

Determination of Risk Factors Affecting Survival of Patients with Gastric Adenocarcinoma in Hamadan, Iran

Ghodratollah Roshanaei*, Farshad Rostampour**,***, Mohammadreza Javadi****, Sepideh Behnoud****, Masoud Sabouri Ghannad*****

*Modeling of Noncommunicable Diseases Research Center, Department of Biostatistics, School of Public Health, Hamadan University of Medical Sciences, Hamadan, Iran

**Student Research Center, Hamadan University of Medical Sciences, Hamadan, Iran

***Health Center, Ilam University of Medical Sciences and Health Services, Ilam, Iran

****Department of General Surgery, Faculty of Medicine, Hamadan University of Medical Sciences and Health Services, Hamadan, Iran

*****Research Center for Molecular Medicine, Department of Microbiology, Faculty of Medicine, Hamadan University of Medical Sciences, Hamadan, Iran

Abstract

Background: Gastric cancer is the second leading cause of cancer death. The aim of this study was to determine the survival rate affected by risk factors in patients with gastric adenocarcinoma.

Methods: We performed this retrospective cohort study on patients diagnosed with gastric adenocarcinoma during 2005-2012 in Hamadan, Iran. All patients with pathological diagnosis enrolled in the study. The effects of patients' demographical and pathological data were assessed in terms of survival. The univariate and multivariate Weibull models were used to determine the effects of these factors on survival rate. Data was analyzed by SPSS16 and STATA10 software.

Results: A total of 112 gastric adenocarcinoma patients were followed. Patients included 74 (66.1%) males. During the follow-up, 102 (91.1) patients died. Patients' had a mean (SD) survival of 21.9 (1.9) months and a median survival of 15 months. The "one-, three- and five-year survival rates were 62%, 16% and 9% respectively. The results showed that metastasis, chemotherapy, tumor site and grade had statistically significant impacts on patient survival.

Conclusion: A potentially important role for tumor grade, tumor site, metastasis, and pathologic stage of disease existed in terms of patient survival after surgery. The current research has indicated that neoadjuvant treatment increased survival in patients with gastric adenocarcinoma. It is expected that the prognostic model based on the mentioned factors may assist individual risk stratification and help in the planning of potential forthcoming studies.

Keywords: Gastric adenocarcinoma, Survival, Adjuvants, Pharmaceuticals, Therapeutics

Corresponding Author:

Masoud Sabouri Ghannad, PhD
Research Center for Molecular
Medicine, Department of
Microbiology, Faculty of
Medicine, Hamadan University
of Medical Sciences, Shaheed
Fahmideh Avenue opposite the
Mardom Park, Hamadan, Iran
Tel: +98-8138380160
Fax: +98-8138380208
Email: sabouri@umsha.ac.ir



Introduction

Gastric cancer (GC) is the fourth most common cancer worldwide¹ and has been reported in Iran.² It is the leading cause of cancer death, with an estimated 875,000 new cases diagnosed annually worldwide.¹ Gastric cancer is the major cause of cancer-related deaths, especially in Asian countries.^{3,4} This study aims to estimate survival and its related factors in patients with gastric adenocarcinoma (GA) during 2005-2012, in Hamadan, a western province of Iran.

Materials and Methods

All patients with pathological diagnosis of GA who referred to Besat Hospital and Mahdiyeh Chemotherapy and Radiotherapy Center in Hamadan during 2005-2012 enrolled in the study. Each patient's survival status was determined by phone contact. We collected patients' demographical and pathological data that included sex, age at diagnosis, tumor site, tumor grade, pathologic stage, numbers of involved lymph nodes, metastasis, chemotherapy, and type of surgery. Their probable roles on patient survival were assessed.

We defined patient lifetime as time of diagnosis until death or end of the current study. Patients'

survival was considered as a censoring event. In this study, Kaplan-Meier was used to determine the patient survival curve. The Weibull regression model was selected as a suitable parametric model due to the Akaike information criteria (AIC). We used the univariate and multivariate Weibull models to analyze and determine the factors that affected patients' survival, as unadjusted and adjusted status. Data were analyzed with SPSS 16 and Stata 10 software. Statistical significance was set at 5%.

