RESEARCH COMMUNICATION

Impact of Age on Prognosis in Iranian Patients with Gastric Carcinoma: Review of 742 Cases

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Abstract

   Background: Gastric carcinoma is one of the most common gastrointestinal malignancies worldwide. Some studies have suggested that it has a worse prognosis in non-elderly than in elderly patients. The aim of the present study was to clarify whether the patient's age is an independent prognostic factor. Methods: A total of 742 patients with gastric carcinoma, who had registered in our cancer registry center between years 2001- 2006 were reviewed to investigate the prognostic significance of age. They were divided into the following two groups: non-elderly (under 70 years) and elderly (70 years or older). The clinicopathological features were reviewed retrospectively and a multivariate analysis was carried out. Results: Lymph node metastasis and differentiated type were more frequently observed in non-elderly than in elderly patients (P<0.0001) and older patients diagnosed with more advanced stages compared with those younger than 70 years old (P=0.015). 5-year survival rates were 27.2 and 15.2% in non-elderly and elderly patients, respectively, the difference being statistically significant (P<0.001). Multivariate analysis showed that age and wall penetration were independent prognostic factors Conclusions: Age clinically serves as an important predictor of survival in patients with gastric carcinoma and elderly patients with gastric carcinoma have a worse prognosis than nonelderly patients.

Keywords: Gastric cancer - prognostic factors - age - Iranian patients

Introduction

   According to the world estimate of cancer incidence in the year 2002 by the International Agency for Research on Cancer, gastric carcinoma is still one of the most common cancers in the world, the fourth most commonly occurring cancer (9% of all cancers) after cancer of the lung, breast, and colorectal, and the second most common cancer related cause of death (10% of all cancer deaths) after lung cancer (Inoue and Tsugane, 2005).The incidence of gastric carcinoma among the old has recently been increasing in many countries. It has been reported that age-adjusted death rates for gastric carcinoma have increased with aging (Arai et al., 1997). Kitamura et al (1996) reported that patients with gastric carcinoma aged 70 years and older increased, despite a plateau in the total number of patients with gastric carcinoma. It is estimated that gastric carcinoma in patients aged 65 years or older accounts for approximately 70% of total gastric carcinoma (Ministry of Health and Welfare of Japan, 2000). This evidence indicates that the relationship between aging and prognosis in older patients with gastric carcinoma is of great importance (Saito et al., 2006).

   Many studies have indicated that the depth of invasion, tumor size, stage, grade and the presence of lymph node metastasis are the most important prognostic factors in gastric carcinoma (Maruyama, 1987; Saito et al., 1999; 2006a; 2006b; Yokota et al., 2002; 2004; Alici et al 2006). Although the relationship between prognosis and age of patients with gastric carcinoma is controversial, a poorer prognosis in nonelderly patients has been suggested by most investigators (Lo et al., 1999). To further examine the hypothesis, a retrospective study was undertaken to analyze a series of patients with gastric carcinoma in Iran.

Materials and Methods

Patients
   This study was based on a retrospective analysis of 742 patients with gastric adenocarcinoma. These patients registered in Taleghani hospital (Tehran, Iran) between 2001 until 2006 and were enrolled in this study. The clinicopathological findings were determined according to the medical records and cancer registry forms. Pathologic stage of tumor was defined as early stage(IA,IB,II,IIA,IIB) and advanced stage(IIIA,IIIB,IV) according to the TNM classification.

Statistical analysis
   Association among factors was evaluated by the

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χ2-test. Survival curves were calculated according to the Kaplan-Meier method. Differences between survival curves were examined with the log-rank test. Multivariate analysis of prognostic factors related to overall survival was carried out using Cox's proportional hazards model and a stepwise procedure. The covariates included age, sex, extent of wall penetration, lymph node metastasis, distant metastasis, grade of tumor, pathologic stage and family history of cancer. The accepted level of significance was $P<0.05$.

Results

Age and clinicopathological factors

The patients' ages ranged from 20 to 88 years with a mean of 59.6±12.9 years; 530 patients were male and 216 were female. A histogram of the patients with regard to age is shown in Figure 1. According to a previous report, patients were divided into two groups as follows: nonelderly patients, age less than 70 years and elderly patients, age over 70 years (Maehara et al., 1995). The correlation between age and clinicopathological factors is shown in Table 1. Poor differentiated type of grade was more frequently observed in nonelderly than in elderly patients ($P=0.016$) and older patients diagnosed with advanced stage compared with younger than 70 years patients ($P=0.015$). Moreover, Regional Lymph Nodes metastasis (N) was seen more frequently in nonelderly than in elderly patients ($P=0.003$).

