and partial crude probability (the probability of failure from a specific cause while other risks eliminated from the population). Assuming a competing risk model with two types of failure, death, and occurrence of digestive cancers, we calculate partial crude probability of digestive cancer occurrence (i.e., the probability of first digestive cancer occurrence when mortality is eliminated). These probabilities were used to construct the current multiple decrement life table and cumulative survival probabilities of digestive cancers occurrence in Mazandaran province.

Mazandaran Province, 23756 km², is 1.46% of the country and surrounded by Caspian Sea from the north and Elburz Mountain range from the south. The Elburz Mountain contains the Caspian Sea humidity to influence the central parts of Iran and causes lots of rainfall on the northern part of Elburz and inside Mazandaran. This climate distinguishes this part of the country from the rest which is much dryer. According to the last official geographic boundary Mazandaran contains 15 districts, 46 cities, and 110 counties. The province population in 2001 was 2,785,229 and 2,942,372

in 2005. From this, the urban population was 1,449,228 in 2001 and increased by 3% to 1,572,678 in 2005, while the rural population, which was 1,390,780 in 2001, increased only by 0.27% to 1,408,349 in 2005. Sixty five percent of the population is younger than 30. According to Statistical Center of Iran latest report, the life expectancy at birth is 67.7 yr for men and 70.5 for women (13).

Materials and Methods

Cancer reporting and Babol cancer registry

The population based cancer registry in Iran does not have a long history. In fact, a country-wide cancer registry started only in 1999 but due to infra-structural difficulties this has not been standardized and practically usable yet (10). However, regional cancer registry, especially those affiliated with Tehran University of Medical Sciences such as Babol cancer registry have longer history dating back to 1969. Until this time, the Babol cancer registry has responsibility of registering cancer cases in Mazandaran and neighboring Golestan Provinces. The major sources of data collection related to cancer cases in Babol cancer registry are reports from pathology laboratories, hospitals, and diagnosis radiology clinics. At the present, all 80 diagnostics and treatment centers in these two provinces cooperating with Babol cancer registry unit. The survey team responsible for collecting reports of new cancer cases had been trained to go to hospitals, pathology laboratories, diagnosis radiology, and out patient public and private clinics and check records for cancer cases monthly. Coding cancer samples are based on the third revision of the international classification of disease for oncology (ICD-O-3) coding (14) and are done by pathology specialists or under their supervisions. The demographic information of cancer patient is collected by trained operators during cancer report process. This information was then sent to the registry office in Babol. Trained operators summarized and saved the information in a data bank.

Quality of Data Collection The survey team enjoyed the close collaboration of all health authorities and physicians in Mazandaran region who

provided all necessary data and documents for the study. All information collected from cooperative centers were again checked carefully in Babol cancer registry for their completeness and accuracy of demographic information and re-checked with pathological records. In addition, the accuracy of cancer codes controls by the Babol center pathologist based on ICD-O method. Reported cancer cases stored in an Excel based data bank monthly, name, age at diagnosis, sex, residential address, race, type of cancer, and method of diagnosis are among collected information. Two independent group of operators are responsible for enter the new cases in separate data bank, these data bank are checked at several time occasion for potential data entry errors. After completion of data collection, all data were alphabetically organized and duplicate cases with the same name, sex, age and place of residence were eliminated by manual and computerized linkage. The quality of the recorded data assessed again by looking at the distribution of the data, the proportions of missing information, the presence of outliers and the proportion of registered cases whose information was obtained from dead certificate. Data processing of this study was based on an existing data bank in Babol Center and took approximately 6 months for completion. In order to make sure of a complete coverage of all cases, all cancers registered in Golestan province which again recorded by the same center and all cases in Gilan which recorded by Ramsar Center rechecked.

Study Population All residence of Mazandaran Province constitutes the research population of this study. The estimated mid- year population between 2001 until 2005, for gender, 5 yr age intervals, and residential place (rural- urban) was obtained from statistical center of Iran (15). In addition, all digestive system cancer patients registered between 2001 until 2005 who reside in Mazandaran province constitute the patients of this study. These cases based on ICD-O coding, including C00-C26. Among these esophageal cancer (C15), stomach cancer (C16), and colorectal cancer (C18, C19, and C20) will be investigated separately because of relatively higher incidences.

