Postoperative life expectancy in gastric cancer patients and its associated factors

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ABSTRACT

Objective: In recent years, the patterns of mortality have changed in Iran, and cancers are playing a greater role in this regard in this country. Various reports indicate that gastric cancer is highly prevalent; it is the second most common cancer in men, and fourth in the general population. The purpose of this study was to determine the 5-year survival rate of gastric cancer patients who had undergone surgical treatment at one of the most important cancer treatment centers, the Iran Cancer Institute, and to assess its associated factors.

Methods: Three hundred and thirty patients with gastric cancer who had been admitted to and operated on at the Iran Cancer Institute, Iran between January 1996 and April 2000 were enrolled in this study. The patients' life expectancy after surgery was determined, and its relationship with variables of age at the time of surgery, gender, and factors related to the disease such as the cancer site, pathologic type, stage, presence of metastasis, and sites of metastases were assessed.

Results: The 5-year survival rate in the studied patients was 23.6%, and the median life expectancy was 19.9 months. Univariate analysis showed that gender, cancer site, and pathologic type did not affect life expectancy significantly. However, the 5-year survival rate significantly decreases with age. As expected, those involved with metastasis had a significantly lower 5-year survival rate, and the disease stage significantly affected the patients' life expectancy ($p<0.001$). The Cox proportional hazards model was used to assess the effect of different variables simultaneously, and it showed that age, lymph node metastasis, and disease stage influenced the rate of survival.

Conclusions: Gastric cancer patients in Iran have a low 5-year survival rate. One of the most important reasons seems to be delayed consultation and diagnosis. Most patients are seen first with the disease in the late stages. At this point, most have lymph node and liver metastasis, which makes treatment even more complex. Thus, it is necessary to employ mass media for extensive public education about the early warning signs of the disease and performing periodic examinations.

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During recent years, improved hygiene in Iran has reduced deaths from infectious diseases, and cancers have become a major contributing factor to the Iranian population death rate. Lack of precise and efficient cancer registries makes the number of cancer patients and the annual occurrence of new cases unknown. However, estimates show that the standardized occurrence in 1999 in the capital, Tehran, was 130.9 in 100,000 for men and 109.8 for women.[1] Considering the probable under estimations, the exact numbers of cancer deaths are not known either, but it has been estimated that in 1999 more than 27 thousand cancer deaths occurred in the 70 million Iranian population.[1] Several reports have stated that gastric cancer is prevalent in Iran, being the second most common cancer in men and the fourth in the general population. Unfortunately, gastric cancer patients in Iran seek medical attention when the disease has reached an advanced stage and is very lethal.[1-3] Determining the survival rate of patients is a very important aspect of cancer research. In this regard, several studies have been

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carried out in different countries. In the case of gastric cancer patients, the postoperative 5-year survival rate has been reported as 29.6% in China, 4.4% in Thailand, 37% in the United States, 22% in Switzerland, and 30% in France.[4-8] The overall 5-year survival rate after gastrectomy is markedly different in the West than in the East. Although many gastric carcinomas in Japan are localized (lymph node negative) cancers, even Japanese patients with regional disease (lymph node positive) have much better overall survival rates than patients with regional disease treated either in the United States or in Europe. Gastric carcinoma survival rates are also much improved in Korea and Taiwan in comparison to the West.[9-11] Various factors affecting survival in these patients have also been investigated; age, disease stage, and occurrence of metastasis has been mentioned.[4-28] Gastric cancer occurs more frequently in men, with a male-to-female ratio of 2.3:1; mortality is approximately double in men.[27] This study was designed and carried out to determine the 5-year survival rate of Iranian gastric cancer patients who received surgical treatment at the most important cancer treatment center in Iran, the Iran Cancer Institute, and to assess some affecting factors.

Methods. In this study, 330 gastric cancer patients admitted and operated on at the Iran Cancer Institute, Iran from January 1996 to April 2000 were enrolled. The postoperative life span of these patients was determined. Diagnosis in all patients was made with biopsies. The median follow-up time for survivors was 37.9 months; right censor was applied from the final day to those who survived the study period, and other certain dates for those who were lost to follow-up. Two hundred and thirty-nine patients died during the study period, in 13 of which death had other causes and so were right censored from their death dates. Staging was based on the tumor node metastasis system.[29] Individual variables such as age (at the time of surgery), gender (male – female), and information regarding the disease such as its site (cardia – antrum – other), stage (I – II – III – IV), presence of metastasis (positive – negative), and site of metastasis (lymph nodes – liver – distant) were assessed for their effect on patients' life expectancy. In the analyses, methods of Life Table, Kaplan Meier, Log-Rank test, and Cox proportional hazards model were used and an alpha level of 0.05 was considered significant. The software used for the analyses were SPSS for Windows version 11.5, and S Plus 2000.

