Treatment Outcomes and Survival of Patients with Gastric Cancer in Hamadan, Iran: A Retrospective Study

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Abstract

This study aimed to evaluate the effect of various factors and treatments protocols' outcomes on the survival of patients with gastric cancer (GC). In a retrospective cohort study Patients with a definite diagnosis of GC who had been hospitalized at the Mahdie Hospital of Hamadan, Iran, from 2005-2017 were investigated. GC-related survival for different factors, types, locations of the tumor, sites of metastasis, and used treatment methods investigated. Data analyze performed by SPSS software version 21. 95 patients, including 66 (71%) male, and 27 (29%) female, were identified. The mean age was 63.88 ± 12.41 years. The largest proportion of tumors was located in the cardia (29.7%), body (18.9%), and antrum (18.9%) of the stomach. The most common site of metastasis was the liver (52.6%), and lung (26.3%). The average survival of patients was 40.64 ± 4.58 months, and the one, two, three, four, and five years' survival of investigated patients were 0.68, 0.49, 0.43, 0.39, and 0.34 years, respectively. The average survival of patients with and without metastasis were 16.35 ± 3.27 and 46.97 ± 5.30 months (P=0.004). The Pearson correlation coefficient between the survival and total dose of RT, total number of CT sessions, and dose of each RT session were -0.003 (P-value=0.98), 0.006 (P-value=0.97), and -0.108 (P-value=0.412), respectively. Results show that there were no statistically significant differences between the average survival of patients and used treatment method, grade, type of cancer, and CT medicine. But survival of patients with metastasis was significantly lower than patients without metastasis (P=0.029).

1. Introduction

Gastric cancer (GC) is an out-of-control growth of malignant cells in the stomach that grows slowly over many years and causes changes in different layers of the stomach (1). Some risk factors for stomach cancer have been identified, including Helicobacter pylori (H pylori) infection, salt-preserved foods, alcohol, obesity, and family history (2). Surgical resection is the main therapy for GC as it offers the best chance for long-term survival. Other treatments such as chemotherapy (CT) and radiation therapy (RT) are often part of treatment protocol as well, either along with or instead of surgery can be used. RT and CT have some side effects cause damage to normal cells and organs around the tumor. Recently some type of nanoparticle is used to enhance effectiveness of conventional methods (3-5). However, RT and CT have used for most of patients during one decades ago, either are the most important part of treatment program of most of the current patients.

Usually, RT is fractionated in 1.8 to 2 Gy per day, 5 days a week. Different RT protocols deliver in various clinics around the world. The two most usual protocols used in The National Cancer are (5-7):

1.   A total dose of 45 Gy during 33 to 36 days, or 50.4 Gy during 38 to 41 days deliver to the patients

2.   A total dose of 45Gy during more than 36 days, or 50.4 Gy during more than 41 days deliver to the patients (8)

In some countries such as Japan the total dose of 40 Gy delivers in dosages of 2 Gy per day (6). On the other hand, there are different delivery techniques. The most common delivery fields used in 3D-conformal RT are the AP-PA technique, and the BOX technique, which includes four fields of AP-PA-left-right lat.

Different CT protocols are used worldwide. In some countries, CT is the only treatment, while in some centers CT is used before or after surgery. In the USA, CT after surgery is most usual, but in East Asia, the CT alone is common (6). Some usual CT medicines are 5-Fluorouracil, Cisplatin, Capecitabine, Fluropyrimidine, and Oxaliplatin. For HER2+ patients in stage four, the trastuzumab is used, but in CT, before surgery, 5-Fluorouracil, Cisplatin, and Capecitabine are common (9).

Although all of these treatments are acceptable according to the recommended protocols, their outcomes have not been fully studied especially in eastern countries. In a study conducted in 2013 by Ashraf et al. In the United States, it was recommended to review the results of various protocols used in Eastern countries and compare them with the results of Western studies (10).