Results

We followed 112 patients with GA, which included 74 (66.1%) males. The mean (SD) follow-up was 21 (18.2) months. The mean (SD) age at diagnosis was 67.1 (12.7) years. The mean age for males was 68 (12.5) years and for females, it was 65.3 (13.1) years. During follow-up 102 (91.1) patients died. Table 1 shows the patients' characteristics. Patients had a mean (SD) survival of 21.9 ± 1.9 months and median survival of 15 months. The "one-, three- and five-year survival rates were 62%, 16% and 9% respectively. Median survival in males was 17 months, whereas in females it was 13 months. Figure 1 shows the patients' survival curve.

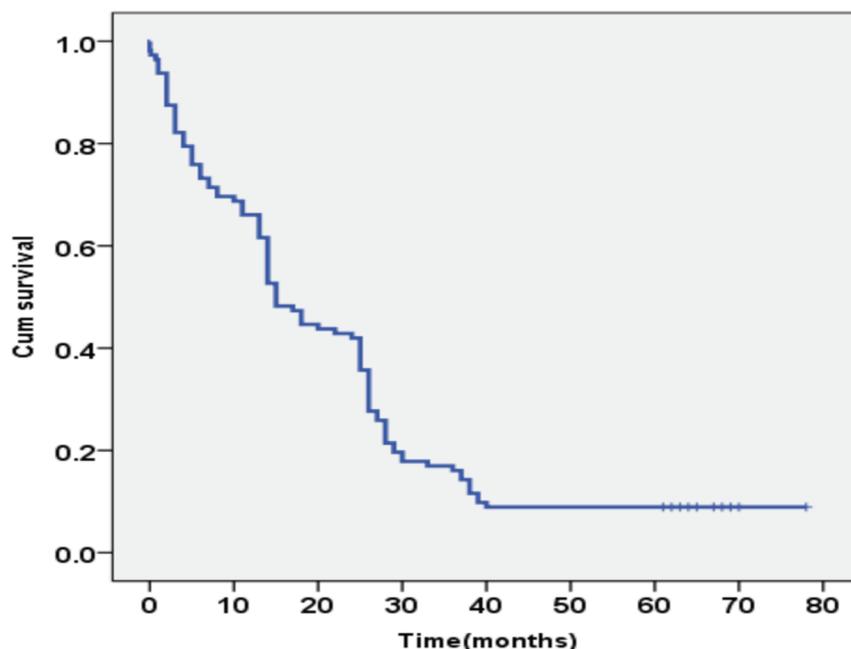


Figure 1. Survival probability of patients with gastric adenocarcinoma (GA).

Table 1. Characteristics of patients with gastric adenocarcinoma (GA) and results of model fit according to univariate Weibull regression model.

Variable	Level	N (%)	Median (months)	HR (95% CI)
Gender	Male	74 (66.1)	17	1
	Female	38 (33.9)	13	1.15(0.76-1.75)
Age at diagnosis (years)	<60	21 (18.8)	15	1
	60-70	34 (30.4)	26	0.7(0.4-1.24)
	>70	57(50.8)	14	1.03(0.61-1.75)
Grade*	Well	16 (14.3)	28	1
	Moderate	59 (52.7)	22	1.97(1.05-3.7)
	Poor	37(33)	13	4.3(1.7-6.3)
Neoadjuvant *chemotherapy	No	91 (81.3)	18	1
	Yes	21 (18.7)	11	1.77(1.07-2.9)
Adjuvant chemotherapy	No	35 (31.2)	4	1
	Yes	77 (68.8)	25	0.7(0.45-1.1)
Neoadjuvant Chemo-radiotherapy	No	98 (86.6)	14	1
	Yes	15 (13.4)	25	0.9(0.65-1.1)
Tumor site*	Cardia	74(66.1)	17	1
	Pylor	25(22.3)	13	0.54(0.32-0.9)
	Other	13 (11.6)	25	1.44(0.78-2.67)
lymph node* Involvement	No	104(92.9)	-	1
	Yes	8(7.1)	14	3.8(1.4-6.7)
Metastasis*	No	33(70.5)	6	1
	Yes	79(29.5)	25	3.94(2.5-7.2)
Pathologic stage* II		9(8)	-	1
	III	70(62.5)	25	3.96(2.5-11.5)
	IV	33(29.5)	6	5.6(2.8-14.9)
Type of Surgery*	Total	28(25)	14	1
	Subtotal	79(70.5)	17	1.55(1.01-2.5)
	Palliative	5(4.5)	13	3.5(1.3-9.4)

*Statistically significant

Initially, we performed the univariate Weibull regression analysis to independently assess the risk factors. The results indicated that tumor grade, use of neoadjuvant chemotherapy, tumor site, involved lymph nodes, metastasis, stage of diagnosis, and surgery type significantly affected GA patients' survival (Table 1). However, evaluation of the significant risk factors simultaneously according to multivariate Weibull regression analysis indicated that only tumor grade, tumor site, metastasis, and stage significantly ($P<0.05$) affected survival (Table 2). Table 2 shows the statistically significant effects of metastasis, chemotherapy, tumor site, and tumor grade in the presence of other variables.