Results. In the studied patients, a total gastrectomy was performed in 55.7% of cases, 27.2% underwent subtotal gastrectomy, and the type of gastrectomy was partial in 8.8%, proximal in 8.5%, and distal in 3.1%. For subsequent reconstruction, esophagojejunostomy was the choice in 50.9% of patients, 27.6% received gastrojejunostomy, and in 13.6% esophagogastrostomy was performed, while colon bypass was carried out in 3.3%, Billroth II in 3.1%, and colostomy 1.5%. Positive nodes were found in 38.8% of patients with a median positive node count of 8. Pathologic stage distribution included stages IA (3%), IB (3.6%), II (18.2%), IIIA (13%), IIIB (3.3%), and IV (58.8%). All stage IV assignments were due to an N3 category, a T4 classification, or a T3 classification with M1. The 5-year survival rate was 23.5%, one-year survival rate was 66.7%, and median life span was 19.9 months (**Table 1, Figure 1**). Comparison of

Table 1 - Life table of patient's survival.

Interval start time (Months)	N of entering this interval	N of withdrawn during interval	N of exposed to risk	N of terminate events	Proportion terminating	Proportion surviving	Cumulative proportion surviving at end	Probability density	Hazard rate	SE of cumulative surviving	SE of probability density	SE of hazard rate
0	330	7	326.5	53	0.1623	0.8377	0.8377	0.0271	0.0294	0.0204	0.0034	0.004
6	270	9	265.5	54	0.2034	0.7966	0.6673	0.0284	0.0377	0.0263	0.0035	0.0051
12	207	16	199	41	0.206	0.794	0.5298	0.0229	0.0383	0.0283	0.0033	0.0059
18	150	7	146.5	26	0.1775	0.8225	0.4358	0.0157	0.0325	0.0287	0.0029	0.0063
24	117	7	113.5	16	0.141	0.859	0.3744	0.0102	0.0253	0.0285	0.0025	0.0063
30	94	5	91.5	9	0.0984	0.9016	0.3375	0.0061	0.0172	0.0282	0.0020	0.0057
36	80	3	78.5	5	0.0637	0.9363	0.316	0.0036	0.011	0.028	0.0016	0.0049
42	72	8	68	9	0.1324	0.8676	0.2742	0.007	0.0236	0.0275	0.0023	0.0079
48	55	7	51.5	6	0.1165	0.8835	0.2423	0.0053	0.0206	0.0272	0.0021	0.0084
54	42	6	39	1	0.0256	0.9744	0.236	0.001	0.0043	0.0272	0.001	0.0043
over 60	35	29	20.5	6	0.2927	0.7073	0.167	**	**	0.0306	**	**

** These calculations for the last interval are meaningless, the median survival time is 19.9 (months)

Table 2 - Univariate analysis of prognostic factors.

Prognostic factor	Patients n	(%)	5-year survival rate %	Median survival time (months)	95% confidence interval for median	Log-rank test *p*-value
Gender						0.278
Male	228	(69.1)	25.8	21.27	15.76 - 26.78	
Female	102	(30.1)	19.2	17.83	11.75 - 23.91	
Age						<0.001
<61	87	(26.4)	38.9	31.93	14.47 - 49.39	
61-70	123	(37.3)	25.2	23.66	17.74 - 29.58	
>70	120	(36.3)	8	12.53	09.96 - 15.1	
Tumor site						0.391
Cardia	145	(43.9)	23	16.9	11.83 - 21.97	
Antrum	63	(19.1)	23.6	23.9	13.25 - 34.55	
Other	122	(37)	25.1	21.69	16.12 - 27.26	
Metastases						0.007
Positive	192	(58.2)	17	17.53	12.69 - 22.37	
Negative	137	(41.5)	33.7	25.87	18.81 - 32.93	
Location of metastases						0.332
Lymph node	128	(38.8)	17.5	17.53	12.08 - 22.98	
Liver	24	(7.3)	(3.5	17.3	0 - 39.82	
Distant*	40	(12.1)	6.4	17.67	17.67 - 22.7	
Stage						0 .004
1	22	(6.7)	56.2	76.43	0 - 174.21	
2	60	(18.2)	36.9	27.7	16.31 - 39.09	
3	54	(16.4)	22.5	16.37	09.6 - 23.14	
4	194	(58.8)	16.7	17.67	13.11 - 22.23	

*diaphragm, spleen, pancreas, lungs, bone

Table 3 - Multivariate analysis of prognostic factors through the backward stepwise* (Likelihood ratio) method of cox proportional hazard model.