Investigating the survival of patients with different kind of cancers, and studying various prognostic factors and treatment methods which have significant effect on their survival is valuable, and show the role of race, economy and medical system ability in controlling cancers. Therefore, this study aimed to evaluate the effect of various factors and used treatment protocols' outcomes on the survival of patients with GC in a radiotherapy center of Hamadan province, Iran during ten years from 2005-2017.

2.1. Theoretical Part

This study was a retrospective cohort study. The data were obtained from the patients' documents with GCs, who were referred to Mahdieh Radiotherapy center from 2005 to 2017. A check list prepared to record information of patients' documents. The inclusion criteria comprised the patients with a definite diagnosis of GC. Demographic data including age, sex, and disease profile, including location of the tumour, stage, grade, and lymph node involvement, treatment methods including RT and CT protocols, and disease outcomes like recovery, recurrence, and metastasis were extracted from the medical records of the patients. Vital status and date of death were determined with official death certificates. Survival time was calculated using the date of diagnosis up to the date of death or last follow-up. The exclusion criteria included incomplete data recorded or lack of access to treatment-related records.

2.2. Statistical analysis

The Kaplan-Meier estimate determined the survival rate. COX regression was used to evaluate the factors influencing survival and the log-rank test was utilized to different survival rates in different groups. To compare the outcome of the disease in terms of nominal and qualitative variables, the Chi-square test (or Fisher's exact test) was used. The T-test (or Mann-Whitney) was employed to compare the low variables. We used the life chart to examine the survival of our subjects. All the statistical analyses were performed with SPSS16.0 (P-value less than 0.05).

3. Results and Discussion

A total number of 95 patients were identified. Among all the cases, 66 (71%) were male, and 27 (29%) were female. The mean age ±standard deviation (SD) was 63.88±12.41 years with a range of 33 to 87 years, and most of the patients were in the age range of 60 to 75 years old (Figure 1). The results of a study were done by Roshanaei et al. in Iran in 2012 indicated that the rate of GC occurrence in males (75.5%) and females (24.5%) was in accordance with the gender distribution in this study (11).
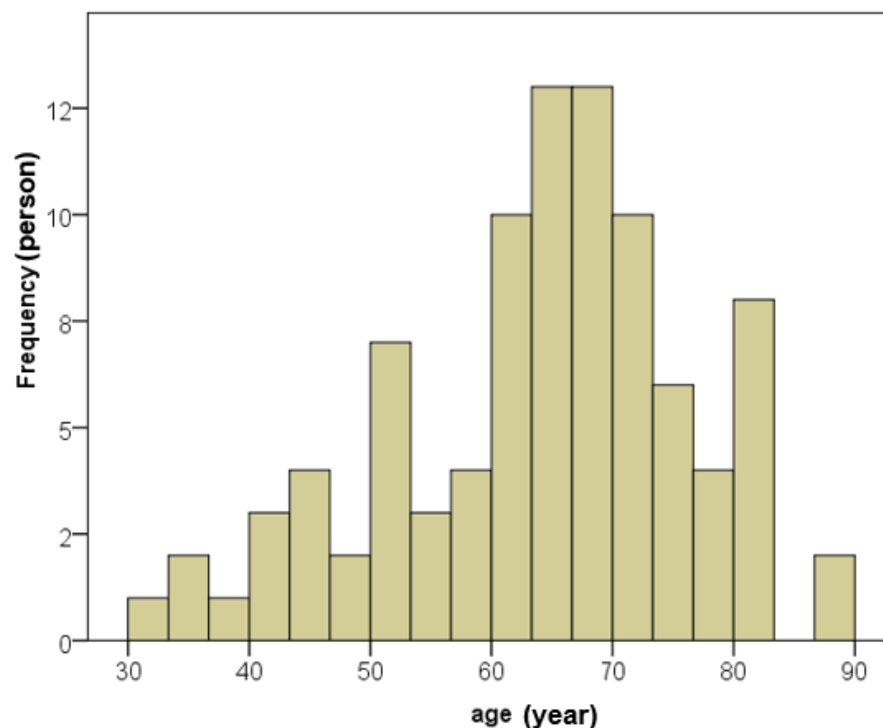
Figure 1: Frequency distribution of GC patients' ages.

