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Original Article

Expected Survival Using Models of Life Table Compared with Survival of Gastrointestinal Tract Cancer Patients in North of Iran

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Abstract

Background: Northern regions of Iran have been encountered to dominate malignancies of gastrointestinal (GI) tract. We came to examine the total excess mortality due to the GI cancer in Mazandaran province.

Methods: Socio-demographic and clinical data of 484 patients with GI cancer collected during the years 1990-1991were available from Babol Cancer Registry. Patients were followed up for 15 years by the year 2006. Using the West Coale-Demeny life table model, a number of five life tables for men and four for women, corresponding to each birth cohort, were constructed. Observed survival was obtained using the Kaplan-Meier method and compared with the Expected survival calculated using the direct adjusted method represented by STEIN et al.

Results: The sample of subjects encompassed 66.3% men and 33.7% women with mean age 58.26 ± 10.90, and endoscopy was the general method for cancer detection. Esophagus accounted for 74.2%, and stomach and colorectal accounted for 22.7% and 3.1% of GI cancers, respectively. Survival rate in 15 years following diagnosis was nearly 6%. Comparing patient and expected survival curves showed a significantly reduced survival for patients of each GI cancer over the whole period and especially during the first two years after diagnosis.

Conclusion: Patients experienced reduced survival associated with the development of GI cancers. Considering individuals in a population come from different cohorts, adjustment by constructing distinct life tables for different birth cohorts is recommended. The West model is recommended as a first choice to represent mortality in countries whose registration systems are exposed to various errors.

Keywords: Expected survival, Excess mortality, Relative survival, Life table models, Coale-Demeny patterns, Gastrointestinal tract cancer

Introduction

Cancer is realized as the third leading cause of death throughout the world, with over 12 million new cases and 7.6 million cancer deaths are estimated to have occurred in 2007 (1). It is approximated that there will be nearly 26 million new cancer cases and 17 million cancer deaths per year, by the year 2030 (2).

Gastrointestinal (GI) tract cancers together accounted for the most common broad group of cancers in 2007 (1). Annually around 50,000 new cases of cancer occur over the 70.4 million population of Iran, in which GI tract is known as the most general organ system involved with over 38% of all cancers. In addition, Stomach, Esophageal, and Colorectal cancers are the three most frequent cancers across Iranian males; however, Iranian females stand at the highest rates of cancers of esophagus, stomach, and colorectal after breast cancer (3, 4).

Expected survival defined as the expected value of future lifetime, estimated based on information from the general population, is an easy and

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convenient way to appraise excess mortality in a group of patients with a specific disease. The method in which observed survival curve of a group of specific patients is compared to expected survival curve, has been generally applied to evaluate the effect of a particular disease on mortality especially when the cause of death is known unreliable or unavailable (5-7).

Life tables as the common tools comprising mortality information of the general population are considered as a standard reference for estimating expected survival. In other words, when estimating expected survival, one usually relies on the published life tables and uses the reference mortality rate that depends on the characteristics of the study patient, such as sex, age, and year of birth (5, 8, 9). One of the limitations of these reference life tables is that individuals in a population basically come from different cohorts with different mortality experiences, while information of mortality rates of different cohorts is as if pooled and combined into a single table. This disparity in the pattern of mortality across cohorts can severely affect life table figures and therefore expected survival measures, which necessitates an adequate adjustment for birth cohort effect during the process of establishing life tables.

Unfortunately, in many developing countries including Iran, registration systems either do not exist or are so affected by omission and other errors. Indeed, there may be little known on the actual age pattern of mortality in these populations, so as measures based on the data that they produce fail to reflect properly either levels or trends of mortality. A number of model life table systems have been developed for use in such cases, but one of the most commonly used is the Coale-Demeny Model Life Tables for Developing Countries (10-12).