Statistical Methods The age specific cancer incidence for all types of digestive system cancers, esophageal, stomach, and colorectal cancer were calculated. This information was used to calculate the life table of digestive cancers incidence age. To model the competing risks we need the age specific mortality probabilities. Because there was no comprehensive death certificate system in Iran (3), the infant mortality information from reports of Ministry of Health of Iran was used (16). This has been proved to be more reliable than the above mentioned death certificates (17). Then using this information, the five-year interval probabilities of mortality for each gender and residential place were calculated based on projections of cohort component techniques by the West UN life table model (18).

In the first step of modeling, a two components model with mortality as a competing risk factor for digestive system cancer incidence was considered. In the second step a five components model with mortality, esophageal, stomach, colorectal and other digestive cancers as competing risks were considered. Assuming a proportional hazard assumption and using the competing risk technique, the partial crude probabilities of cancer occurrence were calculated. Using these probabilities, current life table and cumulative probability of occurrence age of selected digestive system cancers were calculated. Finally, considering the life table radix (l_0) equal to actual population size under risk instead of $l_0=100,000$, the effect of gender, place of residence, and their interaction in time to onset of digestive cancers of interest were investigated. This was done using the log-rank test and Cox proportional hazard model. Furthermore, the hazard ratios together with their 95% confidence intervals were calculated for all comparisons. P was calculated and reported as a measure to assess statistical difference among subgroups, and -2 Log likelihood was used for model comparisons.

Results

A total of 3723 digestive system cancers were registered in Mazandaran province for a period

of 5 years and all this data was used in present analysis. Among these cases, 727 are from year 2001, 765 from 2002, 720 from 2003, 769 from 2004, and 724 cases are from 2005 registry. Also 2330 (62.6 %) were male and remaining 1393 (37.4%) were female. From the registered digestive system cancers 944 (25.4%) had esophageal cancer, 1663 (44.7%) stomach cancer, 713 (19.2%) colorectal cancer, and 403 (10.7%) had other digestive system cancer. The average age for digestive cancer incidence was 63 ± 13.9 for both genders, 61.2 ± 13.9 in men, and 64.1 ± 13.7 in women, this difference was significant (*t*-test, $P < 0.001$). The overall average age of esophageal cancer incidence was 66.2 ± 11.8 , stomach cancer 65.2 ± 12.1 , colorectal cancer 55.6 ± 15.5 and of other digestive cancers was 55.7 ± 16.5 , the observed differences were statistically significant (one-way ANOVA test, $P < 0.001$). Also, 2077 (55.8%) of the digestive cancer cases were from urban areas and 1327 (35.6%) from rural. There was no report on residential places of the other 319 (8.6%) cases. Table 1 indicates the number and percentage of all different types of digestive cancers separated by gender and residential place. Table 2 presents results of life table for digestive cancer incidence: probabilities of age specific incidence of all digestive cancers, partial crude probabilities, and expected time of cancer incidence. The expected time of digestive cancer incidence for less than 5 yr old age category among the study population was 85.2 yr. This time was 84.8 yr for males and 85.6 for females who live in urban areas (log- rank test, $P < 0.001$) while this figure was 84.5 and 85.8, respectively, for males and females who live in rural areas (log-rank test, $P < 0.001$). Therefore, the time to cancer incidence is shorter in males than females also is shorter for those living in cities than in rural places. In fact, this pattern holds for all other age categories so that the excess hazard ratio of digestive cancer in males occurrence was estimated to be 1.31 with 95% CI [1.28- 1.34] more , and for females 0.69 with 95% CI [0.67- 0.71] less than that of the whole population (i.e. baseline). (log- rank test, $P < 0.001$). Furthermore, the ex-

cess hazard ratio of digestive cancer occurrence in urban areas was estimated to be 1.48 with 95% CI [1.44- 1.51] more, and for rural residence 0.62, with 95% CI [0.60- 0.64] less than that of the whole population. (i.e. baseline) (log- rank test, $P < 0.001$). Fig. 1 shows the cumulative survival probabilities of digestive cancer occurrence by gender and place of residence.

In Table 3, the life table of esophageal, stomach, and colorectal cancer were calculated using a five- components competing risk method. Since time to cancer incidence were different in males and females, time to cancer incidences presented separately for each gender in Table 3. The hazard ratio of esophageal cancer was 0.3, 95% CI [0.30-0.31], for stomach cancer was 0.47, 95% CI [0.46-0.48], and finally for colorectal cancer was 0.13, 95% CI [0.12-0.14], less than that of the other types of digestive cancers (i.e., baseline). These differences were all statistically significant. (log- rank test, $P < 0.001$). Fig. 2-4 demonstrate the cumulative survival probabilities of esophageal, stomach, and colorectal cancer for gender and place of residence subgroups separately.

