RESEARCH COMMUNICATION

Survival Rates and Prognosis of Gastric Cancer using an Actuarial Life-table Method

Bijan Moghimi-Dehkordi*, Azadeh Safaee, Mohammad Reza Zali

Abstract

<u>Background and aims</u>: The aim of this study was to calculate survival rates and analyze patterns of survival in gastric cancer. <u>Methods</u>: A total number of 746 patients with gastric cancer registered in the Cancer Registry Center of Research Center of Gastroenterology and Liver Disease of Shahid Beheshti University of Medical Sciences, Iran, from Dec 21, 2001 to Dec 21, 2006 were investigated. 1- to 5-year survival rates were estimated using life-table method and compared by Wilcoxon (Gehan) test. $P < 0.05$ was considered as statistically significant. All calculations were carried out with SPSS (version13.0) statistical software. <u>Results</u>: There were 530 male patients with a mean age of 60.5 ± 12.6 years and 216 females with a mean age of 57.5 ± 13.5 years. Of the total, 454 died and 285 were censored during the investigation. The median survival time was 24.2 months and survival rates at one, two, third, fourth and five years after diagnosis were 73.6, 50.2, 40.6, 33.2 and 29.7%, respectively. Stages of tumor, histology grade, histologic type of cancer, tumor size, age at diagnosis and surgery approach were independent prognostic factors . However, variables such as sex (P=.533), body mass index (P=.214), ethnicity (P=.092), and level of education (P=.762) did not shown significant effects on survival. <u>Conclusion</u>: Early detection of patients at lower age and with primary stages and grades of tumor is important to increase patient's life expectancy.

Key Words: Gastric cancer - prognosis - life-table - Iran

Introduction

Gastric cancer is one of the major causes of cancer related death in the world, even though its incidence has decreased over the past decade (Boring et al., 1994). Although the mortality rate of gastric cancer has been dramatically decreased in the western country since 1930 (Abeloffet al., 2001; Price and Sikore, 2002), cancer of the stomach remains the second most frequent malignancy in the world (Pisani et al., 1999), and an estimate of more than 1 million new cases were identified worldwide in 1997 (World Health Organization, 1997).

The prognosis of gastric cancer is generally poor, especially in Western countries (Akoh et al., 1992; Wanebo et al., 1993) where the overall survival rate at 5 years has not changed, oscillating between 8 and 26 percent, even though the resectability rate has increased (currently 60–80 percent) and the postoperative mortality rate has dropped from 14 to 6 percent (Gouzi et al., 1989; Hangstvedt et al., 1989; Bozzetti et al., 1990; Salvon-Harman et al., 1994; Stipa et al., 1994). The poor survival is related to delayed diagnosis and frequent local and regional recurrence. Several variables representing pathological, clinical and therapeutic characteristics have already been studied in numerous retrospective reports (Cady et al., 1989; Rohde et al., 1989; Shiu et al., 1989;

Arveux et al., 1992; Bollschweiler et al., 1993; Brems-Dalgaard and Clausen, 1993; Michelassi et al., 1994) in an attempt to identify prognostic indicators in patients with gastric cancer and, recently (Fink et al., 1995), to help define high-risk patients who may benefit from adjuvant therapy. The aim of this study was to calculate the survival rates and analyze the factors influencing the patient's prognosis in gastric cancer.

Patients and Methods

Patients

There were 746 patients with stomach cancer registered in the Cancer Registry Center of Research Center of Gastroenterology and Liver Disease(RCGLD), in our university from Dec 21, 2001 to Dec 21, 2006 were investigated with respect to the disease condition, the way of treatment and survival time. Clinopathologic variables and survival times were collected by telephone contact, patient's medical records and cancer registry forms. All patient deaths during this period were considered as a consequence of the gastric cancer. Survival time was calculated in months.

Statistical methods

The total survival rates by the clinopathologic and

Research Center of Gastroenterology and Liver Diseases, Shahid Beheshti Medical University, Tehran, Iran.*For correspondence, email: b_moghimi_de@yahoo.com

Table 1. Survival Rates of Gastric Cancer Patients Using the Life-table Method

Time (yr)	Survival (%)	Number Entering	Number Withdrawing	Terminal Events
1	73.6	739	241	163
2	50.2	335	112	89
3	40.6	134	68	19
4	33.2	47	17	7
5	29.7	23	8	2

Table 2. Survival Rates (%) of Patients by Histology

Time (yr)	Adenocarcinoma NOS	SRCC & M-P A & MA*	Other histology
1	72 ± 0.02#	86 ± 0.05	73 ± 0.04
2	48 ± 0.03	64 ± 0.09	51 ± 0.06
3	38 ± 0.03	54 ± 0.12	41 ± 0.08
4	30 ± 0.04	54 ± 0.12	41 ± 0.08
5	27 ± 0.04	54 ± 0.12	41 ± 0.08