Since a dramatic climb was evident in incidence rate of GI tract cancers in northern regions of Iran during the past a few decades (3, 4, 13-15), we aimed to examine the total excess mortality over time due to the GI tract cancers in Mazandaran province, the province with the dominating rate of GI tract cancers (4, 16). For this purpose, the West life table model of Coale-Demeny was constructed for each birth cohort and sex of patients, and was considered as the basis for estimating expected survival.

Materials and Methods

Babol cancer registration

The Caspian Cancer Registry established in 1969 by joint efforts of the Institute of Public Health Research of Tehran University and the International Agency for Research on Cancer (IARC), in the city of Babol in Mazandaran province. The city is located around 20 kilometers south of Caspian Sea on the west bank of Babol Rood River. As a population-based cancer registry, it has provided a reliable source of data on cancer incidence in the Caspian littoral of Iran (17). These efforts were, however, disrupted by the revolution of Iran and the successive socio-political events of the 1980s, but it initiated the routine practice in the year 1990 as a local cancer registry under the supervision of Tehran University of Medical Sciences. The data sources were mainly reports collected from pathology laboratories, hospitals, and radiology clinics offering samples with cancer progression. The coding of the samples was done under the direct supervision of pathology specialists based on the international classification of disease for oncology (ICD-O) coding (18).

A total of 484 patients diagnosed with GI tract cancer were registered at the Babol cancer registration in Mazandaran province between the years 1990-1991 entered into the study. The collected sample contained 359 cases with esophageal, 110 with stomach, and 15 with colorectal cancers. Patients were followed up for a maximum period of 15 years by the year 2006. The socio-demographic and clinical data were obtained through a structured questionnaire and the patients' clinical records. The data available for analysis included the following: gender, age at the time of diagnosis, current job, education,

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ethnicity, place of residence, pathologic diagnosis, and diagnostic methods. The study was approved by the ethics committee of Tehran University of Medical Sciences.

Creating the West life table model

Since in many countries including Iran, death registration is incomplete or nonexistent, adequate life tables cannot be calculated from the data available. Model life tables have been developed for use in such cases. The Coale-Demeny model life tables are amongst the most commonly used models and consist of four sets or models, each representing a distinct mortality patterns, including North, South, East, and West. As the West pattern is considered to represent the most general mortality pattern, Coale and Demeny recommended its use when reliable information is not available for choosing one of the other patterns (12). Plus, our previous experience reveals that the West life table model can best estimate the actual age pattern of mortality of our population (15). By having in hand the measure of Infant Mortality Rate (IMR) for each year of birth, defined as the number of newborns dying under a year of age divided by the number of live births that year, model life tables can be constructed showing mortality rate for single years of age 0-100. Concerning the Mazandaran province, IMR was available for birth years after 1965; therefore, linear extrapolation methods were invoked to approximate IMR for birth years before 1965. Because the study patients came from different cohorts with experiencing different mortality patterns, men were classified into five distinct cohorts of 1911-1920, 1921-1930,1931-1940, 1941-1950, and 1951-1961, and women into four cohorts of 1921-1930,1931-1940, 1941-1950, and 1951-1961. It should be clarified that an average IMR was obtained for each different cohorts and according to gender. Thus, a number of five West life tables for men and four West life tables for women were constructed corresponding to each birth cohort. Once the West life tables were established, population-based mortality rates were available from the tables for each combination of sex (male or female) and birth cohort (19).

Estimation of observed and expected survivals

Observed survival curve

The ubiquitous estimator of survival function, proposed by Kaplan and Meier in 1958, well known as the Product-Limit estimator, was estimated for the study patients. This is the standard approach for graphical plots of estimated survival curve considered as the observed (patient) survival function (20).