Discussion

In some studies proximal tumors need to be removed by surgery and a number of lymph nodes are reported to be affected.⁵ Unfortunately these tumors are diagnosed at an advanced stage and have a low survival rate in Iran where the five-year survival rate varies from 0.83%-22.6% in different studies.⁶⁻⁸ The current study has attempted to evaluate the probable effects of some factors on the survival of patients with GA. The results of univariate analysis showed that risk factors such as tumor grade, tumor site, neoadjuvant chemotherapy, lymph node involvement, metastasis, surgery type, and pathologic stage of the disease significantly affected the survival of GA patients. However, according to multivariate analysis, neoadjuvant chemotherapy and surgery

Table 2. Assessment of affected factors on survival of patients with gastric adenocarcinoma (GA) according to multivariate Weibull regression model.

Variable	Level	P-value	OR-adjusted (95%CI)
Tumor grade*	Well	1	
	Moderate	0.03	2.04(1.07-3.88)
	Poor	0.009	2.56(1.26-5.2)
Neoadjuvant chemotherapy	No	1	
	Yes	0.16	1.45(0.86-2.44)
Tumor site*	Cardia	1	
	Pylori	0.006	0.27(0.11-0.69)
	Other	0.001	0.26(0.12-0.58)
Metastasis*	No	1	
	Yes	<0.001	14(9.9-35.1)
Pathologic stage*	II	1	
	III	0.011	4.7(1.5-15.2)
	IV	0.001	10.3(2.2-22.8)
Type of surgery	Total	1	
	Palliative	0.58	0.83(0.43-1.6)
	Subtotal	0.7	3.1(0.4-6.5)

*Statistically significant

type were not significant in the presence of the other variables (Table 2). Mean (SD) survival was 21.9 ± 1.9 , whereas median survival was 15 months. The “one-, three- and five-year survival rates were 62%, 16% and 9% respectively. These probabilities were lower than those reported by Akhavan et al. in another cancer center in Yazd, a central province of Iran.⁹ In that study, mean survival of patients with GA was 50.9 months whereas their patients had a median survival of 51 months. The three-year survival rate was 73% and five-year survival rate was 36%. The discrepancy could be due to the higher clinical diagnosis stages of the disease in the Yazd cancer center. The current study showed that the survival probability between males and females did not significantly differ. These results supported those of previous studies in some countries,¹⁰⁻¹² which confirmed that sex had no effect on the survival of patients with GA. However, the results did not support the results of our previous research that showed a significant role of sex in GC patient survival in Tehran, the capital of Iran.¹³ The lower age at diagnosis for female patients in that research might be due to the regional differences in terms of cultural and educational lifestyles in Hamadan compared to Tehran, the capital of Iran. In the current study, 77 (68.8%) patients underwent

adjuvant chemotherapy, 21 (18.7%) underwent neoadjuvant chemotherapy, and 15 (13.4%) received neoadjuvant chemo-radiotherapy. Median survival in these groups was 25 months for those who received adjuvant chemotherapy, 11 months for the group that received neoadjuvant chemotherapy, and 25 months for the neoadjuvant chemo-radiotherapy group. In the Macdonald et al.¹² study, the median overall survival in GC patients who underwent surgery was 27 months. Median overall survival was 36 months in those who underwent adjuvant chemo-radiotherapy. The hazard ratio for death was 1.35 (95% confidence interval: 1.09 to 1.66; $P=0.005$). Cunningham et al.¹³ compared perioperative chemotherapy versus surgery alone for resectable gastroesophageal cancer and reported that in a median follow-up of four years, 149 patients in the perioperative chemotherapy group and 170 patients in the surgery group died. The perioperative chemotherapy group had a higher possibility of overall survival compared with the surgery group [Hazard Ratio (HR) with 95% Confidence Interval (CI)] for death which was 0.75 (0.60 - 0.93). The reason might be due to the perioperative chemotherapy regimen that could decrease tumor size and stage which might significantly improve progression-free and overall

survival. The five-year survival rate was 36% versus 23% progression-free survival (HR (95% CI) for progression, 0.66; 95% confidence interval, 0.53 to 0.81; probability of error $P < 0.001$). In our study patients' survival rate significantly decreased in those with high grade tumors. This finding supported our previous research where we reported a significant relationship between GC survival rate and pathologic stage.¹⁴ Patients with stages 3 and 4 tumors had worse outcome - 2.9 times more for stage 3 and 3.1 times more for stage 4 compared to stage 2 patients.

