• LIVER CANCER •

Changes in survival patterns in urban Chinese patients with liver cancer

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Abstract

AIM: To examine the survival patterns and determinants of primary liver cancer in a geographically defined Chinese population.

METHODS: Primary liver cancer cases (n=13 685) diagnosed between 1981 and 2000 were identified by the Tianjin Cancer Registry. Age-adjusted and age-specific incidence rates were examined in both males and females. Proportional hazards (Cox) regression was utilized to explore the effects of time of diagnosis, sex, age, occupation, residence, and hospital of diagnosis on survival.

RESULTS: Crude and age-adjusted incidence rates in the study period were: 27.4/100 000 and 26.3/100 000 in males; and 11.5/100 000 and 10.4/100 000 in females, respectively. Cox regression analyses indicated that there was a significant improvement in survival rates over time. Industrial workers and older people had relatively poor survival rates. The hospital in which the liver cancer was diagnosed was a statistically significant predictor of survival; patients diagnosed in city hospitals were more likely to have better survival than those diagnosed in community/district hospitals.

CONCLUSION: Patients diagnosed in recent years appeared to have a better outcome than those diagnosed in early times. There were also significant survival disparities with respect to occupation and hospital of diagnosis, which suggest that socioeconomic status may play an important role in determining prognosis.

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INTRODUCTION

Liver cancer is a fairly common malignancy world wide[1-5], especially in developing countries[6-9]. In China, primary liver cancer is the third and fourth most common cancer in men and women with the age-adjusted incidence rates of 28.2/100 000 and 9.8/100 000 respectively in Shanghai[10]. Population-based survival data on cancer are indispensable in providing real, unbiased, average outcome of cancer patients. While liver cancer is a major cause of cancer-related mortality in China, little is known about its survival patterns over time. The objective of this study was two-fold: (1) to examine a specific hypothesis regarding the survival patterns of liver cancer in the studied urban Chinese population; (2) to examine the factors affecting such survival patterns. The objectives were achieved by analysing the data from the Tianjin Cancer Registry. The Tianjin Cancer Registry Centre is one of the members of the International Agency for Research on Cancer (IARC) of the World Health Organization. The cancer incidence data from Tianjin have been included in IARC official publications: "Cancer Incidence in Five Continents" since 1981. As Tianjin Cancer Registry is one of the few internationally accredited cancer registries in China, the results have important implications.

MATERIALS AND METHODS

Data

Tianjin, the third largest city in China, has a population about 10 million, of which about 98 % belongs to the Han ethnic group. The Tianjin Cancer Registry was established in 1978 and became operational in 1981[11-13]. While the registry covers the whole city, data from six urban districts, which include approximately 4-million people, have been computerized and evaluated here. A city by-law requires that all physicians are responsible for filling out a report form for each new diagnosis of cancer. Practically, the task of cancer reporting is delegated to the medical record unit at each hospital. Thus, cancer cases are normally reported when patients are discharged from or die in the hospital. Information collected on the cancer reporting card includes name, sex, current age or date of birth, address, reporting hospital or medical institute, date (month and year) of diagnosis, four digit ICD-9 codes, and occupation. The Centre for Disease Control in Tianjin performs an annual quality control examination in at least 20 randomly selected hospitals in Tianjin to ensure that each hospital meets the standard cancer case reporting protocol. The evaluation results are used as part of the overall hospital report card, which is further used for hospital excellence ranking. A monetary incentive is offered for each cancer case reported, which is normally paid to the medical record unit rather than to individual physicians. Patients from other parts of China or those without permanent residence in Tianjin are not reflected in the current registry data.

All death certificates, which are the second source of cancer registration, are registered both at the district public health unit (DPHU) and the local police station. The DPHU routinely reviews all death certificates and identifies deaths, which are directly or indirectly caused by cancers. All cancer cases identified through death certificates are checked against the existing database at the Tianjin Cancer Institute for possible double or multiple reporting. In this study, we included all primary liver cancer patients (ICD-9 codes 155.1, 155.2). Numbers in each age-sex specific population for the six urban districts were obtained from the Tianjin Police Head Office,

which enumerates the Tianjin urban population based on people's unique resident cards.