Expected survival curve

We took a simple and applicable approach represented by STEIN et al. in 1998 for calculation expected survival function (5). The method is known as the direct adjusted and is theoretically described as the expectation of the Kaplan-Meier estimate for a set of randomly selected controls from the general population, individually matched for sex, age and year of birth with study patients at the time entered into the study. The method requires that population-based mortality rates are available by sex, age and year of birth within the study period, the measures we reached by constructing the West life tables. The expected survival curve was expressed as

$$S^*(t)=\prod_{k=0}^{t}\left(1-\sum_{i=1}^{n}\lambda_i^*(k)\frac{S_i^*(k)}{\sum_{i=1}^{n}S_i^*(k)}\right).$$

The term $\sum_{i=1}^{n}\lambda_i^*(t)S_i^*(t)$ can be interpreted as the expected number of deaths across controls at time *t*, and $\sum_{i=1}^{n}S_i^*(k)$ denotes the expected number of controls at risk (alive) at the start of time interval *t*. Thus, the expression for $S^*(t)$ resembles the usual Kaplan-Meier estimator (5). A simple statistical test, similar to the Mantel-

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Haenszel test, was proposed to test whether patient survival is equal to expected survival. The test (χ^2_M) was assumed to be approximately chi-squared distributed with 1 degree of freedom, as for the Mantel-Haenszel test (5).

For the statistical analysis, the statistical software SPSS version 15.0 for windows (SPSS Inc., Chicago, IL) was used. The statistical package SAS version 9.1 for windows (SAS Institute Inc., Cary, NC, USA) was utilized to depict Expected and Observed survival curves. All *P* values were 2-tailed, with statistical significance defined by $P \leq 0.05$.

Results

We analyzed the data of 484 patients with GI tract cancer including esophagus, stomach, and colorectal in Mazandaran province, one of the northern regions of Iran. Males accounted for 66.3% and females 33.7% of GI tract cancers. The mean age of the patients was 58.26 ± 10.90 (mean ± SD) years [range 40 to 90].

Table 1 shows the socio-demographic and clinical data for the patients according to the three most common cancers in Mazandaran. As can be seen in the table, around 85% of all cancers were detected by the direct endoscopy and biopsy, and a vast majority of patients were illiterate, married, and more than half of them were farmers, and reside in rural areas. Post hoc analysis showed that patients with colorectal cancer were significantly younger, and more literate than patients with other GI cancers. On the other hand, lower proportions of patients with cancer of esophagus resided in Mazandaran, and were Aryan, whereas higher proportions of them were housewives when compared to those with other underlying cancers (Table 1).

By the year 2006, the average follow up was 3.09 ± 3.82 years (range 1 to 15) and a total of 426 (88.0% of the entire sample) mortality occurred. Patients with cancer of esophagus were 2.95 ± 3.64 years on study with 320 (89.1% of 359) mortality and of stomach were 3.33 ± 4.25 years on study with 95 (86.4% of 110) mortality events, and those with colorectal cancer were 4.67 ± 4.62 years on study, of whom 11 (73.3% of 15) died during follow up. The Kaplan-Meier method of survival analysis estimated that the survival rates in 5, 10, and 15 years following diagnosis were 16.9%, 13.80%, and 6.2%, respectively. The overall patient survival rate was not statistically different across the three subgroups of patients with esophageal, stomach, and colorectal cancers (Fig. 1).

Figures 2 through 5 depict the survival curves observed for the GI tract cancer patients versus the expected survival curves for the total patients and for each subgroup of cancer patients. As is clear in all the four figures, a significantly lower survival, comparing the patient curve with the expected curve, is observed for patients throughout the follow-up period, indicating that patients have a reduced survival through the time period. It is also found that the difference is dominant during the first two years after diagnosis of cancer so that the ratio of the expected to the observed survival rates increases during the two years following diagnosis and then declines for about ten years when the ratio gently increases again due to a decrease in the number of patients who survive beyond ten years after diagnosis. In each case, the simple chi-square test (χ^2_M) gave *P*-value< 0.001 for the whole period showing a total excess mortality over time.