The largest proportion of tumors was located in the cardia (29.7%), body (18.9%), and antrum (18.9%) of the stomach.

Table 1 shows the distribution of stages of tumors, lymph node involvement, different sites of distant metastasis, and tumor recurrence.

Table 1: distribution of stages of tumors, lymph node involvement, different sites of distant metastasis, and tumor recurrence.

factor	Number of patients	percentage
T		
1	1	1.1
2	11	11.8
3	51	54.8
4	11	11.8
unknown	19	20.4
Total	93	100
N		
1	24	25.8
2	26	28
3	16	17.2
4	7	7.5
unknown	20	21.5
Total	93	100
Metastasis		
yes	19	20.4
No	74	79.6
Total	93	100
Site of Metastasis		
Liver	10	52.6
Lung	5	26.3
Bone	4	21.1
Total	19	100
Recurrence		
yes	89	95.7
No	4	4.3
Total	100	100

Based on the results of table 1, Out of 93 patients, 89 (95.7%) had recurrence, 19 had metastasis, the most common site of metastasis was liver (52.6%) and lung (26.3%). Results of our study indicate that the most common anatomical site of occurrence was Cardia, body, and antrum, but in the research of Javadi et al. the common places were pylorus, and cardia (12). Results of a study by Behzadpour et al. in 2009 reported that the most common anatomical sites were cardia and antrum, which is in agreement with our results (13). One of the factors that causes poor prognosis and recurrence of the disease is metastasis to distant lymph nodes and other organs. The results of this study shows that metastasis occurred in 95.7% of patients, and the most common cites were liver and lung. Results of Jvadi et al study indicated that the metastasis happened in 65.6% of patients, of these, 34 patients did not metastasize from the beginning and metastasized during the follow-up study. Table 2 shows distribution of metastasis based on the first and second treatment in GC patients.

Table 2: distribution of metastasis based on the first and second treatment method.

Treatment method	metastasis			P.value
	yes	No	Total	
first				
Total Gastrectomy	8 (24.2%)	25(75.8%)	33(100%)	
Sub Total Gastrectomy	2(10%)	18(90%)	20(100%)	
Chemotherapy	4(14.8%)	23(85.2%)	27(100%)	
Radiotherapy	3(50%)	3(50%)	6(100%)	0.23
concurrent chemoradiation therapy	2(28.6%)	5(71.4%)	7(100%)	
Total	19(20.4%)	74(79.6%)	93(100%)	
second				
Total Gastrectomy	2(14.3%)	12(85.7%)	14(100%)	
Sub Total Gastrectomy	0(0%)	6(100%)	6(100%)	
Chemotherapy	6(37.5%)	10(62.5%)	16(100%)	
Radiotherapy	2(25%)	6(75%)	8(100%)	0.286
concurrent chemoradiation therapy	8(17.8%)	37(72.2%)	45(100%)	
Total	18(20.2%)	71(82.2%)	93(100%)	