Finally, simultaneous effects of gender and residential place, as well as, their interaction effect on digestive cancers incidence age were investigated. For this, the Cox regression models were used with all digestive cancers, esophageal cancer, stomach, and colorectal cancer as the end points. In all analyses age, gender, and their interaction were statistically significant. (Table 4) Since these interactions are highly significant, it is not possible to study factors separately. Thus, the rural females group was considered as the baseline for the hazard ratios of group comparisons. Results of these calculations with corresponding 95% confidence intervals are presented in Table 5. In all investigated end points the females resident in rural areas have the lowest risk and males residing in urban areas have the highest risk. In fact, our calculations indicate that risks of all different types of digestive cancers for urban males is 5 times more than the rural females and such risk increases by 7.8 in case of stomach cancer.

Table 1: Number and percentage of selected digestive cancers occurrence during 2001-2005 by gender and place of residence

Type of Cancer	Place of Residence	Sex		Total (%)
		Male	Female	
Esophageal	Urban	249 (26.4%)	242 (25.6%)	491 (52%)
	Rural	205 (21.7%)	154 (16.3%)	359 (38.0%)
	Unknown	53 (5.6%)	41 (4.3%)	94 (10.0%)
	Total	507 (53.7%)	437 (46.3%)	944 (100%)
Stomach	Urban	666 (40.0%)	256 (15.4%)	922 (55.4%)
	Rural	451 (27.1%)	157 (9.4%)	608 (36.6%)
	Unknown	93 (5.6%)	40 (2.4%)	133 (8.0%)
	Total	1210 (72.8%)	453 (27.2%)	1663 (100%)
Colorectal	Urban	239 (33.5%)	208 (29.2%)	447 (62.7%)
	Rural	121 (17.0%)	96 (13.5%)	217 (30.4%)
	Unknown	26 (3.6%)	23 (3.2%)	49 (6.9%)
	Total	386 (54.1%)	327 (45.9%)	713 (100%)
Other digestive cancers	Urban	124 (30.8%)	93 (23.1%)	217 (53.8%)
	Rural	80 (19.9%)	63 (15.6%)	143 (35.5%)
	Unknown	23 (5.7%)	20 (5.0%)	43 (10.7%)
	Total	227 (56.3%)	176 (43.7%)	403 (100%)

Table 2: Crude probability, partial crude probability, and expected time of digestive cancers occurrence for overall population, sex, and residential subgroups

Age Group	Overall Population			Males			Females			Urban			Rural		
	Crude Probability	Partial Crude Probability	Expected Time	Crude Probability	Partial Crude Probability	Expected Time	Crude Probability	Partial Crude Probability	Expected Time	Crude Probability	Partial Crude Probability	Expected Time	Crude Probability	Partial Crude Probability	Expected Time
0-4	0	0	85.2	0.00001	0	84.8	0	0	85.6	0	0	84.5	0	0	85.8
5-9	0	0	81.2	0.00003	0	80.8	0	0	81.6	0	0	80.5	0	0	81.8
10-14	0.00001	0.00001	76.2	0.00010	0.00001	75.8	0.00001	0.00001	76.6	0.00001	0.00001	75.5	0.00001	0.00001	76.8
15-19	0.00003	0.00003	71.2	0.00013	0.00003	70.8	0.00003	0.00003	71.6	0.00003	0.00003	70.5	0.00004	0.00004	71.8
20-24	0.00009	0.00009	66.2	0.00045	0.00010	65.8	0.00007	0.00007	66.6	0.00007	0.00007	65.5	0.00010	0.00010	66.8
25-29	0.00014	0.00014	61.2	0.00072	0.00013	60.8	0.00015	0.00015	61.6	0.00019	0.00019	60.5	0.00011	0.00011	61.8
30-34	0.00039	0.00039	56.2	0.00139	0.00045	55.8	0.00033	0.00033	56.6	0.00042	0.00042	55.5	0.00033	0.00034	56.8
35-39	0.00058	0.00058	51.2	0.00201	0.00073	50.8	0.00044	0.00044	51.6	0.00072	0.00072	50.5	0.00043	0.00043	51.8
40-44	0.00111	0.00112	46.2	0.00414	0.00140	45.8	0.00084	0.00084	46.7	0.00139	0.00140	45.5	0.00076	0.00076	46.8
45-49	0.00169	0.00171	41.3	0.00538	0.00203	40.9	0.00138	0.00139	41.7	0.00209	0.00210	40.6	0.00119	0.00120	41.8
50-54	0.00400	0.00406	36.3	0.00771	0.00422	36.0	0.00387	0.00391	36.8	0.00509	0.00516	35.7	0.00295	0.00300	36.9
55-59	0.00480	0.00492	31.5	0.01355	0.00554	31.1	0.00420	0.00428	31.9	0.00637	0.00650	30.9	0.00295	0.00303	32.0
60-64	0.00686	0.00712	26.6	0.01873	0.00806	26.3	0.00591	0.00610	27.0	0.01039	0.01072	26.0	0.00424	0.00442	27.1
65-69	0.01075	0.01139	21.8	0.03170	0.01444	21.5	0.00773	0.00813	22.2	0.01802	0.01889	21.3	0.00611	0.00652	22.2
70-74	0.01531	0.01668	17.0	0.04733	0.02055	16.8	0.01137	0.01230	17.3	0.02413	0.02596	16.7	0.00959	0.01054	17.3
75-79	0.02344	0.02644	12.3	0.00930	0.03589	12.0	0.01447	0.01625	12.5	0.03220	0.03586	12.0	0.01649	0.01880	12.5
80-84	0.03318	0.03919	7.5	0.00001	0.05572	7.4	0.02015	0.02387	7.7	0.05219	0.06040	7.4	0.01771	0.02127	7.7
85+	0.00547	1	2.7	0.00003	1	2.6	0.00221	1	2.8	0.00768	1	2.6	0.00412	1	2.8