Standard Error *SCC: Signet Ring Cell Carcinoma & M-p A: Mucin-Producing Adenocarcinoma & MA: Mucinous Adenocarcinoma

Table 3. Survival Rates (%) of Patients by Cancer Stage

Time (yr)	Early Stage	Advanced Stage
1	89 ± 0.03#	68 ± 0.02
2	67 ± 0.05	44 ± 0.03
3	51 ± 0.07	36 ± 0.03
4	43 ± 0.10	28 ± 0.04
5	32 ± 0.12	26 ± 0.04

Standard Error

Table 4. Survival Rates (%) of Patients by Grade of Cancer

Time (yr)	Well*	Moderately*	Poorly*	Un*
1	89 ± 0.03	68 ± 0.02	68 ± 0.02	68 ± 0.02
2	67 ± 0.05	44 ± 0.03	44 ± 0.03	44 ± 0.03
3	51 ± 0.07	36 ± 0.03	36 ± 0.03	36 ± 0.03
4	43 ± 0.10	28 ± 0.04	28 ± 0.04	28 ± 0.04
5	32 ± 0.12	26 ± 0.04	26 ± 0.04	26 ± 0.04

*differentiated # Standard Error

demographic variables were calculated by the life-table method (Lee, 1992) and compared by Wilcoxon (Gehan) statistic. P< 0.05 was considered as a significant. The data were analyzed using by SPSS.v.13 software.

Results

There were 530 males and 216 females with mean ages of 60.5±12.6 and 57.5±13.5 years, respectively, in our sample. Some454 dead patients and 285 patients were censored during the term of investigation. Survival information for 7 patients was not available. The median survival time of cases was 24.2 months.

The survival rates are given in Table 1. A histology type report was available for 734 patients. Adenocarcinoma, NOS, was the commonest histology type seen in 71.3 percent. Survival rates by morphology are shown in Table 2. There was seen a statistical significant difference between subgroups of this variable (P=0.02). Survival rates with early (0,I,II) or advanced(III,IV) stage and different grades are shown in

Tables 3 and 4, respectively, again with significance differences (P<0.001 and P=0.036). Statistical analysis of other variables shown that, age at diagnosis (P=.011), tumor size (P=.010), surgery treatment (P<.0001) have a statistical association with survival of patients. Variables such as sex (P=.533), body mass index (P=.214), ethnicity (P=.092), and level of education (P=.762) were without significant effects.

Discussion

Prognostic factors in gastric cancer are a source of controversy in many series. The present study, based upon a prospective data base, indicates that only tumor-related factors are prognostic indicators. We have found that several patient- and treatment-related factors affected survival, but they were not independent prognostic factors. Compared to other tumors, stomach cancer has a dismal prognosis and a low 5-year survival rate. In our research, 5-year survival rate of patients with stomach cancer is 29.7%, which close to the results of some previous research (Ekbom and Gleysteen, 1980; Wu et al., 2000; Souhami et al.,2002; Jun et al., 2004).

The stage of cancer is the most important independent prognostic factor (Msika et al., 2000; Doglietto et al., 2000; Barchielli et al., 2001). The results using COX model in some researches showed that the death hazard of the patients with stage III cancer was 2.82 time as high as that of the patients with stage II cancer, and that with stage IV was 3.29 times as high as that with stage II cancer (Barchielli et al., 2001). The 1- and 2-year survival rates in stage IV stomach cancer were 1.65 and 10 times as high as those in stage III cancer respectively (Haugstvedt et al., 1989). The 5-year survival rate in stage I -stage IV were 81.2%, 50.4%, 24.4% and 5.2%, respectively(Msika et al., 2000). Our research also showed that stage of cancer might make a notable impact on survival rate of stomach cancer and 1- to 5- year survival rates in early stage(I or II) of cancer were higher than those in advanced stage (III or IV).

Some authors (Matley et al., 1988; Mitsudomi et al., 1989; Maehara et al., 1995) consider that age has prognostic value because young patients with gastric cancer have a poorer prognosis than older patients. Perhaps they present with more advanced disease because the index of suspicion for malignant disease is low and so symptoms are allowed to progress for a longer period before investigation is considered, or there may be greater biological activity of the tumor which is more likely to be of the Laurens diffuse type. Other studies (Miller et al., 1992) have shown that age and sex have a significant influence on outcome. In this study, age had an influence on long-term survival but sex did not.

