

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

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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

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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 Mahdīyeh 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.

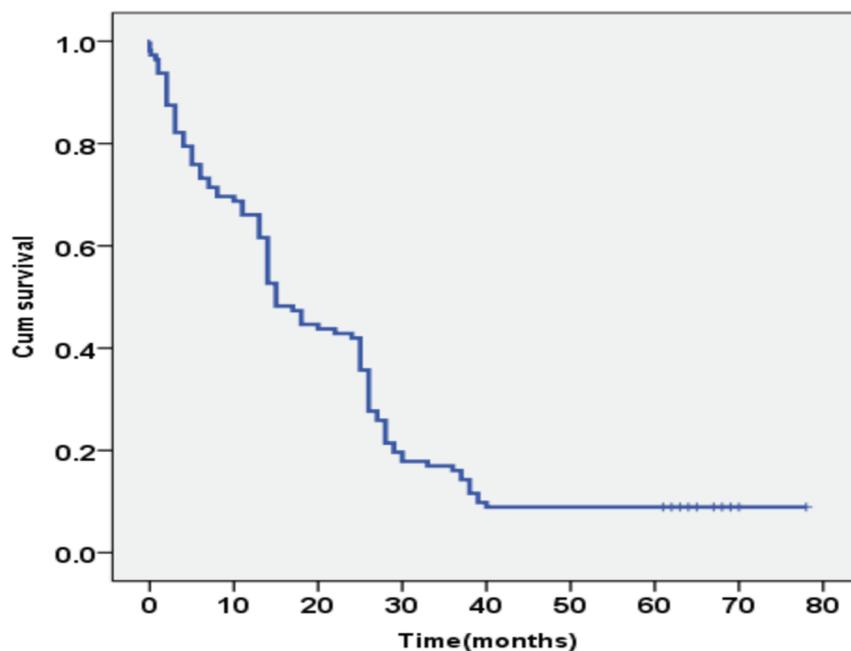


Figure 1. Survival probability of patients with gastric adenocarcinoma (GA).

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.

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Conflict of Interest

No conflict of interest is declared.

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