RESEARCH COMMUNICATION

Prognostic Impact of Risk Factors in Patients with Gastric Cancer in Iran

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Abstract

Background: Gastric cancer (GC) is one the most common causes of death worldwide. Despite the decreasing rate of GC in the world through recent years, it is still the most common cancer in men and the fourth in the general population in Iran. This study aimed to assess the survival of patients with GC and to determine prognostic factors. Materials and Methods: A total of 471 patients with GC were followed from 21 March 2003 to 21 March 2007 in the Cancer Institute of Imam Khomeini Hospital. The patients' survival rate was determined by periodical refers. The survival period considered as the time from diagnosis up to death or the end of the study. The effects of gender, age at diagnosis, tumor site, pathologic stage of disease, type of treatment used, and metastasis were evaluated by log-rank test in a univariate analysis. In addition, all the variables were evaluated simultaneously by the Cox proportional hazard (PH) model. Data were analyzed using SPSS 16 software. Results: 357 (75.8%) out of 471 patients were male and 153 cases (32.5%) experienced death. The mean and median ages at diagnosis were 58.5 and 60.7 years respectively. Also, the survival mean and median were 41.8 (3.1) and 27 (1.7) months respectively. Gender, type of treatment, pathologic stage, the degree of differentiation were significantly related to survival. Conclusions: There was a potential effective role of age at diagnosis, gender of patients and pathologic stage of disease in cancer therapy in this part of Iran. Therefore, to reduce the risk of death in patients with GC, early diagnosis of patients at a younger age and also in primary stages must be targeted.

Keywords: Stomach neoplasia - survival - risk factors - therapy

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Introduction

In the last 20 years, gastric cancer (GC) has been considered as one of the most common causes of death worldwide. In spite of decreasing rate of GC, it is still a very common cause of death in Iran. GC may be kept under control with treatment if it is diagnosed at an early stage, but any delay in diagnosis may lead the disease to metastasis (Mohagheghi et al., 2004; 2005; Sadjadi et al., 2005; Archie et al., 2006). However, without knowledge of all the risk factors involved in cancer, it can not be effectively prevented. The various risk factors such as pathologic stage of disease, age at diagnosis, the number of lymph nodes involved have been the subject of conflicting reports (Manfè et al., 2000; Pacelli et al., 2001; Erturk et al., 2003).

Data on patterns of GC can be used to guide authorities in order to setup cancer prevention programs. Since potential factors involved in survival probability of the patients with GC in Iran may be unnoticed, the main aim of this study was to evaluate the prognostic factors of the cancer using survival analysis in a retrospective study.

Materials and Methods

This study was a retrospective cohort study and performed in the patients diagnosed as GC and treated in the cancer institute of Imam Khomeini hospital in Tehran, the capital of Iran, from March 2003 to February 2010. Demographic and clinico-pathological data of the patients were collected from patients' data files. Total numbers of GC patients referred to the cancer institute was 471 through 5 years. Some demographic and clinical variables like as type and time of treatment, degree of differentiation, pathological stage of disease, relapse and metastasis, treatments (included surgery, chemotherapy and radiotherapy) and finally the number of lymph nodes included in the analysis to find correlated factors and estimate the adjusted prevalence of those factors. To follow the survival status of the patients, phone contact to the relatives of patients and patients' referral to the hospital were the method of research. The data of patients in the cases of impossible contact and also the alive patients were considered as censored observations. The data which obtained in this research was analyzed by Kaplan-Meier

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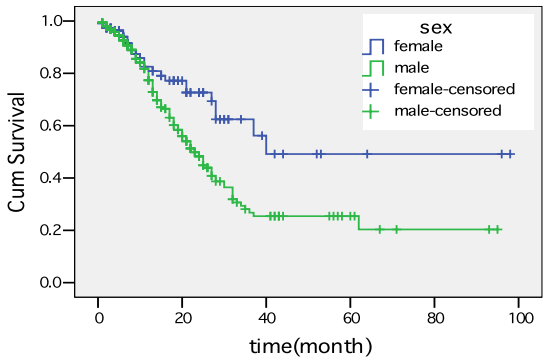