Analyses

Univariate and bivariate descriptive analyses were performed prior to multivariate analyses. Proportional hazards regression (Cox model)[14-20] was used to examine the effects of various factors on survival time for the study population. The proportional hazards model can be expressed as:

$$h(t;X)=h_0(t)exp(\boldsymbol{b}'X)$$

where h(t; X) is the hazard function of T at time t given a regression vector X; h_0 is the unspecified baseline hazard function. The SAS PROC PHREG procedure was used to examine the specified survival model. The time variable (in days) was defined as the interval between the date of diagnosis and date of death. The covariates included in the survival analyses were age, sex, occupation, year of diagnosis, and residence. To best capture the impact of age on survival time, we explored different ways to categorize it in our regression models. As the incidence rates of liver cancer are very low in children, in our final model, we used ages 0-19 years as one group (baseline) and 10-year intervals thereafter to get stable estimates for the regression coefficients. Treating age categories as dummy variables in the model did not result in a better goodness of fit than simply introducing age as an ordered categorical variable with one degree of freedom.

Residence was introduced as a binary variable. As Hexi district is generally regarded as the best neighbourhood in Tianjin, it was used as a reference group and coded as "0". Other districts were coded as "1" and compared to Hexi district. Self-reported occupations were collapsed into 4-broad mutually exclusive categories: professionals and managers (such as teachers, medical doctors), service industry workers (such as

salespeople), industry workers, and others. The professional and manager group was treated as the reference category. Year of diagnosis was treated as single year in Poisson regression and grouped into four categories in Cox regression analysis: 1981-1985 (reference category), 1986-1990, 1991-1995, and 1996-2000. Hospital of diagnosis was dichotomized to community/district hospitals (reference category) and city hospitals. Community hospitals normally provide walk-in service in their districts but do not provide surgical operations. District hospitals provide in-patient service and day-surgery operations in their districts. City general hospitals and speciality hospitals, which normally have advanced technology and research programs, provide a wide range of service to all Tianjin residents referred by community or district hospitals and sometimes patients from other parts of China.

RESULTS

In total, 13 685 cancer cases were identified during the study period (1981-2000) and 70.6 % occurred in males. The mean age at diagnosis for the study population was 62.2 years (61.3 and 64.3 years for males and females, respectively) with a median survival time of 151 days. As shown in Table 1, diagnosis based on death certificate only (DCO) was less than 1 %. Most cancer cases were reported from city (75.1 %) or district hospitals (15.5 %) and most cases were diagnosed based on either medical imaging (60.6 %) or histology (28.4 %). While there are few gender differences with respect to the age at diagnosis and types of hospitals of diagnosis, males were more likely than females to be administrators or professionals.

The crude and age-adjusted incidence rates for the entire study period were 27.4/100 000 and 26.3/100 000 respectively for males. The corresponding rates were 11.5/100 000 and 10.4/100 000 for females.

Table 1 Characteristics of liver cancer cases diagnosed during 1981 to 2000, Tianjin, China

Variable	Category	Male		Female		Total	
		n	%	*n*	%	*n*	%
Sex	Male	-	-	-	-	9666	70.63
	Female	-	-	-	-	4019	29.37
Age	0-19	19	0.20	18	0.45	37	0.27
	20-29	64	0.66	24	0.60	88	0.64
	30-39	360	3.72	119	2.96	479	3.50
	40-49	1118	11.57	284	7.07	1402	10.24
	50-59	2443	25.27	728	18.11	3171	23.17
	60-69	3155	32.64	1395	34.71	4550	33.25
	70-79	2009	20.78	1129	28.09	3138	22.93
	80+	498	5.15	322	8.1	820	5.99
Type of diagnosis	Clinical only	981	10.15	473	11.77	1454	10.62
	Medical imaging only	5934	61.39	2353	58.55	8287	60.56
	Histology at local site	2710	28.04	1176	29.26	3886	28.40
	Surgical examination or autopsy	14	0.14	8	0.20	22	0.16
	Death certificate only	1	0.01	1	0.02	2	0.01
	Unknown	26	0.27	8	0.20	34	0.25
Occupation	Professionals and administrators	3193	33.03	390	9.7	3583	26.18
	Service industry workers	1220	12.62	334	8.31	1554	11.36
	Industry workers	3937	40.73	989	24.61	4926	36.00
	All others	1316	13.62	2306	57.38	3622	26.46
Type of reporting hospital	City general or specified hospitals	7306	75.58	2968	73.85	10274	75.07
	District general hospital	1495	15.47	624	15.53	2119	15.48
	Community hospital	865	8.95	427	10.62	1292	9.44