Variable	Regression coeficient	Standard error	Wald	Degree of freedom	*p* value	Relative risk	95% CI for relative risk
Age	0 .037	0.007	28.329	1	0.000	1.038	1.024 - 1.052
Stage†			14.391	3	0.002		
Stage (2)	0.356	0.363	.963	1	0.326	1.428	.701 - 2.911
Stage (3)	0.767	0.358	4.592	1	0.032	2.153	1.068 - 4.340
Stage (4)	1.027	0.347	8.780	1	0	2.792	1.416 - 5.507
Lymph node metastases	0.339	0.172	3.869	1	0.049	1.404	1.001 - 1.968

*Variables entered at step number 1 = gender, age, location, lymph node metastases, liver metastases, stage
Variable removed at step number = liver metastases,
Variable removed at step number 3= gender,
Variable removed at step number 4 = location,
†Baseline is stage = 1

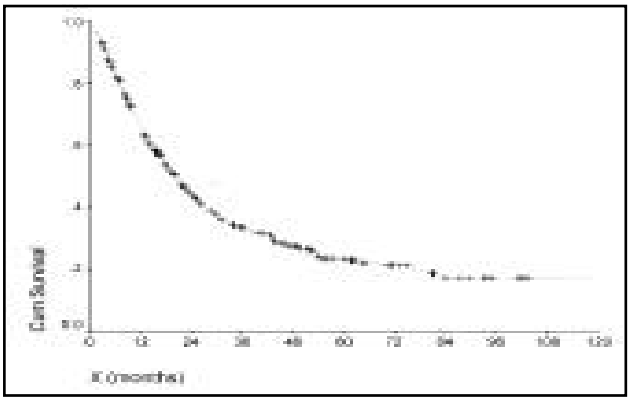

Figure 1 - Kaplan-Meier cumulative survival.

survival based on gender showed the 5-year survival rate to be 25.8% for men and 19.2% for women. The median life expectancy for men was 21.27 months and for women 17.83 months. This difference was not statistically significant (**Table 2**). With age, a significant decrease in 5-year survival rate was seen ($p<0.001$). In the age groups of 60 and under, 61 to 70, and over 70 years, the five-year survival rate was 38.9%, 25.2%, and 8%. (**Table 2**). We also noticed that patients with involvement of the cardia had the lowest 5-year survival rate, followed by those with involvement of the antrum and other sites, although these differences were not statistically significant (**Table 2**). As expected, the 5-year survival rate was significantly reduced by occurrence of metastasis (17% compared to 33.7%, $p<0.01$) and the median life expectancy for patients with metastases was 17.53 months, and without metastases was 25.87 months (**Table 2**). Same as above assessing patients afflicted with metastatic spread of the disease, we found that the 5-year survival rate with involvement of the lymph nodes, liver, and distant sites was 17.5%, 13.5%, and 6.4%. The differences seen here were not statistically significant (**Table 2**). The stage of the disease significantly affected the 5-year survival rate ($p<0.01$) and changed from 56.2% for stage 1 to 16.7% for stage 4 (**Table 2**). Finally, all investigated variables were simultaneously analyzed using the Cox proportional hazards model to determine their relationship with patients' life expectancy. Results (**Table 3**) showed that more advanced disease stages increase mortality risk. Lymph node metastasis increased mortality risk 1.4 times, and aging also increased this risk ($p<0.05$).

Discussion. The 5-year survival rate in this study was 23.6%, which is lower than that found in many other countries such as the United States, Switzerland, France, and China.[4,6-11,26-28] This may be explained by the fact that Iranian patients generally seek medical attention when the disease has reached an advanced stage. Therefore, diagnosis is made when the chance of a full cure is smaller. In this study, comparison of survival and median life span between genders showed that men survived longer, although the difference was not statistically significant. This finding agreed with results of studies carried out in other countries, and the life span difference between male and female gastric cancer patients was not statistically significant.[23-28] As we expected, life expectancy significantly decreased with age ($p<0.001$). A study performed in the United States also showed that older age groups have a shortened life expectancy in comparison to the young.[17] This fact has also been verified by studies performed in Japan and Italy.[18,23-28]

One hundred and ninety-two patients (58.2%) were afflicted with metastasis and their life expectancy was shorter compared to other patients. Presence of metastases usually indicates an advanced disease and therefore a smaller chance of survival. This finding has been confirmed by all studies performed in this regard.[4-6,9,10,21-23] Of these 192 patients, 128 cases had metastasis to the lymph nodes, and in 24 the liver was involved. The site of metastasis did not influence life expectancy. The disease stage affected life expectancy to a great extent; the 5-year survival rate in stage 1 was 56.2%, while it was only 16.7% in stage 4. Unfortunately, 58.8% of patients were initially seen at this stage and therefore the life expectancy was shortened in general. In Thailand, 68.9% of patients were first diagnosed with a stage 4 cancer, and so the 5-year survival rate was as low as 4.4%.[5] In Thailand, where 82% of patients were initially diagnosed with a stage 4 disease, only 16% were operable or curable.[15] The effect of disease stage on life expectancy has been shown in reports concerning Western and developed countries as well.[21,24-28]

Multivariate analysis for detecting the simultaneous effect of different variables on life expectancy showed that age, metastasis to the lymph nodes, and the stage of the disease had significant effects. Older age, later disease stage, and metastatic involvement of lymph nodes proved to lower the chance of survival, while gender, pathologic type, and cancer site had no significant effect. These findings have been confirmed by studies performed in Japan[12,25] and Switzerland.[7] In addition to these variables, metastasis to the liver and tumor site were found related, in China[11] and the United States.[21]

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