Figure 1. Comparison of Survival Probability for Males and Females

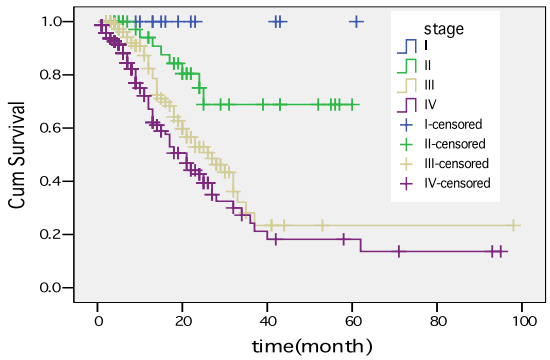

Figure 2. Comparison of Survival Probability for Pathologic Stage of Disease

and Cox PH model utilizing SPSS16 Statistical software. P-value was set as 0.05.

Results

A total of 471 patients entered to this study. 375 cases of participants were male (75.8%) and the rest of them (24.2%) were female. The mean (SD) and median (IQR) age of the patients were 59.7±12 and 61.9±8.8 years respectively. The mean (SD) age at the time of diagnosis were 58.5±12.3 for all patients and it was 59.5±12 and 55.2±12.6 years for males and females respectively. Among these participants 153 (32.5%) died during the current study. Table 1 and Figure 1 showed that there were significant differences between male and female survival rates (= 8.6, p-value=0.003). The results of the Log-rank multivariate analysis in Table 2 showed sex-related survival which was significant (p-value <0.05) so that the hazard rate in male patients was 1.7 times as high as female rate.

Moreover, the position of patients older than 60 years age at time of cancer diagnosis was 1.4 times more hazardous than other patients. The survival rate of disease was also significantly related to pathologic stage (Table 2 and Figure 2), so that patients in stages 3 and 4 were respectively associated with worse outcome as much as 2.9 and 3.1 times higher than those patients in stage 2. Although, tumor site, radiotherapy, type of the treatment (chemotherapy, chemotherapy with surgery), metastasis, degree of tumor of differentiation were not significantly related to the survival of patients. However, the hazard rate was not similar with the different levels of these variables.

Table 1. Evaluation of the Risk Factors Associated with GC using Kaplan-Meier and Log-Rank Test

Variables	Frequency (%)	Median (month)	Log-rank	p-value
Gender				
male	357(75.8)	23	8.6	0.003
female	114(24.2)	40		
Age at diagnosis				
<50	123(26.1)	38	9.7	0.350
50-60	103(21.9)	32		
>60	245(52)	21		
Degree of differentiation				
well	43(9.1)	27	6.3	0.3
moderate	118(25.1)	27		
poor	112(23.8)	23		
unknown	198(42)	23		
Tumor site				
cardia	140(29.7)	28	3.7	0.3
body	107(22.7)	25		
antrum	118(25.1)	27		
Diffuse	39(8.3)	20		
missing	67(14.2)	-		
Metastasis				
No	272(57.7)	30	16.3	0.0001
yes	199(42.3)	21		
Treatment type				
Chemotherapy	196(43.5)	20	7.15	0.0001
Chemotherapy & surgery	255(56.5)	30		
Stage of disease				
II	59(14.5)	-	18.6	0.0001
III	130(31.9)	27		
IV	218(53.6)	21		

Table 2. Evaluation of the Risk Factors Associated with GC Using Cox PH Model

Variables	Relative risk	RR(CI: 95%)
Gender[1]	1.7	(1.44-2.53)*
Metastasis[2]	1.6	(1.2-2.6)*
Age of diagnosis[3]	1.4	(1.1-1.9)*
Stage of disease[4]		
III	2.9	(1.3-6.6)*
IV	3.1	(1.2-7.8)*
Treatment type[5]		
(surgery& chemo)	0.75	(0.42-1.32)

[1]Refernce group females; [2]Negative metastasis; [3]age<60 years old; [4]stage II; [5]chemo; *Statistically significant

