RESEARCH COMMUNICATION

Bayesian Analysis for Survival of Patients with Gastric Cancer in Iran

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Abstract

Background & Objectives: Gastric cancer is one of the most common cancers in the world. The aim of this study was to evaluate prognostic factors using Bayesian interval censoring analysis. Methods: This is a historical cohort study of 178 patients from February 2003 through January 2008, admitted with gastric cancer to one referral hospital in Tehran. Age at diagnosis, sex, histology type, tumor grade, tumor size, pathologic stage, lymph node metastasis and distant of metastasis were entered into the analysis using Bayesian Weibull and Exponential models. The term DIC was employed to find best model. Results: The results showed that as age increased, the risk of death slightly increased significantly in both Weibull and Exponential models with similar results. Patients with grater tumor size were also in higher risk of death followed by advanced pathologic stage. Neither the Weibull nor the Exponential models found sex, distant metastasis, histology type, tumor grade and lymph node metastasis to be prognostic factors. Based on DIC, Bayesian analysis of the Weibull model performed better than the Exponential model. Conclusion: According to these results the early detection of patients at lower ages and in primary stages is important to increase the survival in patients with gastric cancer.

Key words: Gastric cancer - prognostic factors - Bayesian analysis

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Introduction

Despite the universal decline in gastric cancer incidence and mortality, gastric cancer (GC) is still the second most common cancer worldwide (Parkin et al., 2001; Parkin et al., 2004) and is predicted to be the eighth leading cause of all deaths worldwide in the year 2010 (Murray & Lopez, 1997).

Survival analysis is the modeling of time to event of death to evaluate the effects of treatment on survival time. It is important to determine the prognosis factors for patients with gastric cancer. Some potential clinicopathological factors, such as age, tumor size, depth of invasion, distant metastasis, and pathologic type, have been evaluated to identify the factors affecting survival in these patients (Michelassi et al., 1994; Hansson et al., 1999; Yokota et al., 2004).

Most of researches have been done to assess the prognosis factor on survival of patients with GC via right censoring which means that the exact point-time of event (death) is known (Fernandez et al., 2002; Borie et al., 2004; Orsenigo et al., 2007). But in some cases the time of event is not exactly registered. In this mechanism the event of interest cannot be directly observed and it is only known to have occurred during a random interval of time, the censor item called interval censoring (Lindsey, 1998). A number of methods have been proposed in statistical literature for the estimation of a survival in the presence of interval censoring (Pan, 2000; Pan & Chappell, 2002). One of these favorable techniques is Bayesian estimation in which a prior information proposed for unknown parameters of interest (Congdon, 2003).

The aim of this retrospective study was to elucidate what factors affect the survival of patients with GC using Bayesian parametric survival models. Also all models were compared to each other in order to find the best one.

Materials and Methods

This is a historical cohort study of patients treated from February 2003 through January 2008, 178 patients whom were admitted at Taleghani hospital with a diagnosis of GC. This hospital is a referral center for gastrointestinal cancers and all of these patients were diagnosed by endoscopy and biopsies. The exclusion criteria were the patients who had not completed document at hospital registry or treated out of the time February 2003 to January 2008. The study protocol was approved by the ethics committee of the Research Centre for Gastroenterology and Liver Disease of Shaheed Beheshti Medical University. The case of patient's death was confirmed through contact with families of patients by telephone and clinical information was extracted from hospital documents during about two months. Because for some

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Table 1. Demographic Characteristics of Gastric Cancer Patients

Variable	Subgroup	Frequency	
		n	%
Grade of tumor	Well differentiated	49	27.5
	Moderately differentiated	61	34.3
	Poorly differentiated	68	38.2
Tumor size	<35mm	48	27.0
	>35mm	130	73.0
Histology type	Adenocarcinoma NOS	132	74.2
	Signet cell car. &mucin-producing adeno. & mucinous adeno.	24	13.5
	Other type of histology	22	12.4
Regional lymph node metastasis	N1	52	29.2
	N2	105	59.0
	N3	21	11.8
Pathologic distant metastasis	Absent	164	92.1
	Present	14	7.9
Pathologic stage	I(0,IAIB), II	71	39.9
	III(IIIA,IIIB), IV	107	60.1

patients there was no information regarding the exact time of death, the type of censoring supposed to be interval censoring.

Age at diagnosis, sex, histologic type, tumor grade, tumor size, pathologic stage, lymph node metastasis and distant of metastasis were entered to the Bayesian parametric model including Weibull and Exponential censored regression with a priors for shape parameters for all models. The analysis carried out using Winbugs and MCMC technique to estimate the Bayesian Relative Risk (RR) to interpret the risk of death in parametric results. The term of DIC was employed to compare the efficiency of models (Spigelhalter et al., 2002). The DIC is a measure of the goodness of fit for Bayesian estimation. Lower DIC indicates better likelihood.

All P-values less than 0.05 were considered as statistically significant.