Results show that there was no statistically significant relationship between treatment methods and metastasis occurrence. Among 93 investigated patients, 25 (26.9%) were alive up to the end of the study, 35 (37.6%) died, and data of 33 patients were censored. The average survival of patients was 40.64±4.58 months (CI=3.66 to 49.61month), and the median of survival was 24±6.99 months (CI=10.27 to 37.71 months) (Figure 2). One of the factors affecting the survival rate of patients is the age of patients at the time of diagnosis. The research of Javadi et al. in 2014 shows that 53.7% of patients were over 70 years old and the average age of patients was 66.8, which is in the agreement of the results of our research. Also, the one, three, and five year's survival in both genders were in accordance with the current study (12).
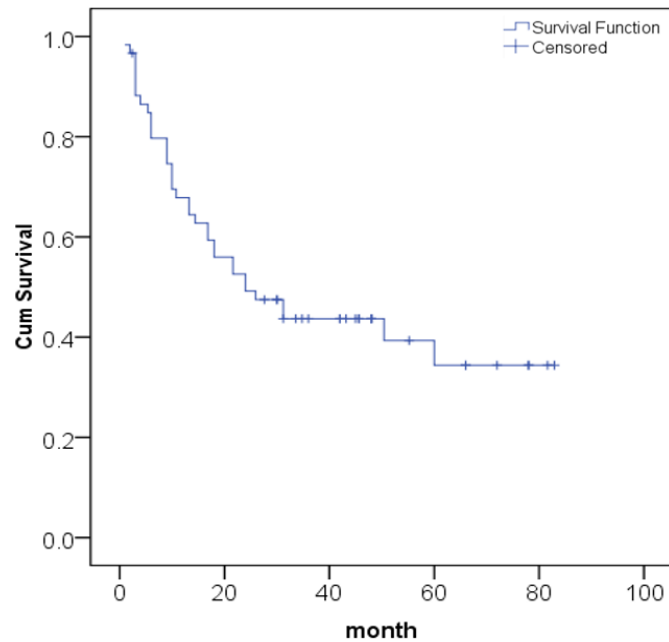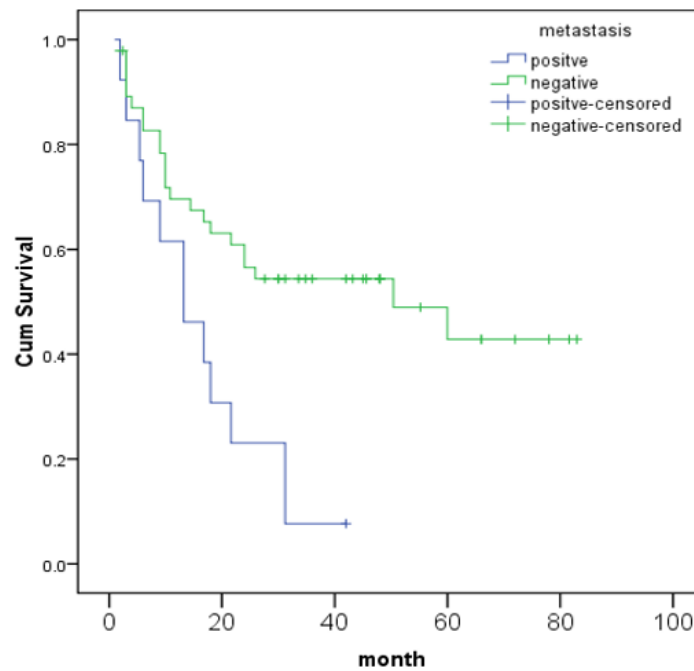
Figure 2: The average survival of patients with GC.