Table 2 displays the results from the proportional hazard regression analyses. Older age and female gender were associated with poor survival rates, with relative risks of 1.06 (95 % CI: 1.01, 1.11) and 1.08 (95 % CI: 1.05, 1.09) respectively. Hospital of diagnosis was a statistically significant predictor of survival time. Patients diagnosed in city hospitals tended to live longer than those diagnosed in district or community hospitals, with relative risk of death of 0.76 (95 % CI: 0.73, 0.79). The results showed that period of diagnosis was a statistically significant predictor of patients' survival time. Patients diagnosed in more recent years were likely to live longer than those diagnosed in earlier years with a relative risk of 0.85 (95 % CI: 0.83, 0.86) for every 5-year increment.

Table 2 Proportional hazards analyses of liver cancer diagnosed between 1981 and 2000 in Tianjin urban districts

Variable	Category	Relative risk	95 % CI
Sex	Male	1	
	Female	1.06	1.01, 1.11
Age	0-19	1	
	Every 10-years increase	1.08	1.05, 1.09
Period of	1981-1985	1	
diagnosis	Every 5-years increase	0.85	0.83, 0.86
Residence	Hexi District (advantaged)	1	
	Other districts	1.02	0.97, 1.08
Occupation	Administrators	1	
	Service industry workers	1.06	0.99, 1.13
	Industry workers	1.08	1.03, 1.13
	All others	0.97	0.91, .102
Hospital	District or community hospitals	1	
	City general or speciality hospitals	0.76	0.73, 0.79

DISCUSSION

In this study, we described the survival patterns for primary liver cancer in a Chinese urban population over the last 20 years. To the best of our knowledge, this was the first study of its kind ever reported from China. Given the inconsistencies in the literature regarding liver cancer incidence trends[21-26] and survival patterns[27-32], this study provides another piece of useful information for this disease. As Tianjin has a first-class cancer treatment centre and facilities, patients from other parts of China often seek treatment in Tianjin. It is relatively uncommon that Tianjin residents travel to other parts of China for treatment. There is no conceivable reason that this pattern had changed during the study period. Moreover, regardless of where a Tianjin patient gets treated, his/her cancer status would eventually be reflected in the death certificates, which are one source of our cancer registration data.

Based on clinical patients in Qidong, which has the highest liver cancer incidence rates in China, Chen *et al*[31] reported that females had a more favourable prognosis than males. In this study, we found that females had slightly poor survival rate than males. As the magnitude of the reported survival difference was small, the results were unlikely to be conclusive. Nevertheless, the discrepancy between the two studies may be related to the differences in study population, such as, clinical setting versus population based or rural (Qidong) versus urban (Tianjin). The last four decades have seen a significant improvement in liver cancer treatment in China[33]. While the current study only had a span of 20 years, the improvement in survival was apparent. The changes may be explained by improvements in liver cancer clinical management in this city. For example, unpublished data indicate the proportion of liver cancer patients who undergo surgery for their condition has

increased substantially in Tianjin.

This study has several limitations. First, we only included urban residents and were unable to compare the differences between rural and urban populations. Since China is a vast country with significant variations in economic conditions, the reported results may only be applicable to urban Chinese residents. Second, as the Tianjin Cancer Registry only records cancer related deaths (direct and indirect), it is possible that liver cancer patients who died from other causes, such as traffic accidents, were not reflected in our data bases. As a result, the observed survival time as reflected in the cancer registry data, might have been inflated. However, given that liver cancer is a fast progressive condition and a dominant majority of liver cancer patients die from it or its complications, it is unlikely that the problem related to non-liver cancer deaths would have altered the observed survival patterns greatly. Furthermore, since the possible artificially better survival caused by omission of non-liver cancer deaths would have been more in evidence for patients diagnosed in early periods, the true survival advantage for the patients diagnosed in recent years could be even greater. Third, we did not have information on cancer stage and treatment and were unable to estimate their impact on the observed survival pattern. It was possible that some of the observed survival advantage in later periods could be attributed to the cancer stage shift over time. Thus, studies on the changes in cancer stage and treatment over time are needed to address these questions.

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