Results

A total number of 178 patients with GC entered to this study, 130 men (73%) and 48 women (27.0%). The mean age at diagnosis was 58.5±12.7 years. In general, up to 80% of patients survived for first year of follow-up, 52.2% for second year and 35.3% for third year. Of this

Table 2. Univariate Model of Bayesian Parametric Regression with Prognostic Factors

	Weibull RR (CI: 95%)	Exponential RR (CI: 95%)
Age at diagnosis	1.02 (1.01-1.04)*	1.02 (1.01-1.04)*
Sex		
Male	1.71 (0.97-3.19)	1.58 (0.89-2.87)
Female	1.00	1.00
Distant metastasis		
Absent	1.00	1.00
Present	2.11 (0.93-4.31)	2.06 (0.92-4.20)
Tumor size		
<35mm	1.00	1.00
>35mm	1.98 (1.08-3.96)*	2.00 (1.07-3.91)*
Histology type		
Adenocarcinoma	0.61 (0.31-1.27)	0.65 (0.33-1.36)
Signet ring cell	0.39 (0.11-1.13)	0.40 (0.12-1.15)
Other	1.00	1.00
Tumor differentiation grade		
Well	0.83 (0.45-1.54)	0.84 (0.45-1.54)
Moderately	0.73 (0.41-1.32)	0.78 (0.43-1.39)
Poorly	1.00	1.00
Lymph node metastasis		
N1	0.86 (0.35-3.29)	0.84 (0.35-2.32)
N2	0.98 (0.45-2.41)	1.01 (0.47-2.57)
N3	1.00	1.00
Pathologic stage		
Early	1.00	1.00
Advanced	1.75 (1.04-3.02)*	1.72 (1.02-3.00)*

* Statistically significant

Table 3. Multivariate Model of Bayesian Parametric Regression with Prognostic Factors

	Weibull RR (CI: 95%)	Exponential RR (CI: 95%)
Age at diagnosis	1.02 (0.99-1.04)	1.01 (0.99-1.04)
Sex		
Male	1.78 (0.97-3.44)	1.64 (0.9-3.12)
Female	1.00	1.00
Distant metastasis		
Absent	1.00	1.00
Present	2.35 (0.93-5.52)	2.13 (0.86-4.77)
Tumor size		
<35mm	1.00	1.00
>35mm	2.29 (1.21-4.83)*	2.15 (1.13-4.42)*
Histology type		
Adenocarcinoma	0.58 (0.28-1.23)	0.63 (0.31-1.36)
Signet ring cell	0.32 (0.09-1.01)	0.36 (0.11-1.10)
Other	1.00	1.00
Tumor differentiation grade		
Well	0.68 (0.34-1.31)	0.71 (0.37-1.31)
Moderately	0.52 (0.26-0.99)	0.58 (0.31-1.1)
Poorly	1.00	1.00
Lymph node metastasis		
N1	2.18 (0.66-7.25)	1.94 (0.66-6.44)
N2	1.24 (0.49-3.34)	1.28 (0.55-3.33)
N3	1.00	1.00
Pathologic stage		
Early	1.00	1.00
Advanced	1.91 (0.94-4.08)	1.78 (0.89-3.83)
DIC	568.73	575.54

* Statistically significant

total patients 7.9% have had pathologic distant metastasis, 73% have more than 35 mm tumor size, 60.1% diagnosed with advanced stage of GC, 38.2% with poorly differentiated grade of tumor, 74.2% with histology type of adenocarcinoma NOS, 14% in T4 level of extent of wall penetration and 11.8% in N3 level of regional lymph nodes metastasis (Table 1). The mean and median of overall survival time were 48.31±7.07 and 25.3 months respectively. According to the univariate analysis (Table II) as age increased, the risk of death slightly increased significantly in both Weibull and Exponential models with similar results. Patients with grater tumor size were also in higher risk of death followed advanced of pathologic stage. Neither Weibull nor Exponential found sex, distant metastasis, histology type, Tumor grade and Lymph node metastasis as a prognostic factor.In multivariate only tumor size still remains significant with similar results drawn from both models. Based on DIC, Bayesian analysis of Weibull model was performed better than Exponential (Table 3).

Discussion

The aim of this study was assess the association between survival of patients with gastric cancer (GC) and prognosis factors including age at diagnosis, sex, histology type, tumor grade, tumor size, pathologic stage, lymph node metastasis and distant of metastasis using Bayesian interval censoring analysis. Some study reported better survival rate for women (Curtis et al., 1985; Ries et al., 1992). Our results indicated no association between sex and risk of death. A study carried out on 2773 patients by Rotterdam cancer registry reported similar results which rates for male and female were similar (Damhuis & Tilanus, 1995). Li et al indicated that there was no association between sex and survival for patients with advanced GC (Li et al., 2009).

Age at diagnosis was another independent prognostic factor, and our finding in univariate analysis was similar as previous reports (Arveux et al., 1992; Haugstvedt et al., 1993; Li et al., 2009) showing a bit better survival for young patients. Metastasis is another important prognostic factor of GC (Shiraishi et al., 2000), however in our results no association was observed according to both univariate and multivariate analysis.

Size of tumor was another significant factor where affected the survival probability of patients in univariate and multivariate analysis. This finding was in confirmed with those where pointed a higher hazard ratio of death for patients with larger tumor (Orsenigo et al., 2005, Coburn et al., 2006, Li et al., 2009).

Histology type, tumor grade and lymph node metastasis did not seem to be significant. The evaluation criteria in our study indicated that Bayesian analysis of Weibull model was most powerful in comparing to Exponential, although it seems that in the term of interpretation the values obtained for both models were similar. Unfortunately we have not a complete overview regarding the treatment that patients received. The site of metastases was another limitation in our study.

In conclusion, this study indicated that age at diagnosis, tumor size and advanced pathology stage are associated factors for survival time of patients with GC. So the early detection of patients in lower ages and in primary stages is important to increase the survival in patients with GC.

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