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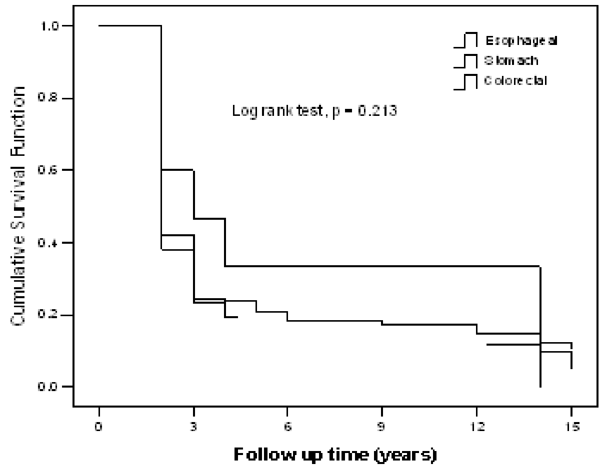

No. at risk

Esophageal	359	70	53	45
Stomach	110	26	20	18
Colorectal	15	5	5	4

Fig.1: Kaplan–Meier plot of cumulative survival of mortality to fifteen years after diagnosis according to the type of GI tract cancer diagnosed in Mazandaran province in Iran

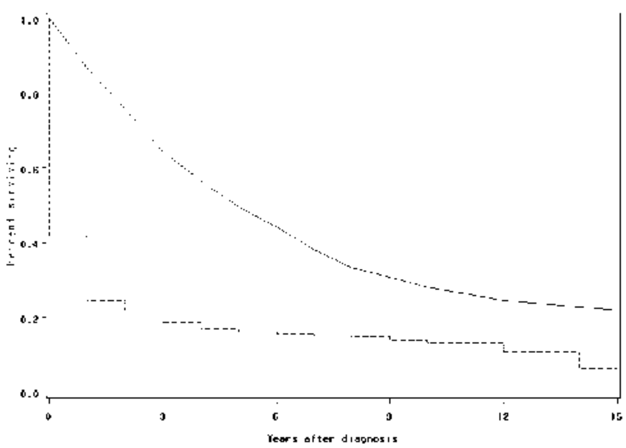

Fig.2: Expected and observed survival curves for 484 gastrointestinal tract cancer patients observed (- - - - -), expected (solid line) χ^2_M = 19.139, df = 1; *P* < 0.001

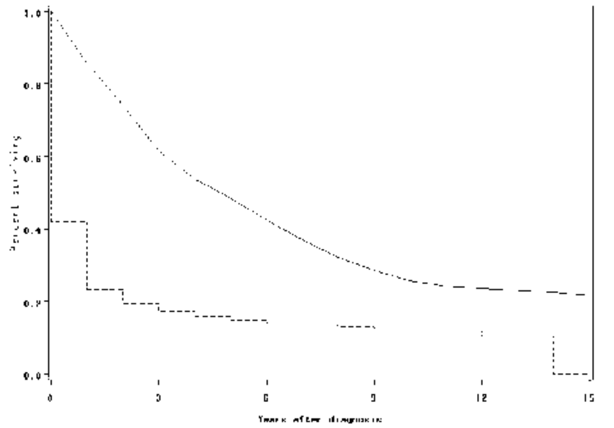

Fig. 3: Expected and observed survival curves for 359 esophageal cancer patients -observed (- - - - -), expected (solid line)- χ^2_M = 23.873, df = 1; *P*< 0.001