Table 3: Crude probability, partial crude probability, and expected time of cancer occurrence for esophageal, stomach, and colorectal cancer in males and females

a) Males									
Age Group	Esophageal Cancer			Stomach Cancer			Colorectal Cancer		
	Crude Probability	Partial Crude Probability	Expected Time	Crude Probability	Partial Crude Probability	Expected Time	Crude Probability	Partial Crude Probability	Expected Time
0-4	0	0	86.4	0	0	85.7	0	0	86.8
5-9	0	0	82.4	0	0	81.7	0	0	82.8
10-14	0	0	77.4	0	0	76.7	0	0	77.8
15-19	0	0	72.4	0	0	71.7	0.00003	0.00003	72.8
20-24	0	0	67.4	0.00002	0.00002	66.7	0.00003	0.00003	67.8
25-29	0	0	62.4	0.00003	0.00003	61.7	0.00006	0.00006	62.8
30-34	0.00003	0.00003	57.4	0.00013	0.00013	56.7	0.00023	0.00023	57.8
35-39	0.00007	0.00007	52.4	0.00021	0.00021	51.7	0.00033	0.00034	52.8
40-44	0.00020	0.00020	47.4	0.00039	0.00039	46.8	0.00043	0.00044	47.9
45-49	0.00022	0.00023	42.5	0.00067	0.00068	41.8	0.00078	0.00079	42.9
50-54	0.00083	0.00085	37.5	0.00206	0.00210	36.8	0.00094	0.00096	37.9
55-59	0.00105	0.00109	32.5	0.00305	0.00314	31.9	0.00077	0.00079	32.9
60-64	0.00174	0.00182	27.5	0.00435	0.00455	27.0	0.00128	0.00134	28.0
65-69	0.00290	0.00311	22.6	0.00808	0.00863	22.1	0.00145	0.00156	23.0
70-74	0.00443	0.00489	17.6	0.01083	0.01192	17.2	0.00215	0.00237	18.0
75-79	0.00767	0.00878	12.7	0.01817	0.02069	12.4	0.00283	0.00324	13.1
80-84	0.01688	0.02014	7.8	0.02297	0.02733	7.6	0.00304	0.00365	8.1
85+	0.00300	1	2.9	0.00450	1	2.7	0.00105	1	3.1