Patients' survival and age

At the time of analysis, the mean survival time of patients were 42.45(CI:35.75-49.17) months. Of 746 patients, 38.6 percent were dead. Kaplan-Meier estimate

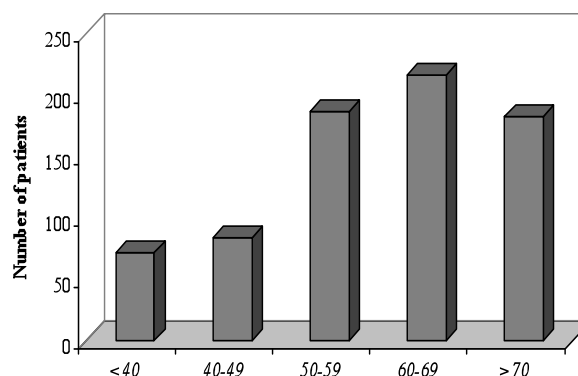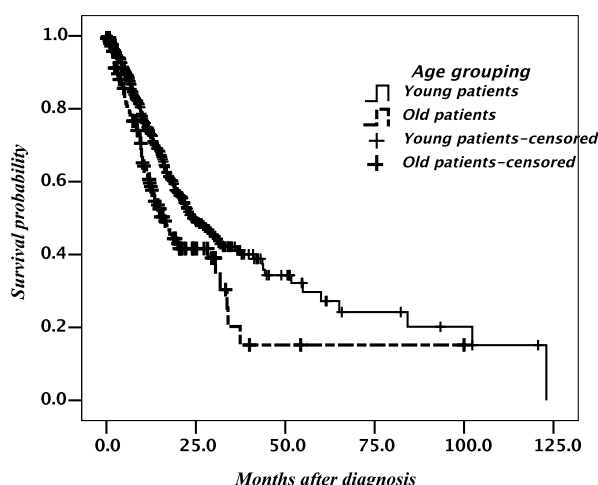**Figure 1. Age-distribution of the Patients**

Figure 2. Cancer-specific Survival Curves. The prognosis of elderly gastric carcinoma patients is significantly worse than that of non-elderly patients, $P<0.001$.

Table 1. Correlation between Age and Clinicopathological Features

Variables	Age (years)		P- value
	Nonelderly (n = 583)	Elderly (n =159)	
Sex (n=742)			
Male	409(70.2%)	120(75.5%)	0.041
Female	174(29.8%)	39(24.5%)	
Family history of cancer (n=699)			
Absent	402(73.2%)	120(80.0%)	0.091
Present	147(26.8%)	30(20.3%)	
Grade of tumor (n=452)			
Well differentiated	83(22.7%)	29(33.3%)	0.016
Moderately differentiated	112(30.6%)	28(32.2%)	
Poor differentiated	171(46.7%)	29(33.3%)	
Extent of wall penetration (T) (n=554)			
T1	14(3.1%)	4(3.5%)	0.153
T2	63(14.0%)	7(6.1%)	
T3	200(44.4%)	57(50.0%)	
T4	173(38.4%)	46(40.4%)	
Regional Lymph Nodes metastasis(N) (n=454)			
N1	117(31.7%)	13(15.3%)	0.003
N2	208(56.4%)	54(63.5%)	
N3	44(11.9%)	18(21.2%)	
Distant Metastasis(M) (n=505)			
Absent	249(63.2%)	72(64.9%)	0.747
Present	145(36.8%)	39(35.1%)	
Stage (n=612)			
Early stage	139 (28.9%)	22(17.7%)	0.015
Advance stage	349(71.5%)	102(82.3%)	

Table 2. Multivariate Analysis of Clinicopathlogical Factors in Patients under Study

Variable	Hazard ratio	95% CI	P-value
Age (years)†	1.02	1.01–1.03	0.025
Extent of wall penetration (T) ‡			
T1	1	-	-
T2	3.03	0.43-11.35	0.251
T3	4.97	0.69-13.90	0.112
T4	9.27	1.26-18.08	0.029

†Continuous variable; ‡T1, tumour has invaded lamina propria or submucosa; T2, tumour has invaded the muscularis propria or the subserosa; T3, penetrating the serosa; T4, invading adjacent organs

showed that, 5-year survival rates were 27.2% and 15.2% in nonelderly and elderly patients, respectively, and the difference was statistically significant (P=0.003; Figure 2). We used Cox's proportional hazards model and a stepwise procedure to assess whether age represents an independent prognostic factor. The results showed that age and extent of wall penetration were independent prognostic factors (Table 2).