Average survival for men and women was 40.23±5.32 and 41.03±8.14 months, respectively (P= 0.744) (Figure 3) Also, the one, two, three, four, and five years' survival of investigated patients were 0.68, 0.49, 0.43, 0.39, and 0.34 years, respectively. Also, it has been reported in another study that the one, three, and five year's survival of GC patients was 0.66, 0.19, and 0.06% that was lower than the result of the current study. This enhancement in the survival of patients in our study can be due to improvements in surgical and treatment methods in recent years compared to the study time of before researches (12).
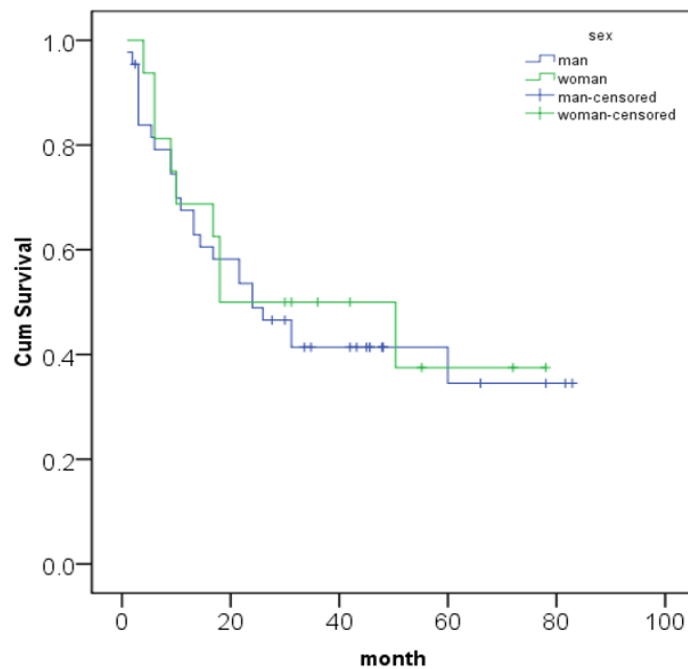
Figure 3: Average survival for men and women.

The average survival of patients with and without metastasis were 16.35±3.27 and 46.97±5.30 months (P=0.004) (Figure 4).

Figure 4: The average survival of patients with and without metastasis.

The average abundance of survival based on the treatment method has shown in table 3.

Table 3: Average abundance of survival based on treatment method.

	average	Standard deviation	95% Confidence Interval		P.value
			Lower Bound	Upper Bound	
Total Gastrectomy	34.65	5.14	24.58	44.71	
Sub Total Gastrectomy	43.51	9.27	5.34	61.68	
Chemotherapy	54.83	8.64	37.91	71.76	
Radiotherapy	4.23	1.61	1.07	7.37	P<0.001
concurrent chemoradiation therapy	9	5.05	0	18.19	
Total	40.63	4.58	31.66	49.61	

The result of the Kaplan-Meyer test showed a statistically significant difference between the average survival of

patients and used treatment method. The Pearson correlation coefficient between the survival and total dose of RT, total number of CT sessions, and dose of each RT session were -0.003 (P-value=0.98), 0.006 (P-value=0.97), and -0.108 (P-value=0.412), respectively, which indicate no significant correlation.

Twenty of the 34 patients did not undergo complementary therapies, including CT (12). In a study conducted by Ahmadloo et al., the effect of using RT after surgery in 58 patients with GC, and lymph node involvement was investigated. Total dose of RT was 54 Gy. Findings from at least 5 years follow-up of patient showed that 41 patients (70.7%) died. The 5-year overall survival of patients was 29.3% and the mean survival of patients was 15 months. The results of these studies showed an increase in the local inhibition of GC due to the use of RT after surgery (14). Soyfer et al. examined the effect of RT duration on localized control of tumor and metastasis in GC patients. The results showed that not only RT after surgery has a significant effect on increasing the survival, but also increasing the duration of radiotherapy and also the time interval between surgery and start of RT, increases the likelihood of recurrence of the disease (15). Table 4 shows the relationship between the mean survival of patients and factors as a grade, type of carcinoma, and type of CT medicine. In a study conducted by McMillan et. al in the United States, the effect of using two types of RT on the survival of patients with GC was investigated. In the first method, a dose of 45 Gy was applied in 33 to 36 days or 50.4 Gy in 38 to 41 days, and in the second method, a dose of 45 Gy was administered over a period of more than 36 days or a dose of 50.4 Gy in 50 days. Results showed that the mean 5-year survival of patients was significantly lower in patients with longer treatment time. Therefore, prolonging the treatment time has negative effects on the patients' survival (16). In the study of Orditura et al., The effect of surgery, and CT or chemoradiotherapy before and after surgery on patients with GC were investigated. The results showed that surgery was the best and only primary treatment for most GCs that had spread to lymphomas. Adjuvant therapies such as CT and chemoradiotherapy can reduce the complications of the disease that has spread to lymphomas (9). In a review study conducted by Repka et al. In the United States, various evidences were examined to evaluate the effect of RT on the treatment of GC. The results of this study showed that radiotherapy has played an important role in treating these patients or relieving the disease (6). In a study by Kraszkicwicz et al., Different treatment methods, radiation protocols, and prognostic factors were evaluated in 60 patients with GC who had metastasized to the brain. Influential prognostic factors were identified as functional status, number of brain metastases, type of treatment, mean time of diagnosis. Results showed that patients treated with combination methods had a longer survival (17-19).