b) Females									
Age Group	Esophageal Cancer			Stomach Cancer			Colorectal Cancer		
	Crude Probability	Partial Crude Probability	Expected Time	Crude Probability	Partial Crude Probability	Expected Time	Crude Probability	Partial Crude Probability	Expected Time
0-4	0	0	88.1	0	0	86.6	0	0	86.9
5-9	0	0	87.1	0	0	82.6	0	0	82.9
10-14	0	0	83.1	0	0	77.6	0	0	77.9
15-19	0.00001	0.00001	78.1	0	0	72.6	0.00002	0.00002	72.9
20-24	0.00000	0.00000	73.1	0.00003	0.00003	67.6	0.00001	0.00001	67.9
25-29	0.00002	0.00002	68.1	0.00003	0.00003	62.6	0.00007	0.00007	62.9
30-34	0.00003	0.00003	63.1	0.00007	0.00007	57.6	0.00019	0.00019	57.9
35-39	0.00011	0.00011	58.1	0.00011	0.00011	52.6	0.00018	0.00018	52.9
40-44	0.00014	0.00014	53.1	0.00017	0.00017	47.6	0.00043	0.00044	47.9
45-49	0.00022	0.00022	48.1	0.00038	0.00038	42.6	0.00065	0.00065	42.9
50-54	0.00098	0.00099	43.1	0.00137	0.00138	37.6	0.00113	0.00115	38.0
55-59	0.00134	0.00137	38.1	0.00137	0.00140	32.7	0.00092	0.00094	33.0
60-64	0.00203	0.00210	33.1	0.00191	0.00198	27.7	0.00114	0.00117	28.0
65-69	0.00334	0.00352	28.1	0.00245	0.00259	22.8	0.00117	0.00123	23.1
70-74	0.00384	0.00417	23.2	0.00438	0.00475	17.8	0.00182	0.00198	18.1
75-79	0.00526	0.00593	18.2	0.00493	0.00556	12.9	0.00241	0.00272	13.1
80-84	0.00663	0.00790	13.2	0.00765	0.00911	8.0	0.00281	0.00335	8.2
85+	0.00123	1	8.2	0.00074	1	3.0	0.00000	1	3.2

Table 4: Estimated relative hazard of sex, residential place, and their interaction on time to selected cancers occurrence: Results of the Cox regressions

Type of Cancer	Factor	Hazard ratio	P
All Types	Sex ¹	2.16	<0.001
	Residency ¹	2.72	<0.001
	Interaction ²	1.17	<0.001
Esophageal	Sex ¹	1.70	<0.001
	Residency ¹	2.38	<0.001
	Interaction ²	1.09	<0.001
Stomach	Sex ¹	3.45	<0.001
	Residency ¹	2.87	<0.001
	Interaction ²	1.26	<0.001
Colorectal	Sex ¹	1.11	0.040
	Residency ¹	3.17	<0.001
	Interaction ²	1.09	0.015

Female and living in rural are baseline, Sex- residency interaction

Table 5: Estimated effects in the Cox models for the time to selected digestive cancers occurrence

Type of Cancer	Factor*	Hazard Ratio	%95 Confidence Interval		P
			Lower Band	Upper Band	
All Types ¹	Urban Females	2.717	2.623	2.814	<0.001
	Rural Males	2.163	2.086	2.243	<0.001
	Urban Males	5.042	4.879	5.210	<0.001
Esophageal ²	Urban Females	2.375	2.240	2.519	<0.001
	Rural Males	1.704	1.602	1.813	<0.001
	Urban Males	3.701	3.502	3.913	<0.001
Stomach ³	Urban Females	2.870	2.705	3.044	<0.001
	Rural Males	3.451	3.258	3.656	<0.001
	Urban Males	7.829	7.417	8.263	<0.001
Colorectal ⁴	Urban Females	3.173	2.919	3.448	<0.001
	Rural Males	1.110	1.005	1.227	0.040
	Urban Males	3.828	3.528	4.154	<0.001

*.Rural Females is considered as baseline,

1. -2 Log likelihood of model is 1152535.9, with 3 degree of freedom ($P < 0.0001$)

2. -2 Log likelihood of model is 354345.7, with 3 degree of freedom ($P < 0.0001$)

3. -2 Log likelihood of model is 559456.5, with 3 degree of freedom ($P < 0.0001$)

4. -2 Log likelihood of model is 168067.1, with 3 degree of freedom ($P < 0.0001$)