Discussion

The results of the univariate analysis showed that the risk factors such as the type of treatment, metastasis, pathologic stage of disease, surgery and gender affected significantly on the survival of GC patients. However, the result of the Cox PH model showed that some of the factors were not affected significantly in comparison to the other factors. The median (IQR) survival of patients was 27(1.7) months, and 1, 3 and 5 years survival rate were 0.79, 0.35 and 0.26 respectively (not shown). These probabilities were higher than those presented by other cancer centers in Iran (Pacelli et al., 2001). The reason could be because of the fact that the cancer

institute of Imam Khomeini hospital has acquired more clinical facilities as the most important center of GC in Iran. Moreover, this center has employed professional staff, modern equipments, and *supplementary* treatment methods. This study showed that the survival probability of males and females was significantly different. This might be associated to the lower age at diagnosis for female patients. As the current research showed, the age at the time of diagnosis was also a significant factor of survival so that the mean age at diagnosis was 4.3 years lower in females than in males. These results are in agreement with previous reports (Munoz et al., 1997; Tuech et al., 1999; Basili et al., 2003; Káposztás et al., 2004; Zhang et al., 2004; Zeraati et al., 2005). However, there is a discrepancy in the latter results obtained with the study performed on GC patients in a Registry of Gastro Intestinal Tract Tumors in France (Fayçal et al., 2008).

The categories degrees of differentiation were not significant in our study in contrast to some other studies at which the moderate and poor degree of differentiation increased the hazard of cancer therapy (Damhuis et al., 1995; Harrison et al., 1995; Jimeno-Aranda et al., 1996; Pacelli et al., 1999; Saito et al., 2006;). This could be due to the high level of diagnosis stage as unknown situation for more than 42% of the patients in the current study. The evaluation criteria in the univariate analysis indicated that there was a significant difference in survival probability between those patients with surgery and chemotherapy and on the other side those with chemotherapy only. Though this variable was not significant in the multivariate analysis in the presence of the other variables, but the hazard ratio was 1.33 for patients with chemotherapy only in comparison to those who use both types of treatment simultaneously (not shown). These findings are in line with results obtained by Cunningham et al. (2006) who concluded that the surgery following chemotherapy increased the patient's lifetime (Erturk et al., 2003)

We found that radiotherapy decreased the death hazard as 40%. It was also confirmed by Sun et al. (2009) and Macdonald et al. (2001) who evaluated the effect of radiotherapy on GC patients with metastasis. In addition the positive effect of supplementary treatment following radiotherapy was concluded by Bilimoria et al. (2007) in GC patients in the United States.

The age of diagnosis was also a significant predictor of survival in our study, so that the age at diagnosis over 60 years increased the hazard about 1.41 times. This is similar with the results obtained in other studies (Macdonald et al., 2001; Sun et al., 2009).

The univariate analysis showed that distant metastasis to other organs was significantly effective in the survival of patients but not in the multivariate analysis. The median survival of metastasic patients was 9 months less than those patients without metastasis (Table 1). The relatively hazard of the patients with distant metastasis was 1.3 times more than other patients (Table 2). This is similar to the findings of the other studies (Arveux et al., 1992; Jaehne et al., 1992; Haugstvedt et al., 1993; Adachi et al., 1994; Adachi et al., 1996; Shiraishi et al., 2000; Bilimoria et al., 2007; Markelis et al., 2009). In the current study, tumour site was not significantly related to the survival in both univariate and multivariate analysis. This may be due to the diagnosis of the most patients in higher clinical stages (384 patients) and there were only 12.6% of patients in stages 1 and 2 (59 patients).

From the data obtained, it could be inferred that there was a potential effective role of age at diagnosis, gender of patients and pathologic stage of disease in cancer therapy in this part of Iran. Therefore, to reduce the risk of death in patients with GC, the early diagnosis of patients at younger age and also in primary stages has been significant. Most patterns of GC obtained in the current research are similar to those reported from high-risk regions worldwide. However, the association among the environmental and other risk factors effective in GC patients' lifetime remains to be investigated.

Finally, an efficient surveillance national wide program is suggested to detect GC cancer in early age especially in a group of high risk population as a way to reduce gastric cancer mortality in Iran.

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