Discussion

Gastric carcinoma is usually a disease of the aged with patients showing a mean age of approximately 50–60 years (Bedikian et al., 1979; Mori et al., 1985; Fujimoto et al., 1994). Furthermore, the incidence of gastric carcinoma is increasing in patients more than 70 years old(Kitamura et al., 1996; Kubota et al., 2000; Otani et al., 2000). Whether gastric carcinoma in elderly patients differs from that in non-elderly patients is controversial. Some authors have reported an inverse relationship between age and prognosis in gastric carcinoma. In the present study, we showed that the prognosis of patients with gastric carcinoma was closely related to age and 79% of all patients with this disease registered in our center were younger than 70 years of age.

In our research, there was a significant difference in the sex ratio between the non-elderly and elderly patients. In the elderly patients, there were a higher proportion of male patients (3.1:1). Other studies have obtained the same results (Maehara et al., 1996; Medina-Franco et al., 2000; Dong-Yi et al., 2005; Wang et al., 2006). The causes of this gender imbalance are not yet clear. Male patients might have a more frequent and prolonged exposure to environmental carcinogens than females, which might explain the male predominance among elderly patients (Ershler and Longo, 1997). Sex hormones may also play a role. Several studies have demonstrated that the presence of estrogen receptor is associated with poor survival in nonelderly patients with gastric carcinoma (Tokunaga et al., 1986; Harrison et al., 1991). On the contrary, for non-elderly patients the sex ratio (females: males) has consistently been reported abut 2.3:1, and this result is compatible with other reports (Grabiec and Owen, 1985; Fujimoto et al.,1994).

Concerning the differentiation of tumor, poorly differentiated type of grade was more frequently observed in nonelderly than in elderly patients. Other studies have

reported similar results[3,Fujimoto et al.,1994; Wang et al., 1996; Medina-Franco et al., 2000). In contrast to elderly patients, the higher incidence of poorly differentiated adenocarcinoma in nonelderly patients found in this study is consistent with the literature.

There were no significant differences in either distant metastasis (M) or extent of wall penetration (T1-T4) between the two groups by univariate analysis. This finding is in contrast with a prior report [20]. Like other studies, finding of multivariate analysis using Cox's proportional hazard model indicate that extent of wall penetration (T) is an independent prognostic factor in gastric carcinoma patients (Saito et al., 2006).

Some authors have suggested a familial form of gastric carcinoma (Bresciani et al., 2003) with an autosomic dominant pattern, although most authors think that the genetic predisposition to gastric carcinoma involves multiple genes and environmental factors (Tahara, 1995). In the present study, there was no significant difference between both groups in regard to the family history of gastric carcinoma.

There were significant differences in either lymph node metastasis or pathologic stage between the two groups. Kubota et al. have shown that the presence or absence of lymph node metastasis is statistically different between the two age groups(>or=80 years) (Kubota et al., 2000). Also, Kim Dong-Yi et al (2005) indicated that the stage of tumor (T1-T4) in time of diagnosis wasn't statistically differing among the two age groups under study. Results of our study are in consistence with their findings.

In this series, 5-year survival rates were 27.2% and 15.2% in nonelderly and elderly patients, respectively, and the difference was statistically significant (P=0.003). In previous reports, the prognosis of elderly patients was poor and the survival rate was low, particularly in patients with advanced gastric carcinoma (Katai et al., 1997; Kubota et al., 2000). Delay in diagnosis and a more advanced stage of gastric carcinoma in elderly patients have been suggested as possible causes of a poor prognosis and low survival.

In conclusion, in this study, elderly patients with gastric carcinoma have a worse prognosis than nonelderly patients. Age clinically serves as an important predictor of survival in patients with gastric carcinoma and should be taken into account along with conventional clinicopathological variables such as extent of wall penetration and lymph node metastasis.

Acknowledgements

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