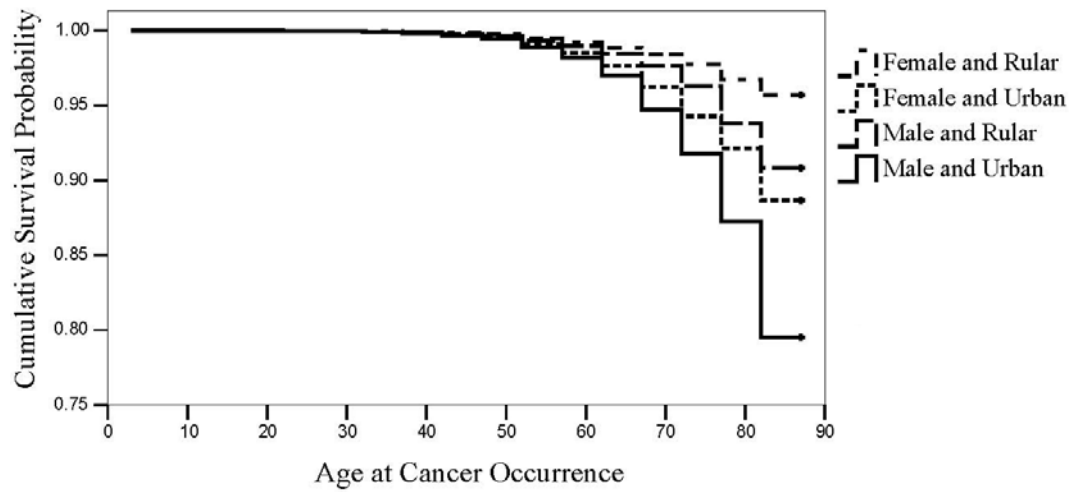


Fig. 1: Time to digestive cancer occurrence by gender and place of residence

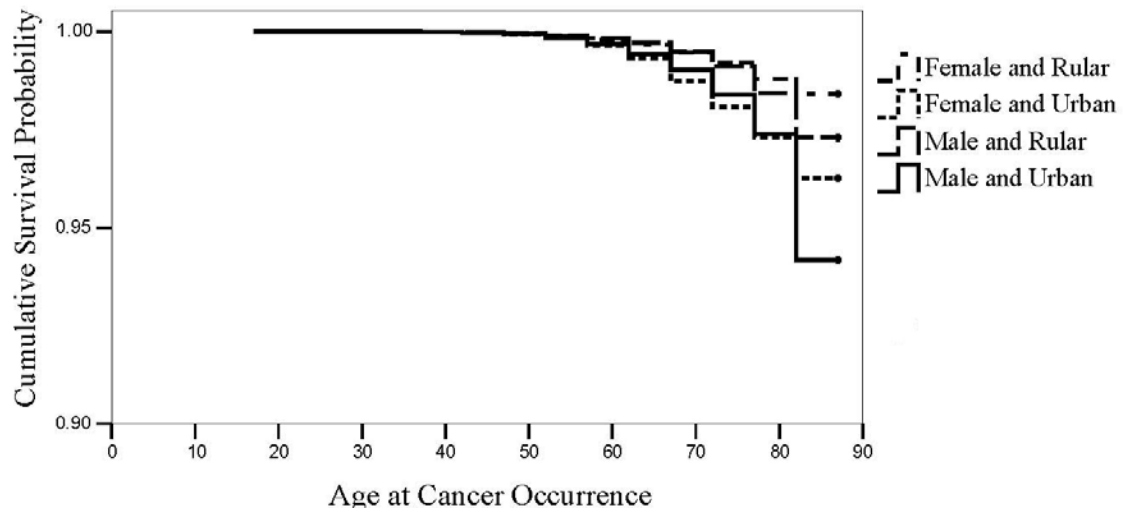


Fig. 2: Time to esophageal cancer occurrence by gender and place of residence

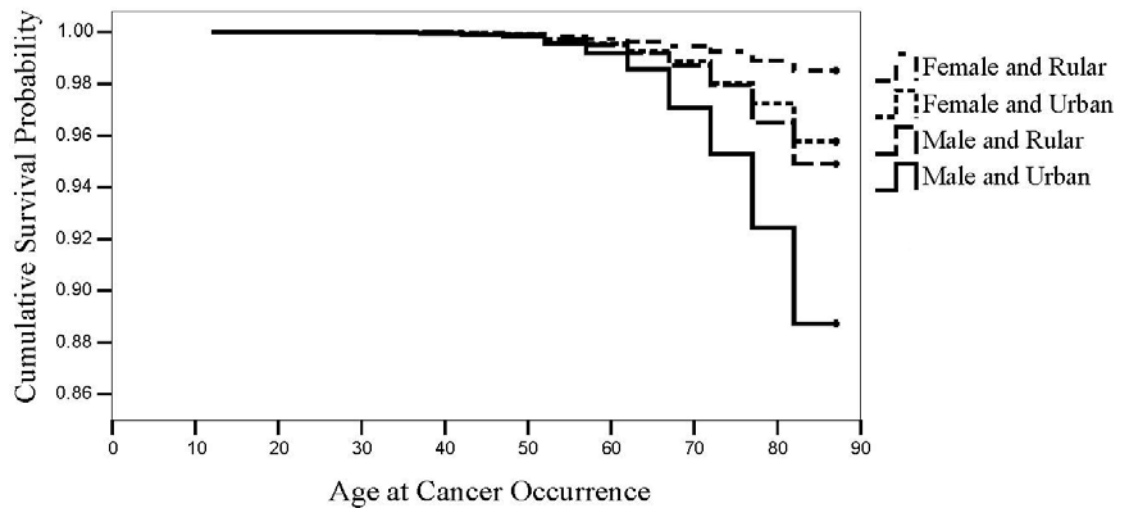


Fig. 3: Time to stomach cancer occurrence by gender and place of residence

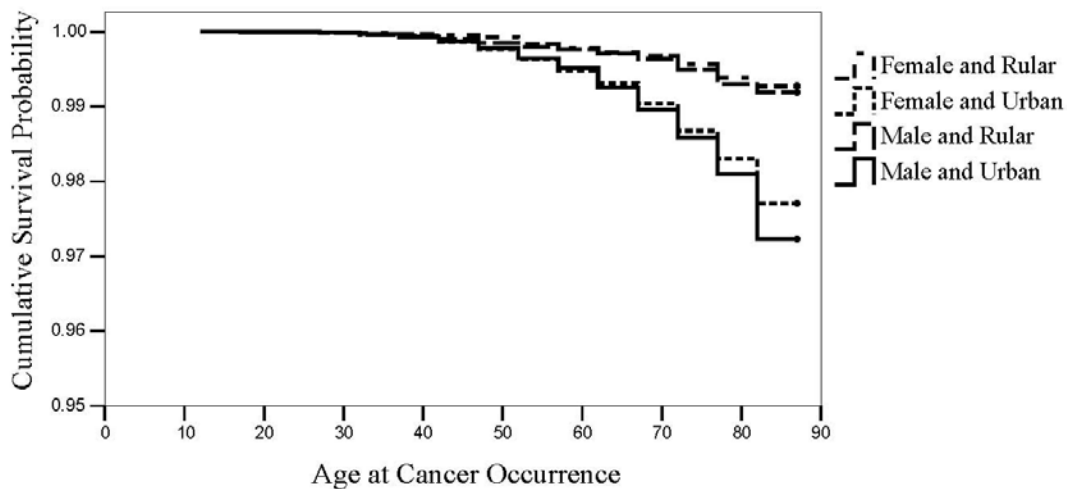


Fig. 4: Time to colorectal cancer occurrence by gender and place of residence

Discussion

This study is the first one which investigates the cancer incidence time based on population data; other similar studies were limited to construction of life tables of the observed cancer cases. Life tables based on observed cancer cases cannot extend to whole study population because the method does not adjust the observed cases for i) censoring (people who died with causes other than cancer), and ii) competing factor of different type of cancers. We use competing risk methodology to address these problems. Lacking such studies in past were due to the following two limitations. 1) A relatively long period of follow up time of healthy residence sufficient for cancer occurrence. Designing such cohort study is very difficult in practice. 2) In theory and in modeling survival data the objective end point should occur for all study cases. If we accept this assumption that all cases eventually get some kinds of digestive cancer, then if death occurs sooner from some other cause, a censored condition will be considered. Modification of survival probabilities due to these types of censored observations and also due to correlations between digestive cancers is not possible by modeling a univariate survival. The first limitation in this study was resolved by calculating age specific mortality probabilities and the related life tables by considering stability of the population in time and using the UN west

method for construction of life tables. Then assuming a constant cancer incidence pattern in time, the age specific probabilities of cancer occurrence were calculated and so a synthetic cohort for residence of Mazandaran province was constructed. In order to overcome the second limitation, we used multivariate survival model methodology through application of nonparametric competing risks modeling. Partial crude probabilities calculate from two components model modify the probabilities of age of digestive cancer occurrence for censored observations due to mortalities. Also, partial crude probabilities calculate from five components model modify the probabilities of age of selected gastric cancers occurrence for censored observations due to mortalities and correlations between all types of digestive cancers.