In conclusion, a number of factors can separately influence survival of GA patients. In the current study, we have observed an important role for tumor grade, tumor site, metastasis, and pathologic disease stage in patient survival after surgery. The current research has indicated that neoadjuvant treatment can increase the survival of patients with GA. It is expected that the prognostic model based on the mentioned factors may assist individual risk stratification and help in the planning of potential, forthcoming studies.

Acknowledgements

The authors wish to thank the authorities and staff of Besat Hospital and Mahdiyeh Chemotherapy and Radiotherapy Center in Hamadan for their cooperation.

Conflict of Interest

No conflict of interest is declared.

References

1. Avital, I; Pisters, PWT; Kelsen, DP; Willett, CG. Cancer of the Stomach. In: DeVita, VT; Lawrence, TS; Rosenberg, SA, editors. DeVita, Hellman, and Rosenberg's cancer: Principles and practice of oncology. 9th ed. Philadelphia: Lippincott Williams & Wilkins; 2011.p.924-54.
2. Nadim, A; Nourai, M. Cancers. In: Azizi, F; Hatami, H; Janghorbani, M, editors. Epidemiology and control of common diseases in Iran. 1st ed. Eshtiagh, Tehran; 2000.p.216-17.
3. Park YS, Jin MY, Kim YJ, Yook JH, Kim BS, Jang SJ. The global histone modification pattern correlates with cancer recurrence and overall survival in gastric adenocarcinoma. *Ann Surg Oncol*. 2008;15(7):1968-76.
4. Jemal A, Siegel R, Ward E, Murray T, Xu J, Smigal C, et al. Cancer statistics, 2006. *CA Cancer J Clin*. 2006;56(2):106-30.
5. Biglarian A, Hajizadeh E, Gohari MR, R. KB. Survival analysis of patients with gastric adenocarcinomas and factors related [article in Persian]. *Kowsar Med J*. 2008;12:345-55.
6. Samadi F, Babaei M, Yazdanbod A, Fallah M, Nouraei M, Nasrollahzadeh D, et al. Survival rate of gastric and esophageal cancers in Ardabil province, North-West of Iran. *Arch Iran Med*. 2007;10(1):32-7.
7. Zeraati H, Mahmoudi M, MK. K. Postoperative survival in gastric cancer patients and its associated factors: A time dependent covariates model. *Iranian J Publ Health*. 2006;35:40-6.
8. Khedmat H, Panahian M, Amini M, Izadi M, Naseri MH. Survival of stomach cancer among patients hospitalized in Baghiyatallah hospital [Article in Persian]. *J Mil Med*. 2007;9:167-77.
9. Akhavan A, Binesh F, Seifaddiny A, Ghannadi F. Characteristics and survival rate of patients with gastric and gastroesophageal junction adenocarcinoma in Yazd, Iran. *Middle East J Cancer*. 2013;4(3):125-9.
10. Zhang XF, Huang CM, Lu HS, Wu XY, Wang C, Guang GX, et al. Surgical treatment and prognosis of gastric cancer in 2,613 patients. *World J Gastroenterol*. 2004;10(23):3405-8.
11. Zeraati H, Mahmoudi M, Kazemnejad A, Mohammed K. Postoperative life expectancy in gastric cancer patients and its associated factors. *Saudi Med J*. 2005;26(8):1203-7.
12. Macdonald JS, Smalley SR, Benedetti J, Hundahl SA, Estes NC, Stemmermann GN, et al. Chemoradiotherapy after surgery compared with surgery alone for adenocarcinoma of the stomach or gastroesophageal junction. *N Engl J Med*. 2001;345(10):725-30.
13. Cunningham D, Allum WH, Stenning SP, Thompson JN, Van de Velde CJ, Nicolson M, et al. Perioperative chemotherapy versus surgery alone for resectable gastroesophageal cancer. *N Engl J Med*. 2006;355(1):11-20.
14. Roshanaei G, Ghannad MS, Jafarabadi MA, Faradmal J, Sadighi S. Prognostic impact of risk factors in patients with gastric cancer in Iran. *Asian Pac J Cancer Prev*. 2011;12(11):3005-8.