Table 4: Relationship between the mean survival of patients and grade, type of carcinoma, and type of CT medicine.

Factor	Survival time (year)		P.value
	mean	Standard deviation	
Grade			
Well	2.13	1.84	
Poorly	2.26	2.36	0.510[*]
Moderate	2.98	1.92	
type of carcinoma			
Adenocarcinoma	2.27	1.87	0.174[**]
Singetring	3.34	2.38	
Chemotherapy medicine			
Iv/5Fu	2.57	1.81	
Cisp/5fu	1.79	2.47	
Carbop/5fu	3.70	4.53	0.393[*]
Cisp	0.47	0.39	
Foifox	0.45	-	

[*]one-way ANOVA
[**]two-way ANOVA

Table 4 shows that there is no significant relationship between the survival of patients and grade, type of cancer, and CT medicine. But the survival of patients with metastasis is significantly lower that patients without metastasis (P=0.029).

Table 5 shows a significant correlation between the survival and stage of the disease (P=0.001).

Table 5: Correlation between the survival and stage of the disease (Test: one way anova).

stage	Number of patients	Mean	Standard. Deviation	Standard. Error	95% Confidence Interval for Mean		Minimum	Maximum
					Lower Bound	Upper Bound		
1b	2	3.3000	0.70711	0.50000	-3.0531	9.6531	2.80	3.80
2a	14	3.9650	2.08854	0.55819	2.7591	5.1709	0.20	6.91
2b	10	2.1770	1.47620	0.46682	1.1210	3.2330	0.75	5.50
3a	5	2.5500	2.24277	1.00300	-0.2348	5.3348	025	6.00
3b	5	0.9466	1.00612	0.44995	-0.3027	2.1959	0.08	2.50
3c	1	6.8000	-	-	-	-	6.80	6.80
4	12	1.4133	1.05359	0.30414	0.7439	2.0827	0.16	3.50
Total	49	2.5535	1.99043	0.28435	1.9818	3.1252	0.08	6.91

4. Conclusions

In this study, the survival rate of patients with GC referred to Mahdieh Center of Hamadan from 2005 to 2017, investigated. Factors such as, the abundance of GC in males and females during this period, 1 to 5 years survival, the mean age of occurrence, the anatomical place of tumors, rate, and site of metastasis investigated and compared to the results of other similar studies. The following different treatment methods used for the patients of this study, and their correlation with the rate of survival investigated and compared to the results of other studies. Totally, it seems that the grade, type of carcinoma, and used CT medicine were not effective factors on the survival of patients, and the only effective factor is the occurrence of far metastasis. The reason for the difference in the prevalence of metastasis among patients with GC who refer to different medical centers at different times can be the difference in the study population, follow-up patients, and variations in treatment methods. Although there was a statistically significant difference between the mean survivals of patients with GC in terms of treatment method, the results of other studies show a significant increase in survival of patients receiving RT and other adjuvant therapies after surgery. The length of treatment and the interval between diagnosis and the start of radiotherapy are also important factors in increasing the patients' survival.

Conflict of Interest
The authors declare that they have no conflict of interest.

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