Mortality due to digestive cancers in Iran is one of the leading causes of mortality (3). Results of a country-wide cancer registry in 2003 which is based on pathology reports indicates that stomach (16%), bladder (11.7%), prostate (8%), colorectal (7.7%), and esophageal (7.3%) cancers have the highest percentage rates in men after skin cancer with 19.4% of rate. In addition, this report indicates that colorectal (8.4%), stomach (7.7%), and esophageal (7.3%) cancer have the highest percentage rate after breast (26.2%), and skin (15.2%) in women (10). These problems

get even worse in southern parts of Caspian Sea, where the stomach and esophageal cancers had the first and second ranks in men in Ardabil and Golestan provinces, respectively. Indeed, this is even higher than skin cancer and higher than breast cancer in women. Table 6 shows the top five common cancers incidences in all four provinces of southern part of Caspian Sea (8, 19, 20). The total number of mortality in 2002 is estimated to be around 35554 from all types of cancer from which 6638 (18.7%) cases are stomach, 6219 (17.5%) cases are esophageal, and 2262(6.4%) cases are colorectal cancer. In other words, these three cancer types were responsible for 42.6% of mortality due to cancer in Iran. So, study of age distribution and life table of occurrence of these three cancers for finding high risk groups by age and gender is very important in future screening and control trials. Furthermore, using the published information of survival rate of gastric cancer patients provides sufficiently good estimates of life table and life expectation of these patients. In general the expected life of Iranian patients with digestive cancer is relatively shorter than of many other countries. This is so that the 5 yr survival rate of gastric cancer patients in a study in Tehran as indicated in Zeraati et al. (21) was 22.6% which is much lower than in many other countries including the US, Switzerland, France, and China (22-26). Unfortunately, the mortality rates in Mazandaran and Golestan provinces are even worse than the above figures. In fact, in a cohort study on 466 gastric patients in Mazandaran and Golestan provinces identified during 1991-1995 and followed for a 10 yr

period, the following results were obtained (27). The follow up cancer cases consisted of 333 esophageal cancers, 100 stomach cancers, and 33 colorectal cancers. The overall 5 yr survival rate was 10%, while this rate was 9% for esophageal cancer, 10% for stomach cancer, and 23% for colorectal cancer. Mortality rates were almost identical in both genders, and increases by age as was expected.

In the present study, we found that the first occurrence of esophageal cancer is in 25-29 yr old age category, and the incidence increases by age. Also, our study shows that the stomach cancer onset is in 20-24 yr age category and this incidence again increases by age. On the other hand, the incidence of first occurrence of colorectal cancer is sooner than the others in 15-19 yr age category. The high incidence of colorectal cancer in young Iranian has also been confirmed by some other studies (28, 29). In this study the cancer incidence probabilities in 5 yr categories and partial crude probabilities of incidences of common cancers after controlling for mortality and occurrence of other digestive cancers were calculated. These calculations were from population-based cancer registry information and so it can be extended to the entire province population. The analytical results of our study indicate that the hazard rates of digestive cancer are higher in males which is consistent with findings in other parts of the world (30- 32). Also in present study living in cities was found to be risk factor digestive cancers. The main reason of this increase in risk in Mazandaran province is not fully known and so demands more field and analytical investigations.

Table 6: Top five cancers percentage (from total) in southern band of Caspian Sea

Ardabil				Gilan				Mazandaran				Golestan			
Male	%	Female	%	Male	%	Female	%	Male	%	Female	%	Male	%	Female	%
Stomach	36.6	Stomach	25.5	Stomach	16.5	Breast	26.4	Stomach	19.9	Breast	25.6	Stomach	21.3	Breast	18.6
Esophagus	11.3	Esophagus	13.7	Bladder	12	Skin	10.5	Skin	10.9	Skin	11	Esophagus	16.6	Stomach	15.1
Skin	7	Skin	10.3	Skin	11.8	Stomach	7.4	Esophagus	8.3	Stomach	10.3	Skin	8.8	Esophagus	10.4
Colorectal	5.9	Breast	8.1	Esophagus	7.8	Colorectal	7.4	Prostate	8.2	Esophagus	8.3	Colorectal	7.7	Colorectal	5.9
Lung	5.9	Colorectal	5.7	Colorectal	5.8	Esophagus	5.5	Colorectal	3.4	Colorectal	3.4	Prostate	5.4	Skin	5.6

Acknowledgements

This study was sponsored by Tehran University of Medical Sciences besides the set up of the Babol Cancer Registry Center. We would like to thank survey team and colleagues of the Babol Cancer Registry Center.

The authors declare that they have no Conflict of Interests.

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