A study conducted in the USA stated that women had better survival rates, that this was more apparent for early-stage tumors (Miller et al., 1992) . Curtis et al. (1985) reported that prognosis was better in women in their study, depending on age and stage. However, no difference with respect to gender was observed in the survival rates for early-stage patients. Male patients had higher mortality rates in a study carried out on patients with gastric cancer

in Canada (Bako et al., 1985) when the results were assessed regarding the gender for patients at the same stage (early stage). Another study reported no differences in survival rates regarding gender in patients at early or advanced stages. Some studies stated that male patients underwent surgery more often (Jonasson et al., 1994; Fuchs and Mayer, 1995). A study carried out on 2773 patients with gastric cancer by the Rotterdam Cancer Registry reported similar resection rates for male and female patients. However, the same study demonstrated significantly lower postoperative mortality rates in female patients (Damhuis and Tilanus, 1995). Jin-Pok Kim et al (1998) stated that women had better prognosis in their study carried out on gastric cancer patients. Also a study stated no statistical differences in survival of patient on the basis of gender. In the present study, no gender-related difference was observed between participants.

With respect to the degree of cellular differentiation, the best prognosis has been found in well differentiated tumors (Cady et al., 1989; Michelassi et al., 1994; Salvon-Harman et al., 1994; Matley et al., 1998). Patients with low-grade tumors had a greater survival rate than those with high-grade tumors, the difference being statistically significant. In this and other studies, the presence of metastatic tumor has a highly significant effect on prognosis and lower survival rates (Msika et al., 1989; Rohde et al., 1989; Maehara et al., 1992; Adachi et al., 1994; Keller et al., 1994; De Manzoni et al., 1996; Kwon and Kim, 1996].

It has been reported that obesity posed an increased risk for certain adenocarcinomas. Four previously case studies (Brown et al., 1995) stated that obesity moderately increased esophageal and gastric cardia adenocarcinoma risk (1.5–3 times). On the other hand, two case studies (Kabat et al., 1993; Chow et al., 1998) stated that no such correlation had been observed. It has often been stated that symptomatic gastro-esophageal reflux (Zhang et al., 1996), a major risk factor for esophagus adenocarcinoma, is associated with obesity. The results of a study carried out by Lagergren et al (1999) are worth noting: while increased BMI revealed a significant correlation with esophagus adenocarcinoma, its correlation with gastric cardia adenocarcinoma was not as strong. This relationship depends on BMI. However, carcinogenic effects have not been completely clarified. The risk was established to be associated with gastro-esophageal reflux. Furthermore, increased gastric cardia and esophageal adenocarcinoma prevalence and its predominantly male incidence may be due to the increased proportion of overweight men. Moriwaki et al (2003) conducted a study which established that median survival rates were significantly higher for stage II patients with lower BMI, whereas median survival rates were significantly higher for stage IIIA patients with higher BMI. In other study, observed that the median overall survival rate of patients whose BMIs were below 20 was significantly lower than that of patients whose BMIs were 20 or higher (Suleyman et al., 2006). The results of our study showed that no association observed between BMI and survival of gastric cancer patients.

Surgery provides the only possibility of cure in stomach cancer patients. The 1- and 2-year survival rates of operated patients were much higher than those of not operated patients (Maetani et al., 1980; Haugstvedt et al., 1989; Pointner et al., 1994; Tuech et al., 1999; Doglietto et al., 2000). Our results also confirmed this. However, whether resection should be performed in patients with the stage IV stomach cancer is still a question (Valen et al., 1988; Haugstvedt et al., 1989; Bonenkamp et al., 2001). Some researchers suggested that surgery could raise 3-year survival rate of patients with stage IV cancer only if tumors were not diffusely infiltrative type, while short-term survival rates could not be raised even though resections were conducted for the patients with diffusely infiltrative type of cancer (Murata et al., 1998). However, surgery did not prolong survival time in patients with peritoneal dissemination, hepatic metastasis, lymph node involvement and invasion to adjacent organs or with 3 of these 4 factors (Haugstvedt et al., 1989; Maekawa et al., 1996). Some other researchers suggested that short-term improvement in survival for resected patients with distant metastases could be obtained and resectional surgery should be undertaken whenever possible in patients with stage IV stomach cancer as both short-term and long-term survival advantages had been demonstrated (Haugstvedt et al., 1989; Huang et al., 2003; Kunisaki et al., 2003; Wan et al., 2003). In conclusion, this survival study has shown that stage of tumor, grading of tumor, histologic type of cancer, tumor size, age at diagnosis and surgery approach are independent prognostic factors in gastric cancer patients. These findings have enabled the elaboration of a prognostic index with which patients can be classified as at low, intermediate or high risk. Also, we suggest that early detection of patients in lower ages and in primary stages and grades of tumor are important to increase patient's life expectancy.

Acknowledgements

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