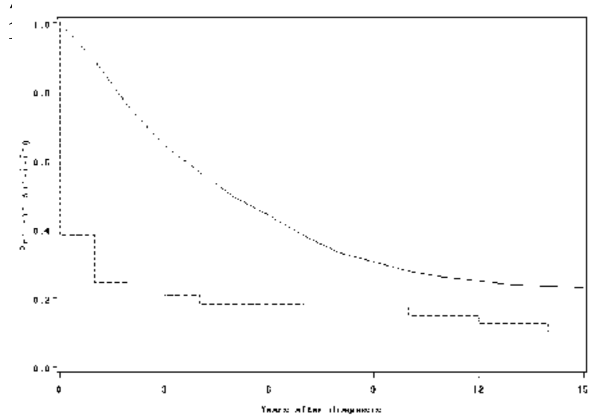

Fig. 4: Expected and observed survival curves for 110 stomach cancer patients-observed (- - - - -), expected (solid line)- χ^2_M = 14.107, df = 1; *P* < 0.001

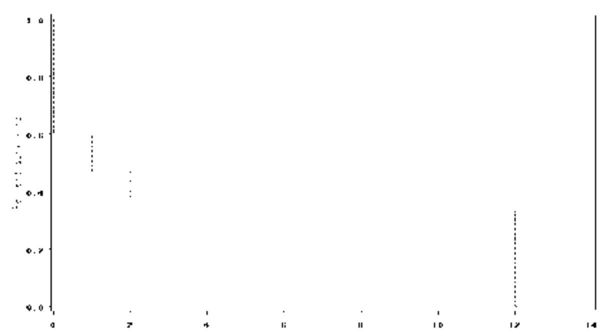

Fig. 5: Expected and observed survival curves for 15 colorectal cancer patients observed (- - - - -), expected (solid line) χ^2_M = 9.493, df = 1; *P*< 0.001

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Table 1: Characteristics of patients according to the type of GI tract cancer diagnosed*

Characteristic	Total (n = 484)	Esophageal (n = 359)	Stomach (n = 110)	Colorectal (n = 15)	P-value†
Gender					0.011
Male	321 (66.3)	225 (62.7)	83 (75.5)	13 (86.7)	
Female	163 (33.7)	134 (37.3)	27 (24.5)	2 (13.3)	
Age (years)	58.26 ± 10.90	57.69 ± 12.17	59.13 ± 11.37	44.93 ± 15.70	< 0.001
Place of residence					0.165
Rural	256 (52.9)	199 (55.4)	50 (45.5)	7 (46.7)	
Urban	228 (47.1)	160 (44.6)	60 (54.5)	8 (53.3)	
Province					< 0.001
Mazandaran	288 (59.5)	188 (52.4)	88 (80.0)	12 (80.0)	
Golestan††	196 (40.5)	171 (47.6)	22 (20.0)	3 (20.0)	
Method of cancer detection					0.014
Clinical diagnosis	35 (7.2)	22 (6.1)	12 (10.9)	1 (6.7)	
Direct endoscopy and biopsy	410 (84.7)	314 (87.5)	86 (78.2)	10 (66.7)	
Conventional chest x-ray	39 (8.1)	23 (6.4)	12 (10.9)	4 (26.7)	
Family history of cancer	142 (29.3)	110 (30.6)	26 (23.6)	6 (40.0)	0.242
Education					0.107
Literate	52 (10.7)	35 (9.7)	13 (11.8)	4 (26.7)	
Illiterate	432 (89.3)	324 (90.3)	97 (88.2)	11 (73.3)	
Job					< 0.001
Farmer	252 (52.1)	186 (51.8)	58 (52.7)	8 (53.3)	
Worker	44 (9.1)	29 (8.1)	14 (12.7)	1 (6.7)	
Employee	7 (1.4)	3 (0.8)	3 (2.7)	1 (6.7)	
Housewife	135 (27.9)	115 (32.0)	20 (18.2)	0	
Others	46 (9.5)	26 (7.2)	15 (13.6)	5 (33.3)	
Marital status					0.920
Married	459 (94.8)	340 (94.7)	105 (95.5)	14 (93.3)	
Single	25 (5.2)	19 (5.3)	5 (4.5)	1 (6.7)	
Cigarette smoking	215 (44.4)	151 (42.1)	57 (51.8)	7 (46.7)	0.194
Ethnicity					< 0.001
Aryan	327 (67.6)	219 (61.0)	95 (86.4)	13 (86.7)	
Torkaman	100 (20.7)	92 (25.6)	7 (6.4)	1 (6.7)	
Others	57 (11.8)	48 (13.4)	8 (7.3)	1 (6.7)	

* Data are presented as mean ± SD or n (%).
† P-value represents comparison across the type of GI tract cancer
†† This new province was created as a result of the division of Mazandaran province into two smaller administrative units in the year 1997.
GI, Gastrointestinal

Discussion

In the present study, our effort was mainly focused on showing the effects of GI tract cancers on excess mortality using the West life table models established for each sex and birth cohort. The direct adjusted method that we applied was described by STEIN et al. in 1998 that measures a total excess mortality over time for a set of patients (5). The method is easy to calculation, has a direct interpretation and does not rely on complicated or unrealistic assumptions.

As was found, a reduced survival rate was seen for patients of each cancer type throughout the whole period, and the most difference between

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the observed and the expected survival curves was established in the first two years of observation, showing that a majority of excess deaths occurred during the first two years following diagnosis. This might be expected because patients with GI tract cancers are generally discovered at a late stage of disease when cancer is difficult to cure successfully at this stage (21, 22). Here, it should be noted that the estimates for patients with colorectal cancer may seem a bit imprecise due to the relatively small sample size of this patients. Nevertheless, an excess mortality was evident through the whole period.
There are a variety of approaches on comparing patients with certain exposure to a general population, including methods of excess mortality, relative survival, and expected survival, and also model-based approaches to the hazard function. The literature is enriched by many studies of each approach showing an increase in mortality rate associated with the development of a particular disease. Not surprisingly, in many of these studies population mortality rates are available through published life tables and no adjustment has been made for birth cohort effect (6, 23-31). Sasieni in estimating excess risk using a proportional excess hazards model for 988 adult patients with non-Hodgkin's lymphoma presentation, population mortality rates from England and Wales were adjusted for cohort effects by dividing patients to 5-year age groups and sex (32).
The focus in our study was directed toward adjustment for confounding effects of birth cohort using establishing the West Coale-Demeny model life table, as registration systems in Iran are so affected by omission and various errors. The basis of the Coale-Demeny life table system is the mortality patterns exhibited in 192 actual life tables by sex. Analysis of 192 life tables revealed four age patterns of mortality labeled North, South, East, and West. The West pattern is, however, derived from the largest set of observed life tables [130] and is considered to represent the most general mortality pattern. According to Coale and Demeny, the West model is very similar to that of the earlier United Nation life tables (11). They recommended its use when the reliability of information is under question for choosing a more deserved model (11, 12, 19, 33).

Limitations

First, we did not carry out computations separately for the two provinces of Mazandaran and Golestan, because the Golestan was created as a result of breakdown of Mazandaran Province into two smaller provinces in the year 1997, while our data was collected by the end of 1991. Second, although the stage of GI cancer can seriously affect the time of death, depending on whether the cancer has spread outside the tract to nearby tissues, the stage of cancer was not determined at the time of data collection. Therefore, we were not able to stratify our analysis based on the stage of cancer and it appears our results here shows an average excess mortality for patients with GI cancers.
In conclusion, patients with GI tract cancer experience reduced survival compared with general population especially during the first two years following diagnosis. Considering the confounding effect of different cohorts on life table figures, in establishing life tables, adjustment for birth cohort effect is highly recommended. Furthermore, in countries whose registration systems either do not exist or are so affected by omission and other errors, the West Coale-Demeny pattern is recommended as a first choice to represent mortality pattern.

Ethical Considerations

Ethical issue principles including plagiarism, informed consent, misconduct, data fabrication and/or falsification, double publication and/or submission, redundancy, etc. have been completely